STATISTICAL ANALYSIS PLAN

VERSION FINAL 01.00, 20DECEMBER2022

A Randomised, Phase 1b, Double-Blind, Placebo-Controlled Study to Evaluate the Safety, Pharmacokinetics, and Antiviral Activity Of RV299 Against Respiratory Syncytial Virus in the Viral Challenge Model

Protocol No: REVD002

hVIVO Study No: VIR-CST-001

CCI [redacted]

For: hVIVO Services Ltd

CONTENTS

1. STATISTICAL ANALYSIS PLAN APPROVAL FORM

	Signature	Date (ddmmmyyyy)	Time (hh:mm)	Local Time Zone
Author(s): PPD Senior Statistician, PPD				
Approval(s): PPD PPD ReViral, a Pfizer Company				
PPD PPD hVIVO Ltd				

2. STATISTICAL ANALYSIS PLAN AUTHOR

PPD BSc (Hons)
Senior Statistician
PPD

3. LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse event
ALP	Alkaline phosphatase
ALQ	Above the limit of quantification
ALT	Alanine transaminase
APTT	Activated partial thromboplastin time
AST	Aspartate transaminase
AUC	Area under the curve
BDR	Blind Data Review
BDRM	Blind Data Review Meeting
β-HCG	Beta human chorionic gonadotropin
BLQ	Below the level of quantification
BMI	Body mass index
BPM	Beats per minute
CI	Confidence interval
CK	Creatinine Kinase
Covid-19	Coronavirus disease 2019
CRF	Case Report Form
CRP	C-reactive protein
CSR	Clinical Study Report
DBP	Diastolic blood pressure
DP	Decimal places
ECG	Electrocardiogram
ET	Early termination
FEV1	Forced expiratory volume in 1 second
FSH	Follicle-stimulating hormone
FU	Follow-up
FVC	Forced vital capacity
GGT	Gamma glutamyl transferase
GM	Geometric Mean
GSD	Geometric Standard Deviation
HbA1C	Glycated haemoglobin
HIV	Human immunodeficiency virus
HR	Heart Rate
HVC	Human Viral Challenge
hVIVO	hVIVO Services Limited
ICF	Informed consent form
IMP	Investigational medicinal product
INR	International normalised ratio
IQR	Inter-quartile range
ITT	Intention-to-Treat
ITT-I	Intention-to-Treat Infected
ITT-A	Intention-to-Treat Infected Analysis Population A
ITT-B	Intention-to-Treat Infected Analysis Population B
LDH	Lactate dehydrogenase
LRT	Lower respiratory tract

Abbreviation	Definition
MCH	Mean corpuscular haemoglobin
MCHC	Mean corpuscular haemoglobin concentration
MCV	Mean corpuscular volume
MedDRA	Medical dictionary for regulatory activities
NCI	New-onset chronic illness
PCR	Polymerase chain reaction
PD	Protocol deviation
PE	Physical examination
PEF	Peak expiratory flow
PFU	Plaque forming units
PK	Pharmacokinetic
PP	Per protocol
PT	Preferred term
PT	Prothrombin time
PTT	Partial thromboplastin time
RR	Respiratory rate
Q1	Lower quartile
Q3	Upper quartile
qicPCR	Qualitative integrative cycler polymerase chain reaction
qRT-PCR	Quantitative reverse transcription polymerase chain reaction
RBC	Red blood cells
RNA	Ribonucleic acid
RSV	Respiratory Syncytial Virus
SAE	Serious adverse event
SAP	Statistical analysis plan
SARS-CoV-2	Sever acute respiratory syndrome coronavirus 2
SBP	Systolic blood pressure
SD	Standard deviation
SE	Standard error
SOC	System organ class
SoE	Schedule of Events
SpO2	Peripheral arterial oxygen saturation
TEAE	Treatment emergent adverse event
TFL	Tables, Figures and Listings
TSS	Total clinical symptoms
ULN	Upper limit of normal
ULOQ	Upper limit of quantification
URT	Upper respiratory tract
VL	Viral load
WBC	White blood cells
WHO	World Health Organisation

4. INTRODUCTION

This statistical analysis plan (SAP) explains in detail the statistical analyses that will performed for the ReViral Limited study REVD002 [hVIVO study no: VIR-CST-001]. The analysis is outlined within the study protocol V3.0 (dated 31 October 2022) and this SAP contains a more technical and detailed description of those analyses. In particular, the SAP provides information on the definitions of the participant populations, analysis methods, and details the list of Tables, Figures and Listings (TFL) that will be produced by S-cubed Biometrics for use and inclusion within the Clinical Study Report (CSR). The SAP has been written and finalised before any unblinding of the study and prior to the database being locked.

Any deviations from the protocol specified analyses, and deviations from analyses stated within this SAP will be described within the CSR.

5. STUDY OBJECTIVES

5.1. Primary Objective

The primary objective is to assess the antiviral activity of RV299 compared to placebo in healthy adult participants infected with RSV-A Memphis 37b.

5.2. Secondary Objectives

- To evaluate the effect of RV299 compared to placebo in healthy adult participants inoculated with RSV in terms of antiviral effect assessed by:
    - viral-load related endpoints;
    - clinical symptom-related endpoints (using the 10 predefined symptoms in the graded symptom scoring system).
- To evaluate the effect of RV299 on nasal discharge in healthy adult participants inoculated with RSV when compared to placebo.
- To evaluate the safety of multiple orally administered doses of RV299 when compared to placebo.
- To monitor the safety of the challenge virus.
- To characterise the PK profile of RV299 after a single oral dose and after multiple oral doses in plasma from healthy participants inoculated with RSV.

CCI [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

6. STUDY DESIGN

6.1. Summary of Study Design

This is a single-centre, randomised, double-blind, placebo-controlled, proof-of-concept study in healthy adult male and female participants from 18 to 55 years of age, inclusive. The primary goal of this Phase 1b study is to assess the antiviral activity of RV299 against RSV in the viral challenge model. In addition, the safety, tolerability, and PK of RV299 will be assessed.

A total of 80 participants is planned to be enrolled in this study: 40 participants on RV299 and 40 participants on placebo.

The study is divided into the following study phases:

- Screening phase: from Day -90 to Day-3 pre-human viral challenge (HVC). Historical generic screening data collected through the hVIVO generic screening process may be transferred to this study after the study-specific consent form has been signed by the participant.
- Inpatient phase: Participants will be resident in the quarantine unit for approximately 15 days (from Day -2 to Day 12). Procedures will include:
    - Pre-HVC:
        - Admission to quarantine unit on Day -2/-1.
        - Baseline assessments will be conducted as per Schedule of Events (SoE) up to Day 0, pre-challenge.
    - HVC: RSV-A Memphis 37b virus inoculation on Day 0.
    - Post-HVC:
        - Randomisation to receive RV299 or matched placebo.
        - Administration of IMP (RV299/placebo). Each participant will receive IMP twice daily (~12 hours interval) for 5 consecutive days:
            - IMP dosing to start on confirmation of RSV infection, i.e., after a positive result by qualitative integrative cycler polymerase chain reaction (qicPCR). The qicPCR of nasal wash will be performed twice daily on Days 2-5 (Day 5 morning only), or until a positive result is received, whichever is sooner. The earliest start of IMP dosing will be in the evening of Day 2 post-HVC (IMP will be initiated 12 hours ± 1-hour post nasal wash confirmation of infection)

            OR

            - IMP would start in the evening of Day 5, if no positive result obtained by qicPCR
        - Day 1 onwards and each day study assessments will be conducted as per SoE.
        - Participants will be discharged from the quarantine unit on Day 12 (or may remain longer at the discretion of the principal investigator [PI]/investigator).
- Outpatient phase:
    - Final visit: Day 28 (±3 days).

The overall study design is depicted in

Table 1.

Table 1: Study Schematic: On-study Participant Progression

SCREENING PHASE	INPATIENT PHASE: QUARANTINE/ISOLATION, HUMAN VIRAL CHALLENGE, AND DOSING				OUTPATIENT PHASE
Day -90 to Day -3 Screening*	Day -2/-1 Admission to quarantine unit	Day 0 Inoculation with challenge agent & assessments as per Schedule of Events	Days 1 to 11 Dosing and assessments as per Schedule of Events	Day 12 Discharge from quarantine unit**	Follow-up visit: Day 28 (±3 days)

NOTES:

*Screening assessments (including repeats, as required), may be performed up to Day -2/-1, defined as the first study day (quarantine admission) at the discretion of the PI/investigator and in accordance with the design of the study.

**Release from quarantine is foreseen at Day 12 (12 days post inoculation) provided that, where appropriate, no virus is detected by qualitative virus antigen test or polymerase chain reaction (PCR) (negative virus antigen test or PCR below Ct cut-off) and the participant has no clinically significant symptoms. If the participant continues to have clinically significant symptoms and/or detectable virus on Day 12, additional extended quarantine stay may be required at the discretion of the PI/investigator.

6.2. Randomisation / Treatment Allocation and Blinding

hVIVO assigns a unique 6-digit number to each participant in the hVIVO database. This number will be used to identify a participant up to the point of randomisation, on source documents, on all study correspondence, and in the study database. A separate randomisation number will be allocated to the participants at randomisation and will be used for allocation to a study arm. The randomisation number encodes the participant's assignment to 1 of 2 study arms (RV299/placebo) in a 1:1 ratio.

Randomisation numbers will be assigned sequentially in ascending order, and once assigned, that randomisation number will not be reassigned. The study site will keep a log of the randomisation number assigned to each participant.

A designated unblinded statistician, separate from the conduct or analysis of the study, will be responsible for the computer-generated randomisation schedule. Sealed copies of the randomisation code will be stored in a secure location.

Randomisation numbers will follow a 3-digit format e.g., 001. If participants are replaced as per Section 7.4, Participant Replacement Strategy, the replacement participant will be assigned a new, unique randomisation number equalling the randomisation number of the replaced participant, plus 100. This will ensure that the replacement participant receives the same allocated, blinded treatment as the participant who is being replaced.

A copy of the randomisation code list will be sent to the unblinded pharmacist/designee preparing the IMP, so that IMP can be prepared for each participant as appropriate. An independent statistician prepares the randomisation schedule, and the GMP pharmacy provider's pharmacy/designee will prepare the participant level IMP doses in line with the randomisation schedule.

Each participant will be dispensed blinded IMP, labelled with his/her unique randomisation number, throughout the study. With the exception of the unblinded pharmacist, unblinded IMP management personnel at the clinical site, the unblinded statistician preparing the randomisation code list, and the quality assurance auditors where necessary, the PI/investigator and all other clinical and nonclinical staff, (including the study statistician, data management staff), and the participants will remain blinded to the treatment allocation until after the database has been locked and approval for study unblinding has been given.

Following database lock, on receipt of authorisation from the Sponsor, a copy of the randomisation code list will be provided to the study statistician to conduct study unblinding for analysis.

6.3. Time and Events Schedule

Details of the timing of study assessments and procedures can be found in Table 2.

Table 2: Schedule(s) of Events (SoE)

Study Phase ➔	Screening Phase*	Inpatient Phase (Quarantine Isolation and Human Viral Challenge [HVC])																	Clinic Visit Follow-up	Early Withdrawal
Study Day ➔ Procedure ↓	D -90 to D -3	D -2	D -1	D 0			D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11	D12 (Discharge)	D 28 (±3 days)	
				Pre-HVC	HVC	Post-HVC														
Written informed consent (a)		X																		
Eligibility criteria (+)	X	X		X																
Medical & medication history	X	X																		
Demographics	X																			
Height & body weight, body mass index (BMI) (b)	X	X																(X)	(X)	(X)
Complete physical examination	X	X																X	X	X
Directed physical examination (incl. nasal)				(X)		(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)	(X)			
Vital signs (heart rate [HR], respiratory rate [RR], systolic blood pressure [BP], diastolic BP, oxygen saturation [SpO_2]) and tympanic membrane temperature	X	X		X			X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead ECG	X	X											X				X		X	X
Spirometry	X																			
Patient Health Questionnaire (PHQ-9)	(X)	(X)																		
Generalised Anxiety Disorder Questionnaire (GAD-7)	(X)	(X)																		
Alcohol breath test	X	X																	X	
Urinalysis	X	X																X	X	X
Urine drugs of abuse and cotinine screen	X	X																	X	
Urine pregnancy test	X																	X	X	X
Symptom diary card (c)		(X)	3X	3X			3X	3X	3X	3X	3X	3X	3X	3X	3X	3X	3X	X		
24-hour paper tissue collection & nasal discharge weight (d)			X	X			X	X	X	X	X	X	X	X	X	X	X	X		(X)

Study Phase ➔	Screening Phase*	Inpatient Phase (Quarantine Isolation and Human Viral Challenge [HVC])																	Clinic Visit Follow-up	Early Withdrawal
Study Day ➔ Procedure ↓	D -90 to D -3	D -2	D -1	D 0 Pre-HVC	D 0 HVC	D 0 Post-HVC	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11	D12 (Discharge)	D 28 (±3 days)	
Product Administration																				
Randomisation								(X)	(X)	(X)	(X)									
RSV299/placebo dosing (k)								(X)	(2X)	(2X)	(2X)	(2X)	(2X)	(2X)	(2X)	(X)				
Challenge virus inoculation					X															
Collection Of Blood Samples																				
Serum follicle-stimulating hormone (FSH) (post-menopausal women)	X																			
Serum β-human chorionic gonadotrophin (β-hCG) pregnancy test (all females)		X																		
Hepatitis B, & C, human immunodeficiency virus (HIV) serology	X																			
Blood Pharmacokinetics (e)								(X)	(X)	(X)	X	X	X	X	X	X	X	X		
Haematology (f)	X	X											X				X		X	X
Biochemistry (f)	X	X											X				X		X	X
Coagulation	X																			
Cardiac enzymes	X	X											X				X			
Thyroid function test	X																			
[redacted] CCI [redacted]	[redacted]	[redacted]																	[redacted]	[redacted]
[redacted]		X																		

Study Phase ➔	Screening Phase*	Inpatient Phase (Quarantine Isolation and Human Viral Challenge [HVC])																Clinic Visit Follow-up	Early Withdrawal
Study Day ➔ Procedure ↓	D -90 to D -3	D -2	D -1	D 0 Pre-HVC	D 0 HVC	D 0 Post-HVC	D 1	D 2	D 3	D 4	D 5	D 6	D 7	D 8	D 9	D 10	D 11	D12 (Discharge)	D 28 (±3 days)	
Collection Of Respiratory Samples																				
Nasopharyngeal swab - respiratory pathogen screen incl. SARS-CoV-2 (h)		X																		
Nasopharyngeal swab- RSV discharge test																	(X)	(X)		
CCI [redacted]		■						■	■	■	■	■	■	■	■	■	■	■		
qicPCR (i)								2X	2X	2X	X									
Safety Assessments																				
Adverse event (AE) recording (j)		←																→		X
Concomitant medications (j)		←																→		X

KEY NOTES FOR TIME AND EVENTS SCHEDULE:

(X)	The assessment may be optional, or at the PI's discretion. The PI may perform additional safety assessments as required.
X	Once daily, at approximately the same time each day, where applicable.
2X	Twice daily (~12 hours between assessments [± 1 hour]).
3X	Three times daily (at the same times each day [± 1 hour]).
*	Potential participants will be screened using the hVIVO generic screening process, and individuals who pass this screen will be admitted to the quarantine unit 1 to 2 days before challenge with study virus and provide study-specific informed consent. They will then be screened for eligibility for this study before viral challenge on Day 0. Results of tests or examinations performed under hVIVO generic screening process may be used to determine eligibility without the need to repeat the assessment if it is within 28 days prior to viral challenge/dosing with IMP.
+	Only the applicable inclusion/exclusion criteria will be reviewed at each time point.
a	Study-specific consent may occur on the day of admission, providing all required eligibility information has been collected through the Health Research Authority -approved hVIVO generic screening process.

b	Height will be taken at screening only.
c	After the baseline has been set, assessments will be performed at the same time each day (±1 hour from baseline) during quarantine. • Symptom diary card baseline: Day -1 (measurements on this day will be taken approximately 8 hours apart, ±1 hour). • Nasal wash baseline: Day 2 (sampling will be performed approximately 12 hours apart, ±1 hour).
d	Distribution of paper tissues and bags will start on Day -1, with the first collection on Day 0. Thereafter, collection of paper tissues will occur at the same time each day (±1 hour) with tissues distributed 24 hours ahead.
e	Blood Pharmacokinetics: plasma samples for RV299 assay will be collected as follows: • First dose (Dose 1): 0.5 hours pre-dose, and at the following hours post-first dose: 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8,10, 12, 24, 36, 48, 60, 72, 84 and 96 hours (note samples taken up to and including 10 hours post-dose should be taken at the indicated time point ±5 minutes. Samples taken thereafter at 12, 24, 36, 48, 60, 72, 84, and 96 hours post-first dose should be taken within the 30 minutes before the next IMP intake). • Last dose (Dose 10): 0.5 hours pre-dose, and at the following hours post-last dose: 1, 1.5, 2, 2.5, 3, 4, 5, 6, 7, 8,10, 12, 24, 36, 48, 60, 72, 84, and 96 hours (note samples taken up to and including 10 hours post-dose should be taken at the indicated time point ±5 minutes; samples taken thereafter should be taken at the indicated time point ±30 minutes). For participants who started dosing on Day 4, am, onwards, the 60-hour, 72-hour, 84-hour, or 96-hour timepoints after Dose 10 could occur after the participant has met the discharge criteria on Day 12. Thus, for a subset of participants, these timepoints could be after discharge. The guidance for the 60-hour, 72-hour, 84-hour, and 96-hour PK sample collection is as follows: • For participants who started dosing on Day 4, am, onwards, and who meet the discharge criteria on Day 12, the 60-hour, 72-hour, 84-hour, and 96-hour timepoint samples may be omitted, as applicable, if it occurs after discharge. • For participants who started dosing on Day 4, am, onwards, and who do not meet the discharge criteria on Day 12 the 60-hour, 72-hour, 84-hour, and 96-hour PK timepoint samples should be collected up to the point where participant meets the discharge criteria.
f	Blood will be drawn under non-fasted conditions. Repeat bloods may be drawn under fasted conditions if a lipid profile (triglyceride) or glucose is required (at the PI's discretion). All participants will be dosed under fasted conditions. For all doses, a pre-dose and post-dose fasting period of 0.5 hour to 1 hour applies. No fluid intake (including water) is allowed for 1 hour pre-dose to 1-hour post-dose).
g	Virus serology (RSV neutralisation antibody assay) will be performed to determine eligibility and seroconversion.
h	Upper respiratory tract swab (e.g., nasopharyngeal swab, mid-turbinate swab, oropharyngeal swab) for respiratory virus screen to assess for the presence of respiratory pathogens; if found positive for any pathogen in the panel, the participant will not be eligible for the current quarantine.
i	Post inoculation nasal wash virology samples will be collected at the same time each day during quarantine (± 1 hour from baseline on Day 2) and used for qRT-PCR and viral culture assay (as appropriate). Samples may be used for related viral genomics CCI [redacted]. Samples collected between the morning of Day 2 and the morning of Day 5 will also be used for qicPCR until a positive result is received (to support triggered dosing).
j	Adverse events and concomitant medications are reviewed throughout the study including pre- and post-dosing with IMP and pre- and post-RSV virus inoculation.

k	IMP doses as oral solution/suspension will be taken with 140 mL of water (50 mL water rinse of IMP bottle following administration, and 90 mL post-dose). All participants will be dosed orally, in the seated position, under fasted conditions, under the direct supervision of the investigator (or delegate), and in accordance with the randomisation schedule. Each participant will receive IMP twice daily (~12 hours interval) for 5 consecutive days, in total 10 doses, IMP dosing to start on confirmation of RSV infection. The earliest start of IMP dosing will be in the evening of Day 2 post-HVC or IMP dosing will start in the evening of Day 5, if no confirmation of RSV infection.
Note:	Parenthesis indicates the assessment may be optional, or at the PI's discretion. The PI/investigator may perform additional safety assessments as required. Where any nasal sampling time points occur together, the order of sampling will typically be (1) nasopharyngeal swab followed by (2) nasal wash.

