Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP) Amendment

Title	:	Reporting and Analysis Plan for a randomized, double-blind, single ascending dose study to determine the safety and tolerability, pharmacokinetics and pharmacodynamics of GSK3772847 administered subcutaneously in healthy participants
Compound Number	:	GSK3772847
Clinical Study Identifier	:	209635
Effective Date	:	Refer to Document Date

Description:

The purpose of this RAP is to describe the planned analyses and output to be included in the Clinical Study Report for Protocol 209635 (Document Number 2020N427367_02).

This RAP is intended to describe the safety, tolerability, pharmacokinetics and pharmacodynamics analyses required for the study.

This RAP will be provided to the study team members to convey the content of Statistical Analysis Complete (SAC) deliverables.

This version of the RAP includes amendments to the originally approved RAP.

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1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol Revision Chronology		
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Amendment 1 includes a COVID-19 measures appendix, increased outpatient visit windows and defines a sample collection window for free sST2 and total sST2 blood samples.

Amendment 2 reduces the age range from 18 – 65 to 18 – 50 to ensure older populations, potentially more at risk of COVID-19 are not recruited into the study and to update secondary pharmacodynamics endpoint to specify nominal day as maximum timepoint.

1.1. RAP Amendments

- To drop interim analysis due to the termination of aIL33r clinical development
- To remove some of the data displays due to the termination of aIL33r clinical development
- To add Covid-19 related data displays
- To remove 'Randomised Population' from Section 4. Analysis Population because this population is not used in any data display.

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

Changes from the originally planned statistical analysis specified in the protocol are outlined in Table 1.

Table 1 Changes to Protocol Defined Analysis Plan

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
The PKPD population	The PKPD population has been defined as two separate populations (A PK and PD population)	Having two separate populations will make things clearer. For example if a subject has a PK sample taken, but no PD sample and vice versa.
Section 9.4.3 Maximal decrease from baseline in free sST2 and maximal increase from baseline in total	The formal analysis has been removed but the endpoint will still be summarised.	Comparisons with placebo are not of interest

Protocol	Reporting & Analysis Plan	
Statistical