6.4. Interim Analysis / Data Monitoring

No interim analysis (i.e., an analysis of early trial data, before enrolment is completed, to detect trends that might warrant modification of the protocol, change in data being collected or trial termination) is planned for the study.

7. STUDY ENDPOINTS

7.1. Primary Endpoint

The primary endpoint is:

The area under the curve (AUC) for RSV viral load measured in nasal washes by quantitative real time reverse transcription polymerase chain reaction (qRT-PCR) in participants inoculated with RSV-A Memphis 37b, starting at initial administration of investigational medicinal product (IMP) up to planned discharge from quarantine (Day 12, am).

7.2. Secondary Endpoints

The secondary endpoints are:

- Additional viral load endpoints relating to antiviral effect include but are not limited to:
    - Peak viral load of RSV as defined by the maximum viral load determined by qRT-PCR measurements in nasal samples starting from initial administration of IMP up to planned discharge from quarantine (Day 12, am).
    - Time (days) to confirmed negative test by qRT-PCR measurements in nasal samples starting at initial administration of IMP to first confirmed undetectable assessment after peak measure.
    - Time (days) to confirmed negative test by qRT-PCR measurements in nasal samples starting from peak qRT-PCR after initial administration of IMP to first confirmed undetectable assessment after peak measure.
    - Time (days) to peak qRT-PCR in nasal samples, starting from initial administration of IMP.
    - Area under the viral load-time curve (VL-AUC) of RSV challenge virus as determined by viral culture on nasal samples, starting at initial administration of IMP up to planned discharge from quarantine (Day 12, am).
    - Peak viral load of RSV as defined by the maximum viral load determined by viral culture measurements in nasal samples starting from initial administration of IMP up to planned discharge from quarantine (Day 12, am).
    - Time (days) to confirmed negative test by viral culture measurements in nasal samples starting at initial administration of IMP to first confirmed undetectable assessment after peak measure.
    - Time (days) to confirmed negative test by viral culture measurements in nasal samples starting from peak viral culture after initial administration of IMP to first confirmed undetectable assessment after peak measure.
    - Time (days) to peak viral culture in nasal samples, starting from initial administration of IMP.
- Clinical symptom-related endpoints include, but are not limited to:
    - Area under the curve over time of total clinical symptoms (TSS-AUC) as measured from 10 symptoms within the graded symptom scoring system collected 3 times daily starting at initial administration of IMP up to planned discharge from quarantine (Day 12, am).
    - Area under the curve over time of total clinical symptoms change from baseline (TSS-AUCCFB) as measured from 10 symptoms within the graded symptom scoring system

collected 3 times daily starting at initial administration of IMP up to planned discharge from quarantine (Day 12, am).

- Peak symptoms diary card score: peak total clinical symptoms (TSS) as measured from 10 symptoms within the graded symptom scoring system collected 3 times daily starting from initial administration of IMP up to planned discharge from quarantine (Day 12, am).
- Peak daily symptom score: individual maximum daily sum of symptom score from initial administration of IMP up to planned discharge from quarantine (Day 12, am).
- Time (days) to symptom resolution as measured from 10 symptoms within the graded daily symptom scoring system starting at initial administration of IMP to time of returning to baseline score.
- Time (days) to symptom resolution as measured from 10 symptoms within the graded daily symptom scoring system starting at peak symptoms after initial administration of IMP to time of returning to baseline score.
- Time (days) to peak as measured from 10 symptoms within the graded daily symptom scoring system starting from initial administration of IMP to the time of peak daily symptom score.
- Total weight of mucus produced starting at initial administration of IMP up to planned discharge from quarantine (Day 12, am).
- Total number of tissues used by participants starting at initial administration of IMP up to planned discharge from quarantine (Day 12, am).

- Safety data including, but not limited to:
  - Occurrence of adverse events (AEs) from initial administration of IMP up to the Day 28 follow-up.
  - Occurrence of serious AEs (SAEs) from initial administration of IMP up to the Day 28 follow-up.
  - Occurrence of AEs related to the viral challenge from viral challenge (Day 0) up to the Day 28 follow-up.
  - Occurrence of SAEs related to the viral challenge from viral challenge (Day 0) up to the Day 28 follow-up.
  - Use of concomitant medications from viral challenge (Day 0) up to the Day 28 follow-up.
- Secondary endpoints related to PK include, but are not limited to:
  - Time to maximum plasma concentration (t_{max}), terminal half-life ($t_{1/2}$), maximum observed plasma concentration (C_{max}), area under the plasma concentration-time curve from time zero to the end of the dosing interval (AUC_{τ}), area under the plasma concentration-time curve over the last 24 hours dosing interval (AUC_{0-24h}) and area under the plasma concentration-time curve from time zero to infinity ($AUC_{0-\infty}$).

CCI [redacted]

[redacted]

- [redacted]
- [redacted]

- CCI [redacted]
- [redacted]

[redacted]

CCI [redacted]

[redacted]

[redacted]

- [redacted]

[redacted]

[redacted]

9. STUDY POPULATIONS

Populations defined below will be reviewed against the study database at a blinded data review meeting (BDRM). The database at this time will be nearly final (i.e., the meeting may result in further data queries/changes post meeting), so inclusion/exclusion of participants from populations defined at this meeting will be further checked (post meeting) against a final locked database and will then be finalised prior to unblinding.

9.1. Intent-to-Treat (ITT) Population

The intent-to-treat (ITT) population will consist of all randomised participants who received challenge virus and at least 1 dose of IMP. Participants will be analysed in the treatment group they were randomised to.

9.2. Intent-to-Treat Infected (ITT-I) Population

The intent-to-treat infected (ITT-I) population will consist of all randomised participants who received challenge virus and at least 1 dose of IMP, and meet the criterion for RSV infection. Participants will be analysed in the treatment group they were randomised to.

As per Section 10.7.2 in the protocol, a laboratory-confirmed RSV infection requires one or both of the following definitions to be met:

- At least 2 positive detections by viral load qRT-PCR assay specific for the challenge virus, reported on 2 consecutive days;
- One positive detection by viral load qRT-PCR assay, specific for the challenge virus, in which an aliquot of the same sample has also tested positive in a viral culture assay appropriate for detecting the challenge virus.

For qRT-PCR and the viral culture assay a positive detection is any positive numeric or “detected” value.

9.3. Intent-to-Treat Infected Analysis Population A (ITT-A) Population

The intent-to-treat infected analysis population A (ITT-A) population will consist of all randomised participants who received challenge virus and at least 1 dose of IMP, and meet the criterion for laboratory-confirmed RSV infection as defined for the ITT-I, using only assessments prior to taking IMP. Participants will be analysed in the treatment group they were randomised to.

The assessments prior to taking IMP includes all qRT-PCR assessments performed before dosing, including the assessment immediately before dosing. In addition, if the infection was seen (via a positive qRT-PCR value) before dosing but the confirmatory value (as per the first part of the viral shedding definition in Section 10.7.2 of the protocol) was taken after dosing, then the participant will be declared as infected before IMP administration, and hence will form part of the ITT-A Population.

Note: The assessments prior to dosing with IMP will include all qRT-PCR and viral culture assessments performed on samples collected before dosing, including the sample collected immediately prior to dosing.

9.4. Intent-to-Treat Infected Analysis Population B (ITT-B) Population

The intent-to-treat infected analysis population B (ITT-B) population will consist of all randomised participants not already in the ITT-A Population, who received challenge virus and at least 1 dose of IMP, and meet the criterion for laboratory-confirmed RSV infection as defined for the ITT-I, using only assessments after taking IMP. Participants will be analysed in the treatment group they were randomised to.

Note: The assessments after dosing with IMP will include all qRT-PCR and viral culture assessments on samples that are collected after dosing and will not include the sample collected immediately prior to dosing.

9.5. Per Protocol (PP) Population

The per-protocol (PP) population will consist of all ITT-I population participants who have no major protocol deviations, and who completed the quarantine period up to the final day of quarantine (Day 12) and received all 10 doses of IMP. Participants will be analysed in the treatment group they were randomised to.

9.6. Safety Population

The safety population will consist of all randomised participants who received challenge virus and at least 1 dose of IMP. Participants will be analysed according to the treatment they received.

9.7. PK Population

The PK population will consist of all ITT population participants with at least one post-dose PK result. Participants will be analysed according to the treatment they received.

10. PLANNED STATISTICAL METHODS

10.1. Statistical Considerations

10.1.1. General Definitions

In all applicable summary/analysis presentations of safety endpoints, Baseline is defined as the last non-missing assessment value for a participant, for that particular parameter, that is prior to inoculation of challenge virus, unless over-ruled after review of data at the BDRM or otherwise stated in the appropriate endpoint sections below, whatever the reason for that assessment (e.g. if it is a repeat assessment, then it should be used as the baseline). For efficacy endpoints, the baseline definition is as per the appropriate endpoint sections below. For the derivation of most efficacy endpoints, the first assessment to be used should be the assessment that was taken at the time of first administration of IMP. For example, if a participant was first dosed on the morning of Day 3 then the first qRT-PCR value to be used in the AUC of qRT-PCR viral load (from time of first administration) derivation should be the Day 3 morning assessment. For endpoints using symptom diary card data, the definition of baseline will be defined in greater detail within the appropriate sections of the SAP.

A participant will be classed as infected, and therefore randomised to be dosed, when they have a positive result for RSV-A Memphis 37b by qualitative integrative cycler polymerase chain reaction (qicPCR) from nasal wash sample. IMP administration will be initiated 12 hours after a positive result. However, if a participant remains uninfected, IMP administration will begin on the evening of Day 5.

For participants that extend their time in quarantine beyond Day 12, the additional assessments beyond Day 12 will be listed only, and will not be used for the derivation of any efficacy endpoints. For the avoidance of doubt, the assessment performed on the morning of Day 12 will be the final assessment used for all analyses and summaries for all participants. If additional assessments are taken on Day 12, then they will be listed only. However, the use of data beyond the morning of Day 12 will be discussed at the BDRM.

A participant will be considered to have completed the study after their attendance at the last planned study visit (Day 28 (± 3 days)), or the last unscheduled visit (if any occur), as applicable.

Data recorded for replaced participants will be listed. However, these participants will only be included in tables where they meets the inclusion criteria for the relevant population.

Within summary presentations/analyses it is envisaged that only scheduled protocol visit values will be used for post-baseline time points and unscheduled visits will not be summarised in tables. All unscheduled visits will be listed. However, at the BDRM the occurrence of such non-scheduled data will be reviewed for each participant to decide if (and how) any such data point(s) should be included within summary presentations/analyses. Any such decisions will be documented in the BDRM minutes.

For assessments made on Day 0 (either pre or post challenge), the date and time of inoculation will be compared to the date and time of assessment to ensure they are assigned to either pre or post challenge accurately.

10.1.2. Data Presentation

The specific format and content of each data presentation is shown in Section **Error! Reference source not found.**.

Summary tables will be presented by treatment group. For demographic, baseline, and safety data these will also be summarised for all participants.

Within all Tables and Figures, the treatment groups will be labelled and ordered as follows:

- RV299
- Placebo
- Overall (including RV299 and placebo participants, for demographic, baseline and safety data)

The scheduled protocol visits will be labelled in report presentations as follows:

- "Admission (Day-2/Day-1)"
- "Day 0 (pre-HVC)"
- "Day 0 (HVC)"
- "Day 0 (post-HVC)"
- "Day x" (where x=1 to 12)
- "Follow-up (Day 28)"
- "Early Withdrawal"

As the study day of IMP administration day will differ between participants, "x Days from IMP Administration" (where x=0 to 11) will be presented for efficacy outputs relating to clinical symptoms and PK. These assessments should be presented in relation to the IMP administration, rather than the inoculation day.

For data with multiple assessments on one study day, each assessment will be numbered sequentially (e.g. Assessment 1, Assessment 2 etc.) and will be relative to the first administration of IMP. Further details will be provided in the relevant sections of the SAP.

Within some tables, only "Baseline" may be shown (as applicable) instead of the scheduled visits Day 0 (pre-HVC) and Day-2/Day-1 (with baseline being chosen as defined in Section 10.1.1 and in the relevant endpoint sections).

Where duplicate information is collected on both the database and on the vendor data transfer(s) (e.g., sampling date and time) this information will be reconciled by data management and then the information from the vendor data transfer(s) will be included in Participant Listings.

All variables will be listed to the same number of decimal places as reported. Continuous endpoints will be summarised by: n, n missing, mean, standard deviation (SD), %CV, median, lower quartile (Q1), upper quartile (Q3), minimum (Min) and maximum (Max). Where appropriate, 95% confidence intervals (CIs) for the mean and/or median may be presented. For selected summaries the geometric mean (GM) and geometric standard deviation (GSD) will also be presented to aid interpretation. The SD will only be presented in summaries where the corresponding n is greater than or equal to 3.

The number of decimal places (DP) each summary statistic is rounded to for display in the summary tables, relative to the number of DP the parameter is recorded to, is shown in Table 3.

Table 3: Number of decimal places to use to display each summary statistic.

Statistics	Number of DP for display
Min, Max	Same as recorded
Mean, GM, Median, Q1, Q3	1 more DP than recorded

SD, GSD, %CV, 95% CI	2 more DP than recorded

For endpoints that require a geometric mean to be produced, and those endpoints can have raw values of 0 (zero), the GM calculation will add an appropriate constant value to all raw values prior to logging and will subtract that constant value from the final calculated anti-logged mean. The constant value used will be documented in the footnote of the tables. The value is typically 1 however it may be another small value which is in line with the scale of the data should a value of 1 be unsuitable. The GM and GSD are calculated as follows:

$$GM = \text{anti-log}\left(\text{mean}\left(\log_{10}\left(\text{endpoint values} + \text{constant} \right) \right) \right) - \text{constant}$$

$$GSD = \text{anti-log}\left(SD\left(\log_{10}\left(\text{endpoint values} \right) \right) \right)$$

The %CV will be calculated as $\%CV = 100 * (SD / \text{mean})$ using untransformed values.

Categorical variables will be summarised using proportions (counts and percentages). The specific approach to calculating percentages (relevant denominator) is detailed within each (relevant) Table template (Section **Error! Reference source not found.**).

All collected data will be included within participant listings.

10.1.3. Early Withdrawal Visit

If a participant withdraws prior to Day 28 they will complete an early withdrawal visit. The data collected at this visit will be summarised as the nearest scheduled visit, unless the nearest visit already has data, in which case it will be summarised as the next scheduled visit. The data collected at the early withdrawal visit will be listed as the early withdrawal visit.

For example, if a participant withdraws at the Day 8 visit the data collected at the early withdrawal visit will be included in the summaries of Day 8. If, however, the participant withdrew between Day 8 and Day 9, after attending as normal on Day 8, the data collected at their early withdrawal visit will be included in the Day 9 summaries.

10.1.4. Statistical Testing and Estimation

Statistical analyses for the primary and secondary endpoints will be performed using appropriate two-sided hypothesis tests at the 5% significance level.

For continuous data, an analysis of covariance (ANCOVA) will be used to compare means between the RV299 and placebo groups. The ANCOVA will have treatment group as a fixed effect and baseline viral load as a covariate, unless stated otherwise in the relevant endpoint section. Should data not satisfy the assumptions, an appropriate alternative test, e.g., Wilcoxon Rank-Sum test will be used.

P-values will be rounded to 4 decimal places. All p-values that round to 0.0000 will be presented as <0.0001 and p-values that round to 1.000 will be presented as >0.9999.

10.1.5. Handling of Dropouts or Missing Data

No imputation methods will be used to manage the occurrence of missing data. Only observed data at each scheduled visit will be reported.

For adverse events and concomitant medications the approach to handle missing data has been described in Sections 10.9.1 and 10.5 respectively. For any other data which has partial dates, these dates will be completed using a suitably conservative approach.

Any other mechanisms to adjust for missing data will be outlined within the relevant endpoints section.

10.1.6. Interim Analysis and Data Monitoring

No interim analyses are planned to be performed.

10.1.7. Multiple Comparison/Multiplicity

As this is an early phase study, no adjustments will be made to address multiplicity.

10.1.8. Model Checking and Sensitivity Analyses

Statistical hypothesis testing will be presented using parametric tests where an ANCOVA will be the preferred statistical method. However, if the parametric test assumptions fail, non-parametric alternatives will be presented.

The normality of the error term from fitted models will be checked by performing the Shapiro-Wilk's test of normality of the residuals and producing normality probability plots of the residuals.

For cases where the normality assumption fails to hold, the treatment effect will be assessed by the non-parametric Wilcoxon rank-sum test.

10.1.9. Data Conversion (CDISC)

For the reporting of this study there is no requirement for CDISC SDTM and/or ADaM standards to be applied.

10.1.10. Software

Data will be reported using SAS version 9.4 (SAS Institute Inc, Cary, North Carolina, USA).

10.2. Participant Disposition

The number of participants enrolled (signed ICF), the numbered receiving challenge agent inoculation, the number randomised, the number receiving at least one dose of IMP and receiving all doses of IMP, the number discontinuing IMP early, the number withdrawing from the study, those completing the study (Day 28 visit), and the numbers in each population will be summarised for all participants and by treatment group. The reasons for early discontinuation of IMP and reasons for withdrawal from the study will also be summarised by treatment group.

A listing will be provided including details of informed consent, randomisation and quarantine admission.

10.3. Protocol Deviations

Participants data will be reviewed for major protocol deviations by a qualified clinical reviewer prior to database lock and unblinding, at the BDRM. Participants with any major protocol deviations will be documented within the BDRM minutes, and such participants will be excluded from the PP population.

All protocol deviations will be listed.

10.4. Demographic and Other Baseline Characteristics

The safety population will be used in summaries of demographic and baseline data. No statistical testing will be used to compare treatment groups for different baseline characteristics.

10.4.1. Demographics

Demographic variables collected at Screening; sex, age, ethnicity, race, height (cm), weight (kg) and body mass index (BMI) will be summarised by treatment group and across all participants.

Age at screening and BMI are recorded in the database and do not need require derivation.

10.4.2. Substance Use History and Recreational Drugs of Misuse

Substance use history and any recreational drug misuse will be collected at screening and listed for all participants.

10.4.3. Reproductive Status and Contraceptive Use

The reproductive status and use of contraception will be collected at screening and listed for all participants.

10.4.4. Medical History

Medical history data will be coded using MedDRA, Version 25.0 (March 2022) and all data will be listed.

10.5. Prior and Concomitant Medications

Prior and concomitant medication terms will be coded using the World Health Organisation (WHO) Drug Dictionary Enhanced (WHO Drug Global, Version March 1 2022). A medication will be assigned as being prior to inoculation based on the start and stop dates of the medication and the date of challenge agent inoculation. If the medication stop date is before the inoculation date, the medication will be assigned as being prior to inoculation. A medication will be assigned as being prior to IMP or concomitant with IMP, based on the start and stop dates of the medication and the IMP. If the medication stop date is before the IMP start date and after the date of inoculation, the medication will be assigned as being prior to IMP. In all other situations, the medication will be assigned as being concomitant with IMP. If a participant has separate periods of taking specific medications, then that medication is only counted once within the specific period of observation (i.e., prior, or concomitant) where it is taken.

Note: Start and Stop times will not be used for determining if a medication is concomitant or not.

Concomitant medications up to the Day 28 visit will be summarised, using the Safety Population, by treatment group (and across all participants), Drug Class (L3) and preferred base name (01001). If Level 3 is missing for a medication then Level 2 will be used instead.

Prior medications will not be summarised but these will be listed.

10.6. IMP Exposure and Compliance

The study consists of 10 doses of IMP administered twice daily for 5 consecutive days. The expected number of doses will be calculated using the start/stop dates and times for each participant. Compliance with IMP will be derived as:

(number of doses received/number of doses expected) * 100.

Compliance will be summarised by treatment group and for all participants as a continuous variable and will also be summarised categorically in the following classifications: <80%, 80-120% and >120%.

10.7. Statistical Analysis

All efficacy analyses will be based on the ITT-I population as the primary analysis. Where the populations differ to ITT-I population by 1 participant within a treatment group, the primary and selected secondary analyses will be repeated for the ITT-A, ITT-B, ITT and PP populations. This will be reviewed and documented at the BDRM.

10.7.1. Primary Endpoint

10.7.1.1 Main Analysis

The primary endpoint is the AUC of RSV-A Memphis 37b viral load measured in nasal washes by qRT-PCR, from the last measurement collected prior to the first administration of IMP until the last measurement collected up to the morning of Day 12 (Quarantine discharge). The viral load data will be supplied as $\log_{10}$ copies/mL and will be used for this main analysis and to calculate the AUC using the trapezoidal rule [1].

The AUC will be summarised for RV299 and placebo using descriptive statistics and an ANCOVA with treatment group as a main effect and the baseline value as a covariate. The baseline value will be the qRT-PCR viral load value from the last measurement collected prior to the first administration of IMP. The treatment comparison will be presented, including the LS mean treatment difference with the corresponding two-sided 95% confidence interval and p-value. The equivalent Wilcoxon rank-sum tests will be provided in place of the ANCOVA where the assumptions of the parametric test are not met.

As nasal washes are scheduled to be taken twice daily for Days 2 to 11 (and once on Day 12), in order to calculate the AUC, the actual time that the assessment was collected will be used within the AUC calculation. The AUC calculation will be based on the available non-missing assessment values between the start and end of the defined AUC time period. However, for an AUC to be derived, a participant should have at least one non-missing data recording at the start of the AUC period (e.g. date of first administration of IMP) and also at the end of the AUC time period (e.g. Day 12). In addition, the participant should have at least 1 non-missing data recording on each day between the start and end of the defined AUC time period (i.e. at least 1 out of the 2 possible assessments on each Day)). Any missing data will be reviewed at the BDRM, for its potential impact on this endpoint, and any decisions to exclude participants as a result of these criteria will be documented in the BDRM minutes. For the reporting of AUC, where appropriate, qRT-PCR values that are 'Not Detected' or 'Detected' will be re-assigned using the substitution values shown in the table in Appendix 15.1.

As well as a descriptive statistics summary of AUC values, the mean qRT-PCR values (+/- 1 Standard Error (SE)) will be displayed graphically by day (relative to first dose of IMP) and assessment, and treatment group. In order to calculate the time point that each assessment will be presented against,

a relative day and relative assessment will be assigned. The last qRT-PCR measurement collected prior to the first dose of IMP will be assigned to be the value at time point 1, while measurements collected on subsequent assessments and days will be assigned to subsequent time points in sequential order (i.e. time point 2, 3 and so on). Time point 1 will be presented against Day 0 assessment 1, while subsequent time points will be presented against Day 0 assessment 2, Day 1 assessment 1, and so on.

[Line graph: y-axis = mean of qRT-PCR (log_{10} copies/mL), x-axis = day relative to dosing, one line for each treatment on same plot].

A boxplot will also be presented by day (relative to first dose of IMP) and assessment, plotting the median and mean qRT-PCT values for each treatment group, with the corresponding summary statistics.

[Box plot: y-axis = mean of qRT-PCR (log_{10} copies/mL), x-axis = day relative to dosing, one box-and-whisker for each day, with each treatment panelled with RV299 at the top and placebo below].

Note: For multiple assessments taken within each day, so as to be able to plot mean values across participants (within a treatment group) by day, the actual collection time point (which may differ across participants) will not be used. Rather all first and second assessments will have mean values separately calculated and plotted as two means within each day. These two means will be shown equally spaced along the x-axis within the graph.

10.7.1.2 Sensitivity Analyses

1. The first sensitivity analysis of the AUC of RSV viral load measured in nasal washes by qRT-PCR will be presented for a fixed time period, from the last measurement collected prior to the first administration of IMP to the scheduled assessment occurring 6.5 days afterwards (e.g. if a participant does not have a positive qicPCR then they will be dosed on Day 5 (evening) and they will be followed up to the morning of Day 12 with 14 assessments in total) – which represents the AUC over the longest possible time period over which all subjects are sampled.
2. A second sensitivity analysis of the AUC of RSV viral load measured in nasal washes by qRT-PCR will be presented for a fixed time period, which will include data from the morning assessment on Day 2 (i.e. the first qRT-PCR assessment measured) through to the morning of Day 12.
3. A third sensitivity analysis of the AUC of RSV viral load measured in nasal washes by qRT-PCR, from the last measurement collected prior to the first administration of IMP until the last measurement collected up to the morning of Day 12 (Quarantine discharge), will be presented where the AUC will be calculated using unlogged viral load data (i.e. the supplied value will be anti-logged to get a value as copies/mL).

The AUC analyses will be summarised by treatment group. The same statistical testing methods as applied to the main analysis of the primary endpoint will be applied to each sensitivity analysis. For the third sensitivity analysis, the data will be log-transformed (base 10) prior to statistical analysis.

10.7.2. Secondary Endpoints

10.7.2.3 Viral Load Endpoints

Peak Viral Load of RSV as Defined by the Maximum Viral Load Determined by qRT-PCR Measurements in Nasal Samples Starting from Initial Administration of IMP up to Planned Discharge from Quarantine

Using the scheduled protocol assessments from the last measurement collected prior to the first dose of IMP to morning of Day 12 (Quarantine discharge), the highest qRT-PCR viral load value observed in nasal samples for each participant will be summarised and analysed in a similar fashion to the primary efficacy endpoint described in Section 10.7.1.

Participants who stay undetectable (i.e. a 'Not Detected' value) during quarantine will be replaced with the 'Not Detected' value shown in the table in Appendix 15.1.

Time to Confirmed Negative Test by qRT-PCR Measurements in Nasal Samples Starting from Initial Administration of IMP to First Confirmed Undetectable Assessment after Peak Measure

The time from the first administration of IMP to the first confirmed negative qRT-PCR test after the peak qRT-PCR measurement will be calculated in days as:

Date and time of first confirmed negative test after peak qRT-PCR measurement – Date of and time of first IMP administration.

A negative test is defined as two consecutive 'Not Detected' results in the qRT-PCR test, with the date and time of the first negative test being utilised in the calculations. The peak qRT-PCR is defined as the highest viral load value obtained by a participant after their first administration of IMP. Participants who did not have a confirmed undetectable assessment after first administration of IMP are censored at their last detectable assessment after their peak qRT-PCR measurement. Participants who stay undetectable during quarantine will be excluded from this analysis. Participants who return a positive result after two consecutive 'not detected' results will remain within the analysis.

The time to confirmed negative test will be summarised descriptively by treatment group. Kaplan Meier [2] curves will be produced for each treatment group, overlayed on one plot. A supporting table will include the median, 25th and 75th percentiles for each group and will be accompanied by a log rank test to compare between RV299 and placebo with the corresponding p-value presented.

[Kaplan-Meier plot: y-axis = cumulative proportion of participants without a negative test, x-axis = day relative to initial administration of IMP, one line for each treatment overlayed on the same plot].

Time to Confirmed Negative Test by qRT-PCR Measurements in Nasal Samples Starting from Peak qRT-PCR after Initial Administration of IMP to First Confirmed Undetectable Assessment after Peak Measure

The time from the peak qRT-PCR measurement after administration of IMP to the first confirmed negative qRT-PCR test will be calculated in days as:

Date and time of first confirmed negative test – Date and time of first IMP administration.

A negative test is defined as two consecutive 'Not Detected' results in the qRT-PCR test, with the date and time of the first negative test being utilised in the calculations. The peak qRT-PCR is defined as the highest viral load value obtained by a participant after their first administration of IMP.

Participants who did not have a confirmed undetectable assessment after their peak qRT-PCR after first administration of IMP are censored at their last detectable assessment. Participants who stay undetectable during quarantine will be excluded from this analysis.

The time to confirmed negative test will be summarised descriptively by treatment group. Kaplan Meier curves will be produced for each treatment group, overlayed on one plot. A supporting table will include the median, 25th and 75th percentiles for each group and will be accompanied by a log rank test to compare between RV299 and placebo with the corresponding p-value presented.

[Kaplan-Meier plot: y-axis = cumulative proportion of participants without a negative test, x-axis = day relative to initial administration of IMP, one line for each treatment overlayed on the same plot].

Time to Peak qRT-PCR in Nasal Samples Starting from Initial Administration of IMP

The time to the peak qRT-PCR measurement starting from the initial administration of IMP will be calculated in days as:

Date and time of peak qRT-PCR measurement – Date and time of first IMP administration.

The peak qRT-PCR measurement is defined as the highest viral load value obtained by a participant after their first administration of IMP. Participants who stay undetectable during quarantine will be excluded from this analysis.

The time to peak qRT-PCR measurement will be summarised descriptively by treatment group. Kaplan Meier curves will be produced for each treatment group, overlayed on one plot. A supporting table will include the median, 25th and 75th percentiles for each group and will be accompanied by a log rank test to compare between RV299 and placebo with the corresponding p-value presented.

[Kaplan-Meier plot: y-axis = cumulative proportion of participants not yet reaching peak qRT-PCR, x-axis = day relative to initial administration of IMP, one line for each treatment overlayed on the same plot].

Area under the Viral Load-Time Curve (VL-AUC) of RSV Challenge Virus as Determined by Viral Culture in Nasal Samples, Starting from Initial Administration of IMP up to Planned Discharge from Quarantine

The area under the viral-load curve (VL-AUC) for RSV-A Memphis 37b measured in nasal washes by viral culture, from the last measurement collected prior to the first dose of IMP until the morning of Day 12 (Quarantine discharge) will be summarised and analysed as described in Section 10.7.1.

Viral culture analysis is only carried out on samples where the qRT-PCR results is at least detectable. Any missing viral culture results will be imputed with 'Not Detected' if the corresponding qRT-PCR result is not detected.

Peak Viral Load of RSV as Defined by the Maximum Viral Load determined by Viral Culture Measurements in Nasal Samples Starting from Initial Administration of IMP up to Planned Discharge From Quarantine

Using the scheduled protocol assessments from the last measurement collected prior to the first dose of IMP to the morning of Day 12 (Quarantine discharge), the highest viral culture measurement observed in nasal samples for each participant will be summarised and analysed in a similar fashion to the primary efficacy endpoint described in Section 10.7.1.

Participants who stay undetectable (i.e. a 'Not Detected' value) during quarantine will be replaced with the 'Not Detected' value shown in the table in Appendix 15.1.

Time to Confirmed Negative Test by Viral Culture Measurements in Nasal Samples Starting from Initial Administration of IMP to First Confirmed Undetectable Assessment after Peak Measure

The time from the first administration of IMP to the first confirmed negative viral culture measurement after the peak viral culture measurement will be calculated in days as:

Date and time of first confirmed negative test after peak viral culture measurement – Date and time of first IMP administration.

A negative test is defined as a 'Not Detected' result in the viral culture test, with the date and time of the first negative test being utilised in the calculations. The peak viral culture measurement is defined as the highest viral load value obtained by a participant after their first administration of IMP. Participants who did not have a confirmed undetectable assessment after first administration of IMP are censored at their last detectable assessment after their peak viral culture measurement. Participants who stay undetectable during quarantine will be excluded from this analysis.

The time to the confirmed negative test will be summarised descriptively by treatment group. Kaplan Meier curves will be produced for each treatment group, overlayed on one plot. A supporting table will include the median, 25th and 75th percentiles for each group and will be accompanied by a log rank test to compare between RV299 and placebo with the corresponding p-value presented.

[Kaplan-Meier plot: y-axis = cumulative proportion of participants without a negative test, x-axis = day relative to initial administration of IMP, one line for each treatment overlayed on the same plot].

Time to Confirmed Negative Test by Viral Culture Measurements in Nasal Samples Starting from Peak Viral Culture after Initial Administration of IMP to First Confirmed Undetectable Assessment after Peak Measure

The time from the peak viral culture measurement after administration of IMP to the first confirmed negative viral culture measurement will be calculated in days as:

Date of and time first confirmed negative test – Date and time of first IMP administration.

A negative test is defined as two consecutive 'Not Detected' results in the viral culture test, with the date and time of the first negative test being utilised in the calculations. The peak viral culture measurement is defined as the highest viral load value obtained by a participant after their first administration of IMP. Participants who did not have a confirmed undetectable assessment after their peak viral culture measurement after first administration of IMP are censored at their last detectable assessment. Participants who stay undetectable during quarantine will be excluded from this analysis.

The time to confirmed negative test will be summarised descriptively by treatment group. Kaplan Meier curves will be produced for each treatment group, overlayed on one plot. A supporting table will include the median, 25th and 75th percentiles for each group and will be accompanied by a log rank test to compare between RV299 and placebo with the corresponding p-value presented.

[Kaplan-Meier plot: y-axis = cumulative proportion of participants without a negative test, x-axis = day relative to initial administration of IMP, one line for each treatment overlayed on the same plot].

Time to Peak qRT-PCR in Nasal Samples Starting from Initial Administration of IMP

The time to the peak qRT-PCR measurement starting from the initial administration of IMP will be calculated in days as:

Date and time of peak qRT-PCR measurement – Date and time of first IMP administration.

The peak qRT-PCR measurement is defined as the highest viral load value obtained by a participant after their first administration of IMP. Participants who stay undetectable during quarantine will be excluded from this analysis.

The time to peak qRT-PCR measurement will be summarised using a descriptive summary. Kaplan Meier curves will be produced for each treatment group, overlayed on one plot. A supporting summary table will include the median, 25th and 75th percentiles for each group and will be accompanied by a log rank test to compare between RV299 and placebo with the corresponding p-value presented.

[Kaplan-Meier plot: y-axis = cumulative proportion of participants not yet reaching peak qRT-PCR, x-axis = day relative to initial administration of IMP, one line for each treatment overlayed on the same plot].

10.7.2.4 Clinical Symptom-Related Endpoints

Area under the Curve over Time of Total Clinical Symptoms (TSS-AUC) as Measured from 10 Symptoms within the Graded Symptom Scoring System Collected 3 Times Daily Starting at Initial Administration of IMP up to Planned Discharge from Quarantine

Total symptom scores (from 10 items of the 13-item symptom diary card) will be used to calculate the AUC, from the assessment nearest to the time of the first administration of IMP (can be prior to or after dosing, depending on whether dosed in the morning or evening), i.e. baseline, until Day 12 (Quarantine discharge), for each participant using the trapezoidal rule [1].

Symptoms are assessed 3 times daily for Day 1 to Day 11 (and once for Day 12) and recorded on the symptom diary cards at each assessment. The following types of symptoms are recorded (on a grading scale, 0 to 3 (or 0 to 4 for the Shortness of Breath symptom)):

- Upper Respiratory Tract (URT): runny nose, stuffy nose, sore throat, sneezing, earache.
- Lower Respiratory Tract (LRT): cough, shortness of breath.
- Systemic: headache, malaise, muscle/joint ache/stiffness.
- Not used for analyses: chilliness/feverishness, chest tightness, wheeze.

A total symptom score will be derived for each participant, separately for each assessment (symptom diary card) on each day (Day 0 to Day 12) as follows:

- For each assessment, sum the 10 observed symptom grade values for each symptom diary card to obtain a total symptom score for each symptom diary card. If the participant does not have all 10 observed values on a specific symptom diary card being considered, then total symptom score will not be calculated for that symptom diary card. It is expected that participants will not have missing data.
- The AUC calculation will be based on the available non-missing calculated total symptom scores between the start and end of the defined AUC time. However, for an AUC to be derived, the participant should have at least 1 non-missing calculated total symptom scores at the start of the AUC period (e.g. date of first dose of IMP) and also at the end of the AUC time period

(e.g. Day 12). In addition, the participant should have at least 2 non-missing data recording on each day between the day after the start, and the day before the end, of the defined AUC time period (i.e. at least 2 out of the 3 possible assessments on each Day)). Any missing total symptom score data will be reviewed at the BDRM, for its potential impact on this endpoint, and any decisions to exclude participants as a result of these criteria will be documented in the BDRM minutes.

- As symptoms are scheduled to be taken 3 times daily for Days 0 to 11 (and once on Day 12), in order to calculate the AUC, the actual time that the assessment was collected will be used within the AUC calculation starting from the assessment at the time of the first administration of IMP.

The AUC of the total symptom score will be summarised by treatment group and modelled in the same way as the main analysis of the primary endpoint described in Section 10.7.1, including sensitivity analyses 1 and 2, as described therein.

The total symptom scores and the change from baseline scores will be summarised by timepoint (i.e. day relative to first administration of IMP and assessment) and treatment group. The symptom scores and the visual analogue score (VAS) in millimetres from the 13-item symptom diary card will be listed.

As well as a descriptive statistics summary of total symptom score values, the mean total symptom score values (+/- 1 Standard Error (SE)) will be displayed graphically by day (relative to first dose of IMP) and assessment, and treatment group. In order to calculate the time point that each assessment will be presented against, a relative day and relative assessment will be assigned. The last total symptom score measurement collected at the time of the first dose of IMP will be assigned to be the value at time point 1, while measurements collected on subsequent assessments and days will be assigned to subsequent time points in sequential order (i.e. time point 2, 3 and so on). Time point 1 will be presented against Day 0 assessment 1, while subsequent time points will be presented against Day 0 assessment 2, Day 0 assessment 3, Day 1 assessment 1, and so on. Negative timepoints relative to dosing will also be included and will be presented as Day -1 assessment 1.

[Line graph: y-axis = mean of total symptoms score, x-axis = day relative to dosing (the axis will be negative to include days prior to IMP administration), one line for each treatment group on same plot].

A boxplot will also be presented by day (relative to first dose of IMP) and assessment, plotting the median and mean qRT-PCT values for each treatment group, with the corresponding summary statistics.

[Box plot: y-axis = mean of qRT-PCR (log_{10} copies/mL), x-axis = day relative to dosing, one box-and-whisker for each day, with each treatment panelled with RV299 at the top and placebo below].

Note: For multiple assessments taken within each day, so as to be able to plot mean values across participants (within a treatment group) by day, the actual collection time point (which may differ across participants) will not be used. Rather all first, second and third assessments will have mean values separately calculated and plotted as three means within each day. These three means will be shown equally spaced along the x-axis within the graph.

Area under the Curve over Time of Total Clinical Symptoms Change from Baseline (TSS-AUC-CFB) as Measured from 10 Symptoms within the Graded Symptom Scoring System Collected 3 Times Daily Starting at Initial Administration of IMP up to Planned Discharge from Quarantine

The change from baseline will be calculated for each assessment following administration of IMP and an AUC calculated using these scores will be analysed in the same manner as described above

(including sensitivity analyses 1 and 2), where the baseline assessment is the assessment nearest to the time of the first administration of IMP (can be prior to or after dosing, depending on whether dosed in the morning or evening).

Peak Symptoms Diary Card Score: Peak Total Clinical Symptoms (TSS) as Measured from 10 Symptoms within the Graded Symptom Scoring System Collected 3 Times Daily Starting from Initial Administration of IMP up to Planned Discharge from Quarantine

Using the scheduled protocol assessments from the assessment at the time of the first dose of IMP to Day 12 (Quarantine discharge), the highest total symptom score (defined as the sum of all 10 individual composite symptoms) will be summarised by treatment group and modelled in the same way as the main analysis of the primary endpoint.

Participants who do not record any symptoms will be assigned a peak of 0.

Peak Daily Symptom Score: Individual Maximum Daily Sum of Symptom Score from Initial Administration of IMP up to Planned Discharge from Quarantine

The highest total symptom score recorded on each day, across the three assessments, for each participant will be summarised descriptively by treatment group and assessment day.

Time to Symptom Resolution as Measured from 10 Symptoms within the Graded Daily Symptom Scoring System Starting at Initial Administration of IMP to 24-hours Symptom Free

Symptom resolution is defined as a participant scoring 0 for the total symptom score for a 24 hour period (e.g a minimum of three consecutive symptom diary cards, each with a score of 0) after their peak symptom score.

The time from the assessment at the time of the first administration of IMP until symptom resolution will be calculated in days as:

Date and time of symptom resolution – Date and time of assessment at IMP administration.

The time to symptom resolution will be summarised by treatment group using descriptive summaries.

If the peak symptom score occurs on more than one day then the first occurrence will be selected. Participants who do not record 24 hours symptom free after their highest total symptom score during the quarantine period will be censored at their last assessment and participants who record no symptoms during quarantine will be excluded from this analysis.

Time to Symptom Resolution as Measured from 10 Symptoms within the Graded Daily Symptom Scoring System Starting at Peak Symptoms after Initial Administration of IMP to 24-hours Symptom Free

The time from the highest total symptom score following administration of IMP until symptom resolution will be calculated in days as:

Date and time of symptom resolution – Date and time of highest total symptom score.

The time to symptom resolution after the peak symptom score will be summarised by treatment group using descriptive summaries.

If the peak symptom score occurs on more than one day then the first occurrence will be selected. Participants who do not record 24 hours symptom free after their highest total symptom score during the quarantine period will be censored at their last assessment and participants who record no symptoms during quarantine will excluded from this analysis.

Time to Peak as Measured from 10 Symptoms within the Graded Daily Symptom Scoring System Starting from Initial Administration of IMP to the Time of Peak Daily Symptom Score

The time from the assessment at the time of the first dose of IMP (can be prior to or after dosing, depending on whether dosed in the morning or evening) until the highest total symptom score will be calculated in days as:

Date and time of highest total symptom score – Date of and time of assessment at IMP administration.

The time to peak daily symptom score will be summarised by treatment group using descriptive summaries.

If the peak symptom score occurs on more than one day then the first occurrence will be selected. Participants who record no symptoms during quarantine will be censored at their last assessment.

10.7.2.5 Nasal Discharge Endpoints

Total Weight of Mucus Produced Starting at Initial Administration of IMP up to Planned Discharge from Quarantine

Total weight of nasal mucus (grams) will be calculated as the sum of mucus weights taken from the assessment at the time of the first administration of IMP (can be prior to or after dosing, depending on whether dosed in the morning or evening) to morning of Day 12 (Quarantine discharge). Total mucus weight will be summarised by treatment group and will include the change from baseline, where baseline is the last assessment recorded prior to receiving a positive result for RSV by qicPCR. For participants who did not receive a positive result, the final assessment prior to the first administration of IMP will be defined as the baseline score.

Total Number of Tissues Used by Participants Starting At Initial Administration of IMP up to Planned Discharge from Quarantine

Total number of tissues will be counted from the assessment at the time of the first dose of IMP (can be prior to or after dosing, depending on whether dosed in the morning or evening) to morning of Day 12 (Quarantine discharge). This count will be summarised by treatment group and will include the change from baseline, where baseline is the last assessment recorded prior to receiving a positive result for RSV by qicPCR. For participants who did not receive a positive result, the final assessment prior to the first administration of IMP will be defined as the baseline score.

CCI [redacted]

[redacted]

[redacted]

CCI [redacted]

CCI [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

CCI [redacted]

10.8. Pharmacokinetic Analysis

Summary of the pharmacokinetic (PK) data and endpoints will not be performed by S-cubed and will therefore not be a part of this SAP. Details of the PK Analysis will be found in the CPAP provided by VENN. Discussion of the PK parameter correlation can be found in Section 10.7.3.1..

10.9. Safety Analysis

All analyses of safety endpoints will be descriptive only. The safety population will be used for all safety presentations.

10.9.1. Adverse Events

All adverse events (AE) will be coded using MedDRA, Version 25.0.

An adverse event is defined as treatment emergent if the onset date is on or after the date of first dosing with IMP. Should any onset date for an adverse event be missing or only a partial date recorded (such that it cannot be determined if the event onset was prior to start of IMP or not) then it will be assumed that the event is treatment emergent, unless the adverse event stop date indicates otherwise.

Similarly, an AE is defined as challenge emergent if the onset date is on or after the date of inoculation. Should any onset date for an adverse event be missing or only a partial date recorded (such that it cannot be determined if the event onset was prior to inoculation or not) then it will be assumed that the event is challenge emergent, unless the adverse event stop date indicates otherwise.

An AE can be both challenge emergent and treatment emergent. Any AE with an onset date earlier than the inoculation date will be classified as a pre-treatment AE.

If a participant experiences more than one adverse event with the same preferred term, that preferred term will be counted only once. It will be assigned the greatest observed severity and the strongest relationship to IMP among those events for the tables in which those characteristics are summarised.

Pre-treatment AEs will be identified in a patient listing.

A summary of treatment-emergent AEs will be presented by treatment group showing the number of events, number of participants with events (also split by severity; mild, moderate, severe), number of participants with SAEs, number of participants with related events, number of participants with events

leading to early withdrawal from the study and the number of participants with events leading to early discontinuation of IMP.

Further summaries will present the treatment-emergent AEs by:

- Treatment group, SOC and PT.
- Treatment group, SOC, PT and severity.
- Treatment group, SOC, PT and relationship to IMP.

Further summaries will present the challenge-emergent AEs by:

- Treatment group, SOC, PT and relationship to challenge agent.

Tables presented by relationship will only include the subset of adverse events that are judged as being 'Related' to IMP or challenge agent, i.e. correspond to adverse events where relationship is recorded on the adverse event page as being 'Unlikely', 'Possibly', 'Probably', 'Definitely', or a relationship is not given.

In all AE summary tables results will be displayed ordered in terms of decreasing frequency of SOC occurrence (based on total across all participants), and within each SOC also ordered in terms of decreasing frequency of preferred term occurrence (also based on total across all participants). In all AE summary tables a total column including data across all participants will also be presented.

10.9.2. Laboratory Variables

For all laboratory variables, baseline is defined as the assessment collected prior to the first administration of IMP.

The following parameters will be included within summary presentations (and presented in the units as shown):

- Haematology: platelet count (10^9/L), white blood cell (WBC) count (absolute) (10^9/L), neutrophils (% and absolute (10^9/L)), lymphocytes (% and absolute (10^9/L)), monocytes (% and absolute (10^9/L)), eosinophils (% and absolute (10^9/L)), basophils (% and absolute (10^9/L)), red blood cell (RBC) count (10^12/L), reticulocyte count (% and absolute (10^9/L), haemoglobin (g/L), haematocrit (%), mean corpuscular volume (MCV) (fL), mean corpuscular haemoglobin (MCH) (PG), mean corpuscular haemoglobin concentration (MCHC) (g/L).
- Coagulation: prothrombin time (PT) (secs), activated partial thromboplastin time (APTT) (secs).
- Biochemistry: sodium (mmol/L), potassium (mmol/L), glucose (mmol/L), albumin (g/L), chloride (mmol/L), bicarbonate (mmol/L), calcium (mmol/L), uric acid (umol/L), total protein (g/L), creatinine (umol/L), total bilirubin (umol/L), indirect bilirubin (umol/L), direct bilirubin (umol/L), inorganic phosphate (mmol/L), blood urea nitrogen (mg/dL), C-reactive protein (CRP) (mg/L), gamma glutamyl transferase (GGT) (IU/L), alkaline phosphatase (ALP) (IU/L), alanine transaminase (ALT) (IU/L), lactate dehydrogenase (LDH) (IU/L), aspartate transaminase (AST) (IU/L), urea (mmol/L).
- Thyroid Function Tests (screening only): Free thyroxine (pmol/L), Thyroid Stimulating Hormone (mIU/L).
- Cardiac Enzymes: creatine kinase (IU/L), troponin T (ng/L).
- Urinalysis: colour, specific gravity, appearance, pH, dipstick presence of: blood, glucose, leukocytes, ketones, nitrite, protein, urobilinogen, bilirubin.

- Human Immunodeficiency Virus and Hepatitis A, B and C: HIV-1 and HIV-2 antibodies, hepatitis A antibodies (HepA IgM), hepatitis B surface antigen (HBsAg), hepatitis C antibodies (HCAb).

Observed parameter values and changes from baseline will be summarised appropriately for the above haematology, chemistry, coagulation and cardiac enzyme parameters. Any other laboratory parameters collected as part of the study will only be included in participant listings. Laboratory data collected in different units to that shown will be converted to the above specified units (if possible) for presentation in tables and listings.

Laboratory values outside the reference range will be identified in the participant listings as above or below the reference range. Laboratory values that are below the limit of quantification (BLQ) will be set to zero in computations for summary presentations but will be noted as BLQ in participant listings. Laboratory values that are missing will remain missing and will be noted as such in listings.

10.9.3. Vital Signs

Vital signs parameters to be summarised are:

- Heart Rate (beats per minute), systolic blood pressure (mmHg), diastolic blood pressure (mmHg), respiratory rate (breaths per minute), peripheral arterial oxygen saturation (%) and tympanic temperature (^{O}C).

Vital signs parameters will be summarised as observed parameter values and changes from baseline, by treatment group for all scheduled protocol visits, where baseline is defined as the assessment performed prior to the first administration of IMP.

10.9.4. Spirometry

Summary statistics for absolute values and change from baseline by time point will be tabulated, by group, for spirometry parameters (FEV_1(absolute), FEV_1(% predicted), Forced vital capacity (FVC) (absolute), FVC (% predicted), FEV_1/FVC ratio (absolute), FEV_1/FVC ratio (% predicted)) and will also be included within participant listings.

The spirometry baseline is the assessment performed at screening.

10.9.5. Physical Examination

Physical examination findings (both for the complete examination and also any directed examination assessments) will be included within participant listings.

10.9.6. 12-Lead Electrocardiograms

Summary statistics for absolute values and change from baseline by time point will be tabulated, by treatment group for the following ECG parameters: (Heart Rate (bpm), PR interval (sec), QRS duration (sec), QT interval (sec), QTc interval (sec), QTcB interval (sec), QTcF interval (sec) and RR interval (sec)). For all ECG parameters, the baseline assessment is defined as the assessment performed prior to IMP dosing. All data will be included within participant listings.

11. CHANGES TO THE PROTOCOL SPECIFIED ANALYSIS DETAILED IN THE STATISTICAL ANALYSIS PLAN

1. Clarity has been added to the definitions for the ITT-A and ITT-B populations to ensure they are mutually exclusive and are accounting for subjects who have a positive detection either side of IMP administration.

2. The protocol incorrectly used median AUC as the main estimator of the primary endpoint. This has been corrected within the SAP to use the mean AUC.

3. Inferential analysis was not required for any time to event secondary endpoints within the protocol. However, this have been deemed as necessary to support the study outcome and log rank tests have been added to the appropriate endpoints.

4. The endpoint 'Time (days) to peak viral culture in nasal samples, starting from initial administration of IMP' had been missed in the list of endpoints within the protocol, though referred to in later sections. This endpoint has been added to the SAP.

5. Symptom resolution was included within the wording of the secondary clinical-symptom related endpoints and referred to as 'returning to baseline score'. This was deemed not to fit the requirements of the endpoint and has instead been amended to be 24-hours symptom free.

6. The endpoint 'Time to symptom resolution … starting at initial administration of IMP to time of returning to baseline score' has been expanded to include the caveat that the symptom-free period must occur after the peak symptom score.

12. REFERENCES

[1] Matthews JNS, Altman DG, Campbell MJ, Royston P. Analysis of serial measurements in medical research. *Br Med J* (1990); 300: 230-5.

[2] Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. Journal of American Statistical Association. 1958; 53:457-481.

13. TABLES, FIGURES AND LISTINGS

13.1. Specific Presentation Details

Tables, listings, and figures will be provided in a WORD document [and programmed off CDISC compliant SDTM SAS data sets.]. All summary tables and figures will have source data footnotes that refer to the relevant listings. Dates will appear as ddmmmyyyy; times as hh:mm. All listings will be ordered by treatment group, participant number, and scheduled visit. For the presentation of summary data, values will be aligned based on the unit column, and not left/right justified. For example:

Parameter			
	n	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)
	GM (GSD)	xx.x (xx.xx)	xx.x (xx.xx)
	%CV	xx.x	xx.x
	SE	xx.xx	xx.xx
	Median	xx.x	xx.x
	Q1, Q3	xx.x, xx.x	xx.x, xx.x
	Min, Max	xx, xx	xx, xx

All tables, listings and figures will have the SAS program name, output filename and date of production in the footnote.

All tables, listings and figures will include the following study header and footer:

CONFIDENTIAL hVIVO Services Ltd Page x of y
REVD002 [VIR-CST-001]

Table x.x
Title
Participant population

Source Data: Listing 16.2.x {Source data footnote only appears for tables, where x references relevant listing number}

Program: xxxxxxxxx Output: xxxxxxx Date: xxxxxxxxx

13.2. List of Tables

For the primary endpoint and selected secondary [redacted] tables will be repeated for the ITT-A, ITT-B, ITT and PP Populations where the difference between the ITT-I is greater than 1 participant within a treatment group. Where tables are to be repeated on any additional populations, an X has been marked in the relevant column. If a table is repeated, the original table number as produced for the ITT-I population will have .1 added and this final digit will be increased by 1 for repeats on the ITT-A. Similarly, for repeats on ITT-B the number will increase by 2, for repeats on ITT the number will increase by 3 and for repeats on the PP the number will increase by 4. For example, table 14.2.1.1 will be produced for the ITT-I population and will be repeated as 14.2.1.2, 14.2.1.3, 14.2.1.4 and 14.2.1.5 for the ITT-A, ITT-B, ITT and PP populations respectively. If no repeats of a table are required then the original table will not require the final .1.

Table Number	Table Title	Repeated for ITT-A	ITT-B	ITT	PP
14.1.1	Participant Disposition – All Participants				
14.1.2	Demography – Safety Population				
14.1.3	IMP Exposure and Compliance – Safety Population				
14.1.4	Concomitant Medications – Safety Population				
14.2.1.1	AUC of RSV Challenge Virus Viral Load by qRT-PCR from Initial Administration of IMP to Quarantine Discharge – ITT-I Population	X	X	X	X
14.2.1.2	AUC of RSV Challenge Virus Viral Load by qRT-PCR from Initial Administration of IMP for 6.5 Days – ITT-I Population	X			
14.2.1.3	AUC of RSV Challenge Virus Viral Load by qRT-PCR from Day 2 to Day 12 – ITT-I Population	X			
14.2.1.4	AUC of RSV Challenge Virus Viral Load by qRT-PCR from Initial Administration of IMP to Quarantine Discharge (Untransformed Data) – ITT-I Population	X			
14.2.2.1	Peak Viral Load of RSV Challenge Virus by qRT-PCR from Initial Administration of IMP to Quarantine Discharge – ITT-I Population	X			
14.2.2.2	Time to First Confirmed Undetectable Assessment of RSV Challenge Virus by qRT-PCR from Initial Administration of IMP – ITT-I Population	X			
14.2.2.3	Time to First Confirmed Undetectable Assessment of RSV Challenge Virus after Peak Measure by qRT-PCR following Initial Administration of IMP – ITT-I Population	X			
14.2.2.4	Time to Peak RSV Challenge Virus by qRT-PCR following Initial Administration of IMP – ITT-I Population	X			
14.2.2.5.1	AUC of RSV Challenge Virus Viral Load by Viral Culture from Initial Administration of IMP to Quarantine Discharge – ITT-I Population	X	X	X	X
14.2.2.5.2	AUC of RSV Challenge Virus Viral Load by Viral Culture from Initial Administration of IMP for 6.5 Days – ITT-I Population	X			
14.2.2.5.3	AUC of RSV Challenge Virus Viral Load by Viral Culture from Day 2 to Day 12 – ITT-I Population	X			

Table Number	Table Title	Repeated for ITT-A	ITT-B	ITT	PP
14.2.2.5.4	AUC of RSV Challenge Virus Viral Load by Viral Culture from Initial Administration of IMP to Quarantine Discharge (Untransformed Data) – ITT-I Population	X			
14.2.2.6	Peak Viral Load of RSV Challenge Virus by Viral Culture from Initial Administration of IMP to Quarantine Discharge – ITT-I Population	X			
14.2.2.7	Time to First Confirmed Undetectable Assessment of RSV Challenge Virus after Peak Measure by Viral Culture starting from Initial Administration of IMP - ITT-I Population	X			
14.2.2.8	Time to First Confirmed Undetectable Assessment of RSV Challenge Virus by Viral Culture starting from Peak Measure - ITT-I Population	X			
14.2.2.9	Time to Peak RSV Challenge Virus by Viral Culture following Initial Administration of IMP – ITT-I Population	X			
14.2.3.1.1	AUC of Total Symptom Score from 10-Item Diary Card from First Administration of IMP to Quarantine Discharge - ITT-I Population	X	X	X	X
14.2.3.1.2	AUC of Total Symptom Score from 10-Item Diary Card from First Administration of IMP for 6.5 Days - ITT-I Population	X			
14.2.3.1.3	AUC of Total Symptom Score from 10-Item Diary Card from Day 2 to Day 12 - ITT-I Population	X			
14.2.3.2.1	AUC of Total Symptom Score Change from Baseline from 10-Item Diary Card from First Administration of IMP to Quarantine Discharge - ITT-I Population	X	X	X	X
14.2.3.2.2	AUC of Total Symptom Score Change from Baseline from 10-Item Diary Card from First Administration of IMP for 6.5 days - ITT-I Population	X			
14.2.3.2.3	AUC of Total Symptom Score Change from Baseline from 10-Item Diary Card from Day 2 to Day 12 - ITT-I Population	X			
14.2.3.3	Total Symptom Score from 10-Item Diary Card by Assessment - ITT-I Population	X	X	X	X
14.2.3.4	Peak Total Symptom Score from 10-Item Diary Card from First Administration of IMP to Quarantine Discharge - ITT-I Population	X			
14.2.3.5	Peak Total Symptom Score from 10-Item Diary Card by Day - ITT-I Population				
14.2.3.6	Peak Daily Symptom Score from 10-Item Diary Card - ITT-I Population				
14.2.3.7	Time to Symptom Resolution by 10-Item Diary Card from Initial Administration of IMP to 24-Hours Symptom Free - ITT-I Population	X			
14.2.3.8	Time to Symptom Resolution by 10-Item Diary Card from Peak Total Symptom Score to 24-Hours Symptom Free - ITT-I Population	X			

Table Number	Table Title	Repeated for ITT-A	ITT-B	ITT	PP
14.2.3.9	Time to Peak Symptom Score by 10-Item Diary Card from Initial Administration of IMP - ITT-I Population	X			
14.2.4.1	Total Weight of Mucus Produced from Initial Administration of IMP to Quarantine Discharge by Assessment - ITT-I Population	X			
14.2.4.2	Total Number of Tissues Used from Initial Administration of IMP to Quarantine Discharge by Assessment - ITT-I Population				
CCI	[redacted]				
[redacted]	[redacted]				
[redacted]	[redacted]				
[redacted]	[redacted]	X			
14.3.1.1	Overall Summary of Treatment Emergent Adverse Events – Safety Population				
14.3.1.2	Treatment Emergent Adverse Events by System Organ Class and Preferred Term – Safety Population				
14.3.1.3	Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity – Safety Population				
14.3.1.4	Treatment Emergent Adverse Events Related to RV299 by System Organ Class and Preferred Term– Safety Population				
14.3.1.5	Adverse Events Related to Challenge Agent by System Organ Class and Preferred Term – Safety Population				
14.3.2	Haematology Parameters: Summary – Safety Population				
14.3.3	Biochemistry Parameters: Summary – Safety Population				
14.3.4	Coagulation Parameters: Summary – Safety Population				
14.3.5	Cardiac Enzymes Parameters: Summary – Safety Population				
14.3.6	Urinalysis Parameters: Summary – Safety Population				
14.3.7	Vital Signs Parameters: Summary – Safety Population				
14.3.8	Spirometry Parameters: Summary – Safety Population				
14.3.9	12-Lead Electrocardiogram Parameters: Summary – Safety Population				

13.3. List of Figures

For the primary endpoint and selected secondary[redacted] figures will be repeated for the ITT-A, ITT-B, ITT and PP Populations where the difference between the ITT-I is greater than 1 participant within a treatment group. Where figures are to be repeated on any additional populations, an X has been marked in the relevant column. If a figure is repeated, the original figure number as produced for the ITT-I population will have .1 added and this final digit will be increased by 1 for repeats on the ITT-A. Similarly, for repeats on ITT-B the number will increase by 2, for repeats on ITT the number will increase by 3 and for repeats on the PP the number will increase by 4. For example, figure 14.2.1.1 will be produced for the ITT-I population and will be repeated as 14.2.1.2, 14.2.1.3, 14.2.1.4 and 14.2.1.5 for the ITT-A, ITT-B, ITT and PP populations respectively. If no repeats of a table are required then the original table will not require the final .1.

		Repeated for			
Figure Number	**Figure Title**	**ITT-A**	**ITT-B**	**ITT**	**PP**
14.2.1.1	Mean RSV Challenge Virus Viral Load by qRT-PCR by Days from IMP Administration – ITT-I Population	X	X	X	X
14.2.1.2	Boxplot of RSV Challenge Virus Viral Load by qRT-PCR by Days from IMP Administration – ITT-I Population	X	X	X	X
14.2.2.1	Peak RSV Challenge Virus Viral Load by qRT-PCR by Days from IMP Administration – ITT-I Population	X			
14.2.2.2	Kaplan-Meier Plot of Time to First Confirmed Undetectable Assessment of RSV Challenge Virus by qRT-PCR from Initial Administration of IMP – ITT-I Analysis Set	X			
14.2.2.3	Kaplan-Meier Plot of Time to First Confirmed Undetectable Assessment of RSV Challenge Virus after Peak Measure by qRT-PCR following Initial Administration of IMP – ITT-I Population	X			
14.2.2.4	Kaplan-Meier Plot of Time to Peak RSV Challenge Virus by qRT-PCR following Initial Administration of IMP – ITT-I Population	X			
14.2.2.5.1	Mean RSV Challenge Virus Viral Load by Viral Culture by Days from IMP Administration – ITT-I Population	X	X	X	X
14.2.2.5.2	Boxplot of RSV Challenge Virus Viral Load by Viral Culture by Days from IMP Administration – ITT-I Population	X	X	X	X
14.2.2.6	Peak RSV Challenge Virus Viral Load by Viral Culture by Days from IMP Administration – ITT-I Population	X			
14.2.2.7	Kaplan-Meier Plot of First Confirmed Undetectable Assessment of RSV Challenge Virus after Peak Measure by Viral Culture starting from Initial Administration of IMP – ITT-I Population	X			
14.2.2.8	Kaplan-Meier Plot of First Confirmed Undetectable Assessment of RSV Challenge Virus by Viral Culture starting from Peak Measure – ITT-I Population	X			
14.2.3.1.1	Mean Daily Total Symptom Score from 10-item Diary Card by Days from IMP Administration – ITT-I Population	X	X	X	X
14.2.3.2.1	Peak Daily Total Symptom Score from 10-item Diary Card by Days from IMP Administration – ITT-I Population	X			
[redacted]	[redacted]				

Figure Number	Figure Title	Repeated for ITT-A	ITT-B	ITT	PP
CCI	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			
[redacted]	[redacted]	[redacted]			

13.4. List of Listings

Listing Number	Listing Title
16.2.1.1	Participant Disposition
16.2.1.2	Failed Inclusion and Exclusion Criteria
16.2.2	Protocol Deviations
16.2.3	Participant Populations
16.2.4.1	Demographics
16.2.4.2	Reproductive Status and Contraceptive Use
16.2.4.3	Smoking History
16.2.4.4	Alcohol Use
16.2.4.5	Recreational Drugs of Abuse
16.2.4.6	Medical History
16.2.4.7	Prior and Concomitant Medications
16.2.5.1	Challenge Virus Inoculation Administration
16.2.5.2	Viral Shedding Results
16.2.5.3	IMP Administration
16.2.6.1.1	Viral Load by Nasal Samples qRT-PCR Results
16.2.6.1.2	Viral Load by Nasal Samples qRT-PCR Derivations
16.2.6.2.1	Viral Load by Nasal Samples Viral Culture Results
16.2.6.2.2	Viral Load by Nasal Samples Viral Culture Derivations
16.2.6.3.1	Symptom Scores from Symptom Diary Card
16.2.6.3.2	Visual Analogue Scale from Symptom Diary Card
16.2.6.3.3	Total Symptom Score: AUC Derivations
16.2.6.3.4	Total Symptom Score: Other Derivations
16.2.6.4	Mucus Weight and Tissue Bag Distribution
16.2.6.5	Nasopharyngeal Swab: Respiratory Virus Screen/Rapid Viral Antigen Test
16.2.6.6	Plasma PK Parameters
16.2.7	Adverse Events
16.2.8.1	Blood Sample Collection
16.2.8.2	Haematology
16.2.8.3	Coagulation
16.2.8.4	Biochemistry
16.2.8.5	Thyroid Function Tests
16.2.8.6	Cardiac Enzymes
16.2.8.7	Human Immunodeficiency Virus and Hepatitis A, B and C
16.2.8.8.1	Other Laboratory Tests: TDL
16.2.8.9.1	Other Laboratory Tests: Urine Pregnancy
16.2.8.9.2	Other Laboratory Tests: Drugs of Abuse Screen
16.2.8.9.3	Other Laboratory Tests: Urine Cotinine
16.2.8.9.4	Other Laboratory Tests: Alcohol Breath Test
16.2.9.1	Urinalysis
16.2.9.2	Urinalysis (TDL): Microscopy

Listing Number	Listing Title
16.2.10	Vital Signs
16.2.11	Spirometry
16.2.12.1	Physical Examination
16.2.12.2	Rhinoscopic Examination
16.2.13	ECG
16.2.14	Visit Dates

14. TABLE AND LISTING SHELLS

Table 14.1.56
Participant Disposition
All Participants

	Treatment Group					
	RV299 (N=xx)		Placebo (N=xx)		Overall (N=xx)	
	n	(%)	n	(%)	n	(%)
Enrolled					XX	
Received challenge agent					XX	
Randomised	XX		XX		XX	
Received at least 1 dose of IMP	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Received all doses of IMP	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
ITT Population [1]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
ITT-I Population [2]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
ITT-A Population [3]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
ITT-B Population [4]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Per Protocol Population [5]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Safety Population [6]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X
PK Population [7]	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Discontinued IMP	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Completed study	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Withdrew from study	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Reason for Discontinuation of IMP:						
Death	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Withdrawal by Subject	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Investigator’s Decision	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Reason for Study Withdrawal:						
Death	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Withdrawal by Subject	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Investigator’s Decision	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Non-compliance with Study Requirements	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Pregnancy	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Study Terminated by Sponsor	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Lost to Follow-up	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Never dosed	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Other	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)

[1] Intent to Treat (ITT) Population = All randomised participants receiving challenge virus and at least one dose of IMP.
[2] Intent to Treat Infected (ITT-I) Population = All randomised participants receiving challenge virus and at least 1 dose of IMP, and meeting the criterion for laboratory confirmed RSV infection.
[3] Intent to Treat Infected Pre-dose (ITT-A) Population = All randomised participants receiving challenge virus and at least 1 dose of IMP, and meeting the criterion for laboratory confirmed RSV infection, using only assessments prior to taking IMP.
[4] Intent to Treat Infected Post-dose (ITT-B) Population = All randomised participants receiving challenge virus and at least 1 dose of IMP, and meeting the criterion for laboratory confirmed RSV infection, using only assessments after IMP.
[5] Per Protocol (PP) Population = All ITT-I population participants who have no major protocol deviations, and who complete the quarantine period up to the final day of quarantine (Study Day 12) and receive all 10 doses of IMP.
[6] Safety Population = All randomised participants receiving challenge virus and at least one dose of IMP.
[7] The PK Population = All ITT participants with at least one post-dose PK result.
[8] Completed Study = Participating in the study up to and including Day 28 (Follow-up).
Note: Percentages are based on all randomised participants.

Table 14.1.2
Demography
Safety Population

		Treatment Group RV299 (N=xx)	Placebo (N=xx)	Overall (N=xx)
Ethnicity				
Hispanic or Latino	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Hispanic or Latino	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Not Reported	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Unknown	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Race				
American Indian or Alaska Native	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Asian	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Black or African American	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Native Hawaiian or Other Pacific Islander	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
White	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Other	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
Height at Screening (m)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX
Weight at Screening (kg)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX
BMI at Screening (kg/m^2)	n	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX

BMI = Body Mass Index
Note: Percentages are based on the safety population.

Programming note: If any categorical parameters have missing values for certain participants, then include a missing value category.

Table 14.1.3
IMP Exposure and Compliance
Safety Population

		Treatment Group RV299 (N=xx)	Placebo (N=xx)	Overall (N=xx)
Number of doses of IMP received	n	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX
Compliance				
<80%	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
80% - 120%	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)
>120%	n (%)	XX (XX.X)	XX (XX.X)	XX (XX.X)

Note: Compliance = (number of doses received / number of doses expected) * 100.

Table 14.1.4
Concomitant Medications
Safety Population

Drug Class (L2)/ WHO Drug Name [1]	Treatment Group: RV299 (N=xx) n	%	Placebo (N=xx) n	%	Overall (N=xx) n	%
Number of Subjects with any Medication	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Drug Class 1	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
WHO Drug Name 1	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
WHO Drug Name 2	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Drug Class 2	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
WHO Drug Name 1	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
WHO Drug Name 2	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)

[1] All medications will be coded using the WHO Drug Global Version March 1 2022.
Note: Concomitant medications correspond to medications where medication stop date is not before the date of IMP treatment.
Note: Table shows distinct number of participants with each WHO Drug Name/Drug Class.
Note: Percentages are based on the safety population.

Table 14.2.1.1
AUC of RSV Challenge Virus Viral Load by qRT-PCR from Initial Administration of IMP to Quarantine Discharge
ITT-I Population

AUC(hours*Log10 copies/mL)	Treatment Group RV299 (N=xx)	Placebo (N=xx)
n	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.XX	XX.XX
Median	XX.X	XX.X
Q1, Q3	XX.X, X.XX	XX.X, X.XX
Min, Max	XX, XX	XX, XX
Difference in LS means [1]	XX.XX	
95% Confidence interval for difference	XX.XXX, XX.XXX	
P-value [1]	X.XXX	

[1] Comparison of RV299 and placebo using an ANCOVA with treatment group as a fixed effect and baseline viral load as the covariate.

This table may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

This layout will be utilised for the following tables:

Table 14.2.1.2 AUC of RSV Challenge Virus Viral Load by qRT-PCR from Initial Administration of IMP for 6.5 Days – ITT-I Population
Table 14.2.1.3 AUC of RSV Challenge Virus Viral Load by qRT-PCR from Day 2 to Day 12 – ITT-I Population
Table 14.2.1.4 AUC of RSV Challenge Virus Viral Load by qRT-PCR from Initial Administration of IMP to Quarantine Discharge (Untransformed Data) – ITT-I Population
Table 14.2.2.1 Peak Viral Load of RSV Challenge Virus by qRT-PCR from Initial Administration of IMP to Quarantine Discharge - ITT-I Population
Table 14.2.2.5.1 AUC of RSV Challenge Virus Viral Load by Viral Culture from Initial Administration of IMP to Quarantine Discharge - ITT-I Population
Table 14.2.2.5.2 AUC of RSV Challenge Virus Viral Load by Viral Culture from Initial Administration of IMP for 6.5 Days – ITT-I Population
Table 14.2.2.5.3 AUC of RSV Challenge Virus Viral Load by Viral Culture from Day 2 to Day 12 – ITT-I Population
Table 14.2.2.5.4 AUC of RSV Challenge Virus Viral Load by Viral Culture from Initial Administration of IMP to Quarantine Discharge (Untransformed Data) – ITT-I Population
Table 14.2.2.6 Peak Viral Load of RSV Challenge Virus by Viral Culture from Initial Administration of IMP to Quarantine Discharge - ITT-I Population

Where appropriate, these tables may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

Programming Note: It is possible that the parametric methods will fail to meet the required assumptions for the main or repeated tables. Therefore, we will provide a Wilcoxon test (see Section 10.1.4). The alternative presentation for this is shown below and will require the following footnote to be updated: [1] Comparison of RV299 and placebo using a Wilcoxon rank sum test.

Median difference in LS means [1]	XX.XX
P-value [1]	X.XXX

Table 14.2.2.2.1
Time to First Confirmed Undetectable Assessment of RSV Challenge Virus by qRT-PCR from Initial Administration of IMP
ITT-I Population

	Treatment Group					
	RV299 (N=xx)			Placebo (N=xxx)		
Time (days)	n	N#	Kaplan-Meier Estimate	n	N#	Kaplan-Meier Estimate
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	xx	0.xxx	xx	xx	0.xxx
X	xx	Xx	0.xxx	xx	xx	0.xxx
X	xx	Xx	0.xxx	xx	xx	0.xxx
X	xx	Xx	0.xxx	xx	xx	0.xxx
X	xx	Xx	0.xxx	xx	xx	0.xxx
X	xx	Xx	0.xxx	xx	xx	0.xxx
25th percentile [1]		xx.x			xx.x	
50th percentile [1]		xx.x			xx.x	
75th percentile [1]		xx.x			xx.x	
p-value [2]		x.xxxx				

n = number of participants with a confirmed undetectable assessment by the end of the period. N# = number of participants at risk.
[1] Percentiles are obtained from the Kaplan-Meier estimates.
[2] P-value obtained from a log-ank test compared RV299 and placebo.
Note: Time to First Confirmed Undetectable Assessment from Initial Administration of IMP = (Date of first confirmed negative test after peak qRT-PCR measurement – Date of first administration of IMP) + 1.

This table may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

This layout will be utilised for the following tables:

Table 14.2.2.3.1 Time to First Confirmed Undetectable Assessment of RSV Challenge Virus after Peak Measure by qRT-PCR from qRT-PCR following Initial Administration of IMP - ITT-I Population
Table 14.2.2.4.1 Time to Peak RSV Challenge Virus qRT-PCR following Initial Administration of IMP - ITT-I Population
Table 14.2.2.7.1 Time to First Confirmed Undetectable Assessment of RSV Challenge Virus after Peak Measure by Viral Culture starting from Initial Administration of IMP - ITT-I Population
Table 14.2.2.8.1 Time to First Confirmed Undetectable Assessment of RSV Challenge Virus by Viral Culture starting from Peak Measure - ITT-I Population

Where appropriate, these tables may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

Table 14.2.3.1.1
AUC of Total Symptom Score from 10-Item Diary Card from First Administration of IMP to Quarantine Discharge
ITT-I Population

AUC(hours*score)	Treatment Group RV299 (N=xx)	Placebo (N=xx)
n	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
GM (GSD)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.XX	XX.XX
Median	XX.X	XX.X
Q1, Q3	XX.X, X.XX	XX.X, X.XX
Min, Max	XX, XX	XX, XX
Difference in LS means [1]	XX.XX	
95% Confidence interval for difference	XX.XXX, XX.XXX	
P-value [1]	X.XXX	

[1] Comparison of RV299 and placebo using an ANCOVA with treatment group as a fixed effect and baseline viral load as the covariate.
Note: Total symptom scores at the time of the first administration of IMP can be prior to or after dosing, depending on whether dosed in the morning or evening.
Note: GM is derived by antilog(mean(exp(TSS-AUC + 1))) - 1.

This table may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

This layout will be utilised for the following tables:

Table 14.2.3.1.2 AUC of Total Symptom Score from 10-Item Diary Card from First Administration of IMP for 6.5 Days - ITT-I Population
Table 14.2.3.1.3 AUC of Total Symptom Score from 10-Item Diary Card from Day 2 to Day 12 - ITT-I Population
Table 14.2.3.2.1 AUC of Total Symptom Score Change from Baseline from 10-Item Diary Card from First Administration of IMP to Quarantine Discharge - ITT-I Population
Table 14.2.3.2.2 AUC of Total Symptom Score Change from Baseline from 10-Item Diary Card from First Administration of IMP for 6.5 Days - ITT-I Population
Table 14.2.3.2.3 AUC of Total Symptom Score Change from Baseline from 10-Item Diary Card from Day 2 to Day 12 - ITT-I Population
Table 14.2.3.4.1 Peak Total Symptom Score from 10-Item Diary Card from First Administration of IMP to Quarantine Discharge - ITT-I Population
[redacted]

Where appropriate, these tables will be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

Programming Note: It is highly likely that the parametric methods will fail to meet the required assumptions. Therefore, we will provide a Wilcoxon test (see Section 10.1.4). The alternative presentation for this is shown below and will require the following footnote update: [1] Comparison of RV299 and placebo using a Wilcoxon rank sum test.

Median difference in LS means [1]	XX.XX
P-value [1]	X.XXX

Table 14.2.3.3.1
Total Symptom Score from 10-Item Diary Card by Assessment
ITT-I Population

		Treatment Group			
		RV299 (N=xx)		Placebo (N=xx)	
Days from IMP Administration Assessment		Observed	Change from Baseline	Observed	Change from Baseline
0 Days Assessment 1	n	XX		XX	
	Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)	
	GM (GSD)	XX.X (XX.XX)		XX.X (XX.XX)	
	%CV	XX.XX		XX.XX	
	Median	XX.X		XX.X	
	Q1, Q3	XX.X, X.XX		XX.X, X.XX	
	Min, Max	XX, XX		XX, XX	
0 Days Assessment 2	n	XX	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	GM (GSD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	%CV	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
[Repeat for all assessments during Quarantine Period]					

Note: Assessments are relative to first administration of IMP.
Note: Total symptom scores at the time of the first administration of IMP can be prior to or after dosing, depending on whether dosed in the morning or evening.

This table may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 respectively.

This layout will be utilised for the following tables:

Table 14.2.3.5.1 Peak Total Symptom Score from 10-Item Diary Card by Day - ITT-I Population

The table may be repeated on the ITT-A, ITT-B, ITT and PP Populations as .2, .3, .4 and .5 as appropriate.

Table 14.2.3.6.1
Peak Daily Symptom Score from 10-Item Diary Card
ITT-I Population

		Treatment Group			
		RV299 (N=xx)		Placebo (N=xx)	
Days from IMP Administration		Observed	Change from Baseline	Observed	Change from Baseline
0 Days	n	XX		XX	
	Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)	
	GM (GSD)	XX.X (XX.XX)		XX.X (XX.XX)	
	%CV	XX.XX		XX.XX	
	Median	XX.X		XX.X	
	Q1, Q3	XX.X, X.XX		XX.X, X.XX	
	Min, Max	XX, XX		XX, XX	
1 Day	n	XX	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X
	GM (GSD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	%CV	XX.XX	XX.XX	XX.XX	XX.XX
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
[Repeat for all days during Quarantine Period]					

Note: Days are relative to first administration of IMP.
Note: Total symptom scores on the day of the first administration of IMP can be prior to or after dosing, depending on whether dosed in the morning or evening.

Table 14.2.3.7.1
Time to Symptom Resolution by 10-Item Diary Card from Initial Administration of IMP to 24-Hours Symptom Free
ITT-I Population

	Treatment Group	
Time (days)	RV299 (N=xx)	Placebo (N=xx)
n	XX	XX
Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)
GM (GSD)	XX.X (XX.XX)	XX.X (XX.XX)
%CV	XX.XX	XX.XX
Median	XX.X	XX.X
Q1, Q3	XX.X, X.XX	XX.X, X.XX
Min, Max	XX, XX	XX, XX

Note: Time to Symptom Resolution from Initial Administration of IMP = (Date and time of symptom resolution – Date of and time of assessment at time of IMP administration) + 1.

This layout will be utilised for the following tables:

Table 14.2.3.8.1 Time to Symptom Resolution by 10-Item Diary Card from Peak Total Symptom Score to 24-Hours Symptom Free - ITT-I Population
Table 14.2.3.9.1 Time to Peak Symptom Score by 10-Item Diary Card from Initial Administration of IMP - ITT-I Population

The layout will be repeated for the following tables, without the GM (GSD) row:
Table 14.2.4.1.1 Total Weight of Mucus Produced from Initial Administration of IMP to Quarantine Discharge - ITT-I Population
Table 14.2.4.2.1 Total Number of Tissues Used from Initial Administration of IMP to Quarantine Discharge by Assessment - ITT-I Population

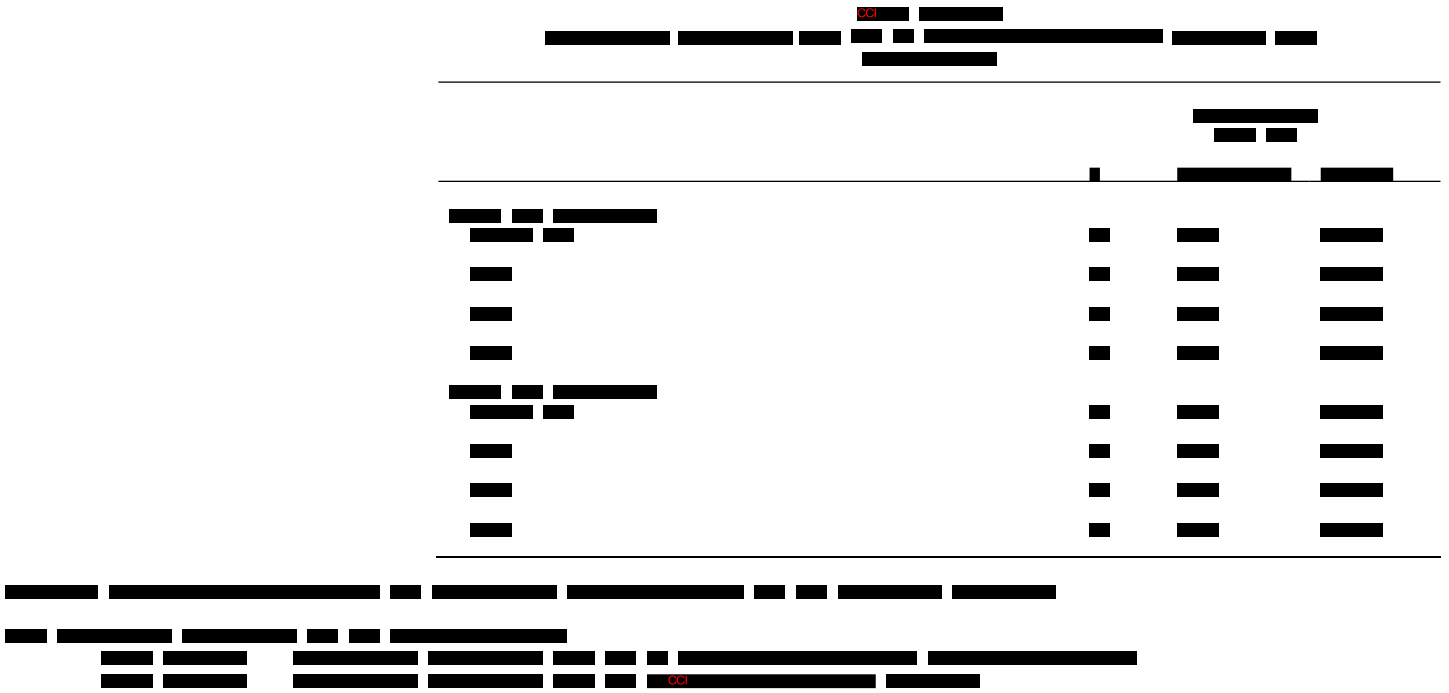

Table 14.3.1.67
Overall Summary of Treatment Emergent Adverse Events
Safety Population

	Treatment Group					
	RV299 (N=xx)		Placebo (N=xxx)		Overall (N=xx)	
	n	(%)	n	(%)	n	(%)
Number of Events	XX		XX		XX	
Number of Participants with any Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Participants with any Serious Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Participants with any Related Adverse Event	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Participants with any Adverse Event Leading to Withdrawal from the Study	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)
Number of Participants with any Adverse Event Leading to Discontinuation of IMP	XX	(XX.X)	XX	(XX.X)	XX	(XX.X)

Note: Treatment emergent events are those events with an onset on or after the start of IMP dosing.
Note: If a participant experiences more than one event, then the event with the worst severity or strongest relationship is included in the relevant level of summarisation.
Note: Related = 'Unlikely', 'Possibly', 'Probably', 'Definitely' or 'Not assessed'.
Note: Adverse Event Leading to Discontinuation from the Study = Participant withdrew from the study due to an adverse event.
Note: Adverse Event Leading to Discontinuation of Dosing = Action taken of 'Trial/Study drug permanently discontinued'.
Note: Percentages are based on the safety population.

Table 14.3.1.68
Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class/ Preferred Term [1]	Treatment Group RV299 (N=xx) n	(%)	Placebo (N=xxx) n	(%)
Number of Events	XX		XX	
Number of Subjects with any adverse event	XX	(XX.X)	XX	(XX.X)
System Organ Class 1	XX	(XX.X)	XX	(XX.X)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)
Preferred Term 2	XX	(XX.X)	XX	(XX.X)
System Organ Class 2	XX	(XX.X)	XX	(XX.X)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)
Preferred Term 2	XX	(XX.X)	XX	(XX.X)

[1] MedDRA Version 25.0.
Note: Treatment emergent events are those events with an onset on or after the first administration of IMP.
Note: Table shows distinct number of participants with events for each system organ class/preferred term.
Note: Percentages are based on the safety population.

Table 14.3.1.3
Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity
Safety Population

System Organ Class/ Preferred Term [1]	Treatment Group: RV299 (N=xx) n	(%)	Placebo (N=xxx) n	(%)
System Organ Class 1	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)
Preferred Term 2	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)
System Organ Class 2	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)
Mild	XX	(XX.X)	XX	(XX.X)
Moderate	XX	(XX.X)	XX	(XX.X)
Severe	XX	(XX.X)	XX	(XX.X)

[1] MedDRA Version 25.0.
Note: Treatment emergent events are those events with an onset on or after the first administration of IMP.
Note: This table shows distinct number of participants with events for each system organ class/preferred term/severity. If a participant experienced a specific event more than once then the event with the worst severity is summarised.
Note: Percentages are based on the safety population.

Table 14.3.1.4
Treatment Emergent Adverse Events Related to RV299 by System Organ Class and Preferred Term
Safety Population

System Organ Class/ Preferred Term [1]/ Relationship	Treatment Group: RV299 (N=xx) n	(%)	Placebo (N=xxx) n	(%)
System Organ Class 1	XX	(XX.X)	XX	(XX.X)
Not Assessed	XX	(XX.X)	XX	(XX.X)
Unlikely Related	XX	(XX.X)	XX	(XX.X)
Possibly Related	XX	(XX.X)	XX	(XX.X)
Probably Related	XX	(XX.X)	XX	(XX.X)
Definitely Related	XX	(XX.X)	XX	(XX.X)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)
Not Assessed	XX	(XX.X)	XX	(XX.X)
Unlikely Related	XX	(XX.X)	XX	(XX.X)
Possibly Related	XX	(XX.X)	XX	(XX.X)
Probably Related	XX	(XX.X)	XX	(XX.X)
Definitely Related	XX	(XX.X)	XX	(XX.X)
Preferred Term 2	XX	(XX.X)	XX	(XX.X)
Not Assessed	XX	(XX.X)	XX	(XX.X)
Unlikely Related	XX	(XX.X)	XX	(XX.X)
Possibly Related	XX	(XX.X)	XX	(XX.X)
Probably Related	XX	(XX.X)	XX	(XX.X)
Definitely Related	XX	(XX.X)	XX	(XX.X)
System Organ Class 2	XX	(XX.X)	XX	(XX.X)
Not Assessed	XX	(XX.X)	XX	(XX.X)
Unlikely Related	XX	(XX.X)	XX	(XX.X)
Possibly Related	XX	(XX.X)	XX	(XX.X)
Probably Related	XX	(XX.X)	XX	(XX.X)
Definitely Related	XX	(XX.X)	XX	(XX.X)
Preferred Term 1	XX	(XX.X)	XX	(XX.X)
Not Assessed	XX	(XX.X)	XX	(XX.X)
Unlikely Related	XX	(XX.X)	XX	(XX.X)
Possibly Related	XX	(XX.X)	XX	(XX.X)
Probably Related	XX	(XX.X)	XX	(XX.X)
Definitely Related	XX	(XX.X)	XX	(XX.X)

[1] MedDRA Version 25.0.
Note: Treatment emergent events are those events with an onset on or after the first administration of IMP.
Note: This table shows distinct number of participants with events for each system organ class/preferred term/relationship. If a participant experiences a specific event more than once then the event with the greatest relationship is summarised.
Note: Only the subset of AEs that are judged to be related to IMP have been considered (i.e. relationship = Possibly Related/Probably Related/Definitely Related/Not Assessed) in the table.
Note: Percentages are based on the safety population.

This layout will be utilised for the following table:

Table 14.3.1.5 Adverse Events Related to Challenge Agent by System Organ Class and Preferred Term – Safety Population
With the following footnote:
Note: Only the subset of AEs that are judged to be related to challenge agent have been considered (i.e. relationship = Possibly Related/Probably Related/Definitely Related/Not Assessed) in the table.

Table 14.3.2
Haematology Parameters: Summary
Safety Population

		Treatment Group			
		RV299 (N=xx)		Placebo (N=xx)	
Parameter (units)		Observed	Change from Baseline	Observed	Change from Baseline
Baseline	n	XX		XX	
	Mean (SD)	XX.X (XX.XX)		XX.X (XX.XX)	
	%CV	XX.XX		XX.XX	
	Median	XX.X		XX.X	
	Q1, Q3	XX.X, X.XX		XX.X, X.XX	
	Min, Max	XX, XX		XX, XX	
Day 7	n	XX	XX	XX	XX
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	%CV	XX.XX	XX.XX	XX.XX	XX.XX
	Median	XX.X	XX.X	XX.X	XX.X
	Q1, Q3	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX	XX.X, X.XX
	Min, Max	XX, XX	XX, XX	XX, XX	XX, XX
[Repeat for all scheduled post-baseline assessments and parameters]					

This layout will be utilised for the following tables:

Table 14.3.3	Biochemistry Parameters: Summary – Safety Population
Table 14.3.4	Coagulation Parameters: Summary – Safety Population
Table 14.3.5	Cardiac Enzyme Parameters: Summary – Safety Population
Table 14.3.6	Urinalysis Parameters: Summary – Safety Population
Table 14.3.7	Vital Signs Parameters: Summary – Safety Population
Table 14.3.8	Spirometry Parameters: Summary – Safety Population
Table 14.3.9	12-Lead Electrocardiogram Parameters: Summary – Safety Population

Listing 16.2.1.1
Participant Disposition

Treatment Group	Participant Number / Randomisation Number	Date/Time of Informed Consent: V2 / V3 / V5.1 / V8 / Genetic testing V1 / Genetic testing V2	Date/Time of: Quarantine Admission / Randomisation / Challenge Agent Administration / First IMP Administration / Quarantine Discharge	Eligible for randomisation? [1] / Completed IMP? / Completed Study? [2]	Reason not randomized / Reason for discontinuation of IMP / Reason for withdrawal
xxxxxxx	xxxxxx / xxxxxx	ddmmmyyyy hh:mm / NA / ddmmmyyyy hh:mm / ddmmmyyyy hh:mm / NA / ddmmmyyyy hh:mm	ddmmmyyyy hh:mm / ddmmmyyyy hh:mm / ddmmmyyyy hh:mm / ddmmmyyyy hh:mm / ddmmmyyyy hh:mm	Yes or No / Yes or No / Yes or No	xxxxxxxxxxxxxxxxx / xxxxxxxxxxxxxxxxx / xxxxxxxxxxxxxxxxx

NA = Not applicable.
[1] Eligible for randomisation based on criteria at Admission (Day -2/-1).
[2] Completed Study = Participating in the study up to and including Day 28 (Follow-up).

Listing 16.2.1.2
Failed Inclusion and Exclusion Criteria

Treatment Group	Participant	Reason for Exclusion
xxxxxxx	xxxxxx	xxxxxxxxxxxxxxxxxxx

Programming note: Listing not required if no participants fail the criteria.

Listing 16.2.74
Protocol Deviations

Treatment Group	Participant	Deviations Reported	Date Occurred (Study Day)	Deviation Category [a]	Other, Specify	Deviation Description	Serious Breach?
xxxxxxx	xxxxxx	Yes/No	ddmmmyyyy (xx)	n	xxxx	xxxxxxxxxx	Yes / No

[a] – Deviation categories: Informed Consent procedure [1] / Subject error [2] / Inclusion/exclusion criteria [3] / Investigational product [4] / Visit window [5] / Concomitant medication/therapy [6] / Study procedure/assessment window [7] / SAE reporting [8] / Study procedure/assessment performance [9] / Randomisation [10] / Missing assessment/sample [11] / Other [12]

Listing 16.2.75
Participant Populations

Treatment Group	Participant	ITT Population [1]	ITT-I Population [2]	ITT-A Population [3]	ITT-B Population [4]	PP Population [5]	Safety Population [6]	PK Population [7]
xxxxxxx	xxxxxx	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No	Yes / No

[1] Intent to Treat (ITT) Population = All randomised participants receiving challenge virus and at least one dose IMP
[2] Intent to Treat Infected (ITT-I) Population = All randomised participants receiving challenge virus and at least 1 dose of IMP, and meeting the criterion for laboratory confirmed RSV infection. A laboratory-confirmed RSV infection is defined as the presence of viral shedding, measured in nasal wash where one or both of the following definitions must be met: At least 2 positive detections by viral load qRT-PCR assay specific for the challenge virus, reported on 2 or more consecutive days; One positive detection by viral load qRT-PCR assay, specific for the challenge virus, in which an aliquot of the same sample has also tested positive in a cell-based assay appropriate for detecting the challenge virus.
[3] Intent to Treat Infected Pre-dose (ITT-A) Population = All randomised participants receiving challenge virus and at least 1 dose of IMP, and meeting the criterion for laboratory confirmed RSV infection, using only assessments prior to taking IMP.
[4] Intent to Treat Infected Post-dose (ITT-B) Population = All randomised participants receiving challenge virus and at least 1 dose of IMP, and meeting the criterion for laboratory confirmed RSV infection, using only assessments after IMP.
[5] Per Protocol (PP) Population = All ITT-I population participants who have no major protocol deviations, and who complete the quarantine period up to the final day of quarantine (Study Day 12) and receive all 10 doses of IMP.
[6] Safety Population = All randomised participants receiving challenge virus and at least one dose of IMP.
[7] The PK Population = All ITT participants with at least one post-dose PK result.

Listing 16.2.4.76
Demographics

Treatment Group	Participant	Age at Time of screening (years)	Sex	Race / Ethnicity	Visit	Date / Time	Height (cm)	Weight (kg)	BMI (kg/m^2)	Comments
xxxxxxx	xxxxxx	xx	Male / Female	xxxxxx / xxxxxx	Screening	ddmmmyyyy / hh:mm	xxx	xx.xx	xx	xxxxxxx

NA = Not Applicable.
Note: Results for height, weight and BMI are shown for all visits at which they were recorded.

Programming note: For height, weight, and BMI if recording is repeated, then all sets of results should be shown.

Listing 16.2.4.77
Reproductive Status and Contraceptive Use

Treatment Group	Participant	Sex	Breast Feeding/ Pregnant Recently / Planning Pregnancy	Child-bearing potential?	Agree to not donate sperm	(Hetero) Sexually active?	Agree to contraception	Contraception methods [1]
xxxxxxx	xxxxxx	Male	NA	NA	Yes / No	Yes / No	Yes / No	1
xxxxxxx	xxxxxx	Female	Yes / No	Yes / No; menopausal / No; incapable	NA	Yes / No	Yes / No	3

[1] 1 Male sterilisation where vasectomised male is the sole partner for that woman.
2 Oral, injected or implanted hormonal methods of contraception (minimum 2 weeks prior to admission).
3 An intrauterine device (IUD) or intrauterine hormone-releasing system (IUS) or bilateral tubal ligation.
4 Male condom with spermicide and female partner using a highly effective method of contraception (e.g. IUD, IUS, bilateral ligation).
5 Other method.

Listing 16.2.4.78
Smoking History

Treatment Group	Participant	Smoking History	Start Date	Stop Date	Date Last Smoked	Category	Amount	Years	Comments
xxxxxxx	xxxxxx	xxxxxxxxxxx	ddmmyyyy	ddmmyyyy	ddmmyyyy	Number of cigarettes smoked per day	xx	xx	xxxxxxxxxxx
						Number of cigars smoked per day	xx	xx	xxxxxxxxxxx
						Tobacco smoked per week (grams)	xx	xx	xxxxxxxxxxx
						Pack years	xx	xx	xxxxxxxxxxx

* Date estimated.
Note: Comments are collected for the combined smoking, alcohol and drugs of abuse module and hence may relate to any of these parameters.

Listing 16.2.4.79
Alcohol Use

Treatment Group	Participant	Alcohol Use History	Weekly alcohol intake (units)	Willing to refrain from alcohol intake	Comments
xxxxxxx	xxxxxx	Never / Current User / Previous User	xx	Yes / No	xxxxxxxxxxx

Note: Comments are collected for the combined smoking, alcohol and drugs of abuse module and hence may relate to any of these parameters.

Listing 16.2.4.80
Recreational Drugs of Misuse

Treatment Group	Participant	Current or recent user of recreational drugs?	Start Date	Stop Date	Recreational drug(s) used	Volume	Route	Comments
xxxxxxx	xxxxxx	Yes / No	ddmmmyyyy*	ddmmmyyyy / hh:mm	XXXX	XXXX	XXXX	XXXX

NA = Not Applicable. * = Date estimated.

Listing 16.2.4.81
Medical History

Treatment Group	Participant	MedDRA SOC / Preferred Term [1] / Medical Condition	Start Date / End Date	Line No.	Frequency	Ongoing	Concomitant medication taken for this condition?
xxxxxxx	xxxxxx	Xxxxxxxxx Xxxxxxxxx Xxxxxxxxxx	ddmmmyyyy / ddmmmyyyy	xxxx	Single Episode / Intermittent / Continuous / Other	Yes / No	Yes / No

* Date estimated.
[1] MedDRA Version 25.0. The modified term is the term that was used for MedDRA coding of the event when the event required multiple codes.

Listing 16.2.4.82
Prior and Concomitant Medications

Treatment Group	Participant	Drug Class (L2)/ WHO Drug Name/ Medication (verbatim)[1]	Start Date / Time	Stop Date / Time	Ongoing	Indication / AE/ Medical History Line	Dose / Dose units	Frequency [2]	Route [3]	PI / P / C [4]
xxxxxxx	xxxxxx	Xxxxxxxxx Xxxxxxxxx Xxxxxxxxxx	ddmmmyyyy / hh:mm	ddmmmyyyy / hh:mm	Yes / No	Xxxxxxxxx / Xxxxxxxxx / Xxxxxxxxx	XX xx	XXX	XXX	PI

* = Date/time estimated.
[1] WHO Drug Global Version 2022:1, March 1, 2022.
[2] QD = Once a day, BD = Twice a day, PRN = As needed, TDS = Three times a day, QDS = Four times a day.
[3] PO = oral, TOP = topical, PRN = Take as needed.
[4] PI = Prior to Inoculation, P = Prior to IMP treatment and after inoculation, C = Concomitant with IMP treatment.
Note: If the medication stop date is before the date of inoculation the medication will be assigned as prior to inoculation. If the medication stop date is before the date of IMP treatment but after the date of inoculation, the medication will be assigned as being prior to IMP treatment. In all other cases, the medication is assigned as concomitant with IMP treatment.

Listing 16.2.5.83
Challenge Virus Inoculation Administration

Treatment Group	Participant	Administration Date / Time	Administered intranasally?	Administered to both nostrils?	Administered successfully?	Change in health in 30 minutes post administration?	Comments
xxxxxxx	xxxxxx	ddmmmyyyy / hh:mm	Yes / No	Yes / No	Yes / No	Yes / No	XXXXXXX

Listing 16.2.5.84
Viral Shedding Results

Treatment Group	Participant	Study day and nasal wash time-point	qicPCR result	Comments
xxxxxxx	xxxxxx	Day X AM/PM	Positive/Negative/Invalid/NA	XXXXXXXX
		Day X AM/PM	Positive/Negative/Invalid/NA	XXXXXXXX
		…		
		Subject to be dosed Day 5 PM	NA	XXXXXXXX

Listing 16.2.5.3
IMP Administration

Treatment Group	Participant	Dose Number	Administered?	Administration Date / Time	Was dose fully administered?	Comments
xxxxxxx	xxxxxx	XX	Yes / No	ddmmmyyyy / hh:mm	Yes / No	XXXXXXXX

Listing 16.2.6.1.1
Viral Load by Nasal Samples qRT-PCR Results

Treatment Group	Participant	Sample Collection Date / Time (Study Day)	Assessment	Virus Titre (Log10 Copies/mL)	Did Participant Bleed?	Comments
xxxxxxx	xxxxxx	ddmmyyyy / hh:mm (xx)	1 / 2	Xxxxx	Yes / No	xxxxxxxxxxx

Programming Note: The Limit of Detection and Lower limit of Quantification will be shown in the footnote.

Listing 16.2.6.1.2
Viral Load by Nasal Samples qRT-PCR Derivations

Treatment Group	Participant	AUC IMP administration to planned discharge (hours*Log10 Copies/mL)	AUC IMP administration for 6.5 days (hours*Log10 Copies/mL)	AUC Day 2 to Day 12 (hours*Log10 Copies/mL)	AUC IMP administration to planned discharge (hours*Copies/mL)	Peak Viral Load (from IMP administration to Day 12) (Log10 Copies/mL)	Time from IMP administration to negative test after Peak measure (days)	Time from Peak measure after IMP administration to negative test after peak measure (days)	Time to Peak Measure (days)
xxxxxxx	xxxxxx	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX	XX	XX

* = Censored value.
Note: For the calculation of AUCs, values that are 'Not Detected', 'Detected' or are at or below the limit of quantification have been re-assigned to 0.

Listing 16.2.6.2.1
Viral Load by Nasal Samples Viral Culture Results

Treatment Group	Participant	Sample Type	Sample Collection Date / Time (Study Day)	Assessment	Virus Titre (Log10 Copies/mL)	Comments
xxxxxxx	xxxxxx	Xxxxxxxxxx	ddmmyyyy / hh:mm (xx)	1 / 2	xxxx	xxxxxxxxxxxxxxxxxx

Programming Note: The Limit of Detection and Lower limit of Quantification will be shown in the footnote.

Listing 16.2.6.2.2
Viral Load by Nasal Samples Viral Culture Derivations

Treatment Group	Participant	AUC IMP administration to planned discharge (hours*Log10 Copies/mL)	AUC IMP administration for 6.5 days (hours*Log10 Copies/mL)	AUC Day 2 to Day 12 (hours*Log10 Copies/mL)	AUC IMP administration to planned discharge (hours*Copies/mL)	Peak Viral Load (from IMP administration to Day 12) (Log10 Copies/mL)	Time from IMP administration to negative test after Peak measure (days)	Time from Peak measure after IMP administration to negative test after peak measure (days)	Time to Peak Measure (days)
xxxxxxx	xxxxxx	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX	XX	XX

* = Censored value.
Note: For the calculation of AUCs, values that are 'Not Detected', 'Detected' or are at or below the limit of quantification have been re-assigned to 0.

Listing 16.2.6.3.1
Symptom Scores from Symptom Diary Card

Treatment Group	Participant	Diary Card Completion Date / Time (Study Day)	Days from IMP Administration	Assessment	LRT Grades [1]	URT Grades [2]	S Grades [3]	10-item Symptom Score [4]		13-item Symptom Score	
								Total	CFB	Total	CFB
xxxxxxx	xxxxxx	ddmmyyyy / hh:mm (xx)	XX	1 / 2 / 3	X/X/X/X	X/X/X/X/X	X/X/X/X	xx	xx	xx	xx

LRT = Lower respiratory tract. URT = Upper respiratory tract. S = Systemic. CFB = Change from Baseline.
[1] Cough/Shortness of Breath/Chest Tightness/Wheeze
[2] Runny Nose/Stuffy Nose/Sneezing/Sore Throat/Earache
[3] Headache/Malaise/Muscle Joint, Ache/Chilliness, Feverishness
[4] Includes Cough/Shortness of Breath/Runny Nose/Stuffy Nose/Sneezing/Sore Throat/Earache Headache/Malaise/Muscle Joint, Ache.
Note: A total symptom score requires at least one symptom to be scored.

Listing 16.2.6.3.2
Visual Analogue Scale from Symptom Diary Card

Treatment Group	Participant	Diary Card Completion Date / Time (Study Day)	Days from IMP Administration	Assessment	LRT Grades (mm) [1]	URT Grades (mm) [2]	S Grades (mm) [3]
xxxxxxx	xxxxxx	ddmmyyyy / hh:mm (xx)	XX	1 / 2 / 3	XX/XX/XX /XX	XX/XX/XX /XX/XX	XX/XX/XX/ XX

LRT = Lower respiratory tract. URT = Upper respiratory tract. S = Systemic.
[1] Cough/Shortness of Breath/Chest Tightness/Wheeze
[2] Runny Nose/Stuffy Nose/Sneezing/Sore Throat/Earache
[3] Headache/Malaise/Muscle Joint, Ache/Chilliness, Feverishness

Listing 16.2.6.3.3
Total Symptom Score: AUC Derivations

		Total Symptom Score AUC [1]			Total Symptom Score Change from Baseline AUC			Total Symptom Score AUC [2]		
Treatment Group	Participant	IMP administration to planned discharge	IMP administration for 6.5 days	Day 2 to Day 12	IMP administration to planned discharge	IMP administration for 6.5 days	Day 2 to Day 12	IMP administration to planned discharge	IMP administration for 6.5 days	Day 2 to Day 12
xxxxxxx	xxxxxx	XX	XX	XX	XX	XX	XX	XX	XX	XX

[1] Derivations made using 10-items of the 13-item symptom diary card.
[2] Derivations made using all 13-items of the symptom diary card.

Listing 16.2.6.3.4
Total Symptom Score: Other Derivations

Treatment Group	Participant	Days from IMP Administration	Sum Total Symptom Score (from IMP administration to planned discharge)	Peak Total Symptom Score (from IMP administration to planned discharge)	Peak Daily Total Symptom Score (from IMP administration to planned discharge)	Time to Symptom Resolution from IMP administration (days)	Time to Symptom Resolution from Peak Symptom after IMP administration (days)	Time to Peak Total Symptom Score from IMP administration (days)
xxxxxxx	xxxxxx	XX	XX	XX	XX	XX	XX	XX

Note: Derivations made for 10-items of the 13-item diary card.

Programming Note: Place the endpoints that are not by study day onto the first row for each participant.

Listing 16.2.6.4.1
Mucus Weight and Tissue Bag Distribution

Treatment Group	Participant	Study Day	Date Collected	Tissue Bag Distribution Time Collected/Dispensed	Tissues Taken	Total Tissues Taken	Mucus Weight (g)	Total Mucus Weight (g)	Comments
xxxxxxx	xxxxxx	xx	ddmmyyyy	hh:mm	xxxx	xxxx	xxxx	xxxx	

Programming note: The Total Mucus Weight and Total Tissues Taken will be listed against the Day 12 observation.

Listing 16.2.6.5.1
Nasopharyngeal Swab: Respiratory Virus Screen/Rapid Viral Antigen Test

Treatment Group	Participant	Sample Collection Date / Time (Study Day)	Result	Comments
xxxxxxx	xxxxxx	ddmmyyyy / hh:mm (xx)	Positive / Negative	xxxxxxxx

Listing 16.2.6.6
Plasma PK Parameters

Treatment Group	Participant	Day	PK Parameter	Units	RV299	Comments
xxxxxxx	xxxxxx	XXX	XXX	XXX	XXX	xxxxxxxx

Listing 16.2.7
Adverse Events

Treatment Group / Participant /AE Number	MedDRA SOC / Preferred Term [1] / Adverse event (verbatim)	Start Date Time (study day) / Stop Date Time (Study day)	TE [2] / CE [3] / Severity / Frequency [4]	SAE / Serious Criteria [5]	Outcome [6] / Action Taken IMP [7] / Action Taken [8] /	Related to [9] IMP / Challenge Agent / Concomitant medication / Procedure / Other	Comments
xxxxxxx / xxxx / xx	xxxxxxxxx/ xxxxxx/ xxxxxx	ddmmmyyyy hh:mm (xx) / ddmmmyyyy hh:mm (xx)	Yes or No / Yes or No / Mild, Moderate, Severe, Life-Threatening / xx	Yes or Blank / xx	x / x / x	x / x / x / x / x	xxxxxxxxxx xxxxxxxxxx

TE = Treatment Emergent. SAE – Serious Adverse Event.
[1] MedDRA Version 24.0.
[2] An AE occurring on or after the first administration of IMP.
[3] An AE occurring on or after the challenge agent inoculation.
[4] Freq = Frequency. For frequency categories, C = Continuous, I = Intermittent, S = Single Episode.
[5] Serious Criteria: 1 = Death; 2 = Life-threatening; 3 = Hospitalization; 4 = Persistent or significant disability/incapacity; 5 = Congenital anomaly/birth defect; 6 = Other.
[6] Outcome: 1 = Resolved; 2 = Resolved with Sequelae; 3 = Ongoing; 4 = Fatal; 5 = Unknown.
[7] Action Taken IMP: 1 = IMP dosage not changed; 2 = IMP dosage adjusted; 3 = IMP administration temporarily interrupted; 4 = IMP administration discontinued.
[8] Action Taken: 1 = None; 2 = Non-drug therapy given; 3 = Concomitant medication taken; 4 = Participant withdrawn; 5 = Participant hospitalized; 6 = Other; 7 = Not applicable.
[9] Related: 1 = Not Related; 2 = Unlikely Related; 3 = Possibly Related; 4 = Probably Related; 5 = Definitely Related.

Listing 16.2.8.98
Blood Sample Collection

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Sample Type(s) [1]	Clinically Significant Result?	Adverse Event associated with Procedure?	Comments
xxxxxxx	xxxxxx		ddmmyyyy / hh:mm (xx)	x x x x x x	Yes / No	Yes / No	xxxxxxxxxxxxxx

* see Time and Events Schedule.
[1] 1 = Biochemistry, 2 = Cardiac enzymes, 3 = Haematology, 4 = Coagulation, 5 = Thyroid function test,
6 = Hepatitis B, & C, HIV serology, 7 = Serum pregnancy test, 8 = Serum follicle-stimulating hormone, 9 = Serum markers humoral immunity, 10 = Paxgene.

Listing 16.2.8.99
Haematology

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Parameter	Result	Change from Baseline	Units	Lower Limit	Upper Limit	Flag	Comments
			ddmmyyyy hh:mm								
xxxxxxx	xxxxxx	xxxx	(xx)	Basophils (%)	x.xx	x.xx	%	x.xx	x.xx	L / H	xxxxxxxxxxxxxxxxxxx
				Basophils (abs)	x.xx	x.xx	X10^9/L	x.xx	x.xx		
				Eosinophils (%)	x.xx	x.xx	%	x.xx	x.xx		
				Eosinophils (abs)	x.xx	x.xx	X10^9/L	x.xx	x.xx		
				Haematocrit	x.xx	x.xx	%	xx	xx		
				Haemoglobin	xxx	xxx	g/L	xxx	xxx		
				Lymphocytes (%)	x.xx	x.xx	%	x.xx	x.xx		
				Lymphocytes (abs)	x.xx	x.xx	X10^9/L	x.xx	x.xx		
				MCH	x.xx	x.xx	pg	xx.x	xx.x		
				MCHC	xxx	xxx	g/L	xxx	xxx		
				MCV	x.xx	x.xx	fL	xx.x	xx.x		
				Monocytes (%)	x.xx	x.xx	%	xx.x	xx.x		
				Monocytes (abs)	x.xx	x.xx	X10^9/L	xx.x	xx.x		
				Neutrophils (%)	x.xx	x.xx	%	xx.x	xx.x		
				Neutrophils (abs)	x.xx	x.xx	X10^9/L	xx.x	xx.x		
				Platelets	xxx	xxx	X10^9/L	xx.x	xx.x		
				RBC Count	x.xx	x.xx	X10^12/L	x.xx	x.xx		
				Reticulocytes (%)	x.xx	x.xx	%	x.xx	x.xx		
				Reticulocytes (abs)	xx.x	xx.x	X10^9/L	xx.x	xxx.x		
				WBC Count	x.xx	x.xx	X10^9/L	x.x	xx.x		

L = below lower limit, H = above upper limit.

This layout will be utilised for the following listings:
Listing 16.2.8.3 Coagulation
Listing 16.2.8.4 Biochemistry
Listing 16.2.8.5 Cardiac Enzymes
Listing 16.2.8.6 Thyroid Function Tests

Listing 16.2.8.100
Other Laboratory Tests: TDL

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Test	Result
xxxxxxx	xxxxxx	xxxx	ddmmmyyyy / hh:mm (xx)	HIV 1 and HIV 2 antibodies	Positive / Negative
				Hepatitis A	Positive / Negative
				Hepatitis B	Positive / Negative
				Hepatitis C	Positive / Negative
				FSH	xx.x
				Beta HCG (IU/L)	Positive / Negative
				Immunoglobulin A antibodies	xx.x
				HbA1C (%)	xx.x
				HbA1C (mmol/mol)	xx.x

L = Low, H = High, ND = Not Done.
Programming Note: Normal Ranges to be displayed in footnote, if available.

Listing 16.2.8.101
Other Laboratory Tests: Urine Pregnancy

Treatment Group	Participant	Visit	Test Date / Time (Study Day)	Participant has data	Result	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	Yes / No / NA - Male	Positive / Negative	xxxxxxxxxxxxxxxxx

Listing 16.2.8.9.2
Other Laboratory Tests: Drugs of Abuse Screen

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Test Performed Time	Drug	Result	Comments
xxxxxxx	xxxxxx	xxxx	ddmmmyyyy hh:mm (xx)	hh:mm	Cocaine	Positive / Negative / Not done	
					Cannabinoids	Positive / Negative / Not done	
					Methadone	Positive / Negative / Not done	
					Ecstasy	Positive / Negative / Not done	
					Opiates	Positive / Negative / Not done	
					Benzodiazepines	Positive / Negative / Not done	
					Barbituates	Positive / Negative / Not done	
					Amphetamine	Positive / Negative / Not done	
					Methamphetamine	Positive / Negative / Not done	
					Tricyclic	Positive / Negative / Not done	

Listing 16.2.8.9.
Other Laboratory Tests: Urine Cotinine

Treatment Group	Participant	Visit	Test Performed Date / Time (Study Day)	Result	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	Positive / Negative	xxxxxxxxxxxxxxxx

Listing 16.2.8.9.
Other Laboratory Tests: Alcohol Breath Test

Treatment Group	Participant	Visit	Test Date / Time (Study Day)	Result	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	Positive / Negative	xxxxxxxxxxxxxxxx

Listing 16.2.9.
Urinalysis

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Test Performed Time	Parameter	Result [1]
			ddmmyyyy / hh:mm			
xxxxxxx	xxxxxx	xxxx	(xx)	hh:mm	Appearance	
					Bilirubin	
					Blood – Dip	
					Blood – Haemolysed / Non-Haemolysed	
					Colour	
					Glucose	
					Ketones	
					Leukocytes	
					Nitrite	
					Protein	
					Specific Gravity	
					Urobilinogen	
					pH	
					Interpretation	
					Sent for Microscopy	
					Comments	

[1] NCS = Not clinically significant, CS = Clinically significant.

Programming note: The physician interpretation and microscopy (Yes/No) will be shown as an additional row at the end of each assessment, with the interpretation/microscopy outcome shown in the result column.
Programming note: for Blood parameter there is a Haemolysed/Non-Haemolysed as well as a result.

Listing 16.2.9.
Urinalysis (TDL): Microscopy

Treatment Group	Participant	Visit	Sample Collection Date / Time (Study Day)	Urine RBC	Urine WBC	Cellular casts	Granular casts	Hyaline casts	Urine culture
xxxxxxx	xxxxxx	xxxx	ddmmyyyy / hh:mm (xx)	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxx	xxxxxxxxx

ND = Not Done, A = Abnormal

Listing 16.2.10
Vital Signs

Treatment Group	Participant	Visit	Date	Assessment	Time Started Supine	Collection Time	Parameter	Result [1]	Change from Baseline	Units	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy	1 / 2 / 3	hh:mm	hh:mm	Systolic BP	xxx	xxx	mmHg	
							Diastolic BP	xx	xx	mmHG	
							Heart Rate	xx	xx	bpm	
							Rep. Rate	xx	xx	breaths/min	
							SpO2	xx	xx	%	
							Tympanic temperature	xx.x	xx.x	deg C	
							Interpretation	xxxxxxxx			xxxxxxx

[1] NCS = Not clinically significant, CS = Clinically significant.* = tympanic temperature >= 37.9 deg C.

Programming note: The physician interpretation will be shown as an additional row at the end of each assessment, with the interpretation outcome shown in the result column. Add * to any temperature result >=37.9 deg C.

Listing 16.2.11
Spirometry

Treatment Group	Participant	Visit	Date / Time (Study Day)	Parameter	Result [1]	Units
xxxxxxx	xxxxxx	xxxx	Ddmmyyyy hh;mm (XX)	FEV1 (abs)	x.xx	L
				FEV1 (% Pred)	xx	%
				FEV1/FVC Ratio (abs)	xx	
				FEV1/FVC Ratio (% Pred)	xx	%
				FVC (abs)	x.xx	L
				FVC (% Pred)	xx	%
				FEV1 decreased by > 15% from baseline	Yes / No	
				FEV1 or FVC < 80% of the predicted value?	Yes / No	

Listing 16.2.12.1
Physical Examination

Treatment Group	Participant	Visit	Date / Time (Study Day)	Parameter	Finding	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy hh:mm (Study Day)	General Appearance Eyes Ears Nose Throat Head and Neck Cranial Nerves/Nervous System Musculoskeletal Skin Cardiovascular Abdomen/GI System Respiratory System Chest – Auscultation Chest – Vocal Resonance Chest – Percussion Other Findings	Normal / Abnormal Not Clinically Significant / Abnormal Clinically Significant / Not Done	

Listing 16.2.12.2
Rhinoscopic Examination

Treatment Group	Participant	Visit	Date / Time (Study Day)	Assessment	Level [1]	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy hh:mm (Study Day)	Nasal Discharge - Left Nasal Discharge – Right Otitis – Left Otitis – Right Pharyngitis Sinus Tenderness – Left Sinus Tenderness – Right New Wheezes, Rhonchi – Left New Wheezes, Rhonchi – Right		

[1] Nasal Discharge: 0 = None, 1 = Clear, serous; scant but slightly increased, 2 = Clear to white, obvious increased volume, + / - minor blood streaks on tissue, 3 = Frankly prudent (yellow or green), or gross blood.
Otitis: NA = Tympanic membrane not visible, 0 = None, 1 = Dulled tympanic membrane, 2 = Inflamed, injected tympanic membrane, 3 = Retracted or bulging tympanic membrane, obvious air, fluid level.
Pharyngitis: 0 = None, 1 = Mild and / or patchy erythema, 2 = Marked and / or confluent erythema, 3 = Erythema and purulent exudate.
Sinus Tenderness: 0 = None, 1 = Mild tenderness, 2 = Moderate tenderness, 3 = Severe tenderness or overlying erythema.
New Wheezes, Rhonchi: 0 = None, 1 = Mild wheezes or rhonchi, 2 = Scattered wheezes or rhonchi, 3 = Widespread wheezes.

Listing 16.2.111
ECG

Treatment Group	Participant	Visit	Date	Time Started in Resting Position	Time Performed	Parameter	Result [1]	Units	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy	hh:mm	hh:mm	HR	xxx	bpm	xxxxxx
						PR	xxx	ms	
						QRS	xxx	ms	
						QT	xxx	ms	
						QTc	xxx	ms	
						QTcB	xxx	ms	
						QTcF	xxx	ms	
						RR	xxx	ms	
						Interpretation	Normal / Abnormal NCS / Abnormal CS		

[1] NCS = Not clinically significant, CS = Clinically significant.

Programming note: The physician interpretation will be shown as an additional row at the end of each assessment, with the interpretation outcome shown in the result column.

Listing 16.2.14
Visit Dates

Treatment Group	Participant	Visit	Date	Source of Unscheduled Visit Comments	Comments
xxxxxxx	xxxxxx	xxxx	ddmmyyyy	xxxxxxxxxx	xxxxxxxxxxxx

Programming note: Unscheduled visits and visit information will be taken from specific database modules and the "Reason for additional collection" will be placed in the comments column in this listing.

15. APPENDICES

15.1. Study VIR-CST-001 assay cut-offs and reporting

Analysis	Assay	Associated units	Assay Reporting		
			Result	Reported result	S-cubed assigned value
RSV titre (Viral Load)	RSV Viral Culture assay (plaque assay)	Log_{10} PFU/mL	ALOQ	ALOQ	6.34
			Quantifiable Titre	Value	Use reported value
			DETECTED	DETECTED	1.00
			NOT DETECTED	NOT DETECTED	0
			INVALID	INVALID	Missing data point
			NOT TESTED	N/A	Missing data point
RSV titre (Viral Load)	qRT-PCR (in saline matrix)	Log_{10} Copies/mL	Quantifiable Titre	Value	Use reported value
			DETECTED	DETECTED	1.69
			NOT DETECTED	NOT DETECTED	0
			INVALID	INVALID	Missing data point
			NOT TESTED	N/A	Missing data point
RSV antibody titre	RSV Neutralisation Assay (virus focus reduction neutralisation assay)	None	Quantifiable Titre	Value	Use reported value
			>4209	>4209	4209
			<156	<156	78
			NDA	NDA	10
			INVALID	INVALID	Missing data point
			NOT TESTED	N/A	Missing data point

N/A = not applicable; NDA = no detectable antibody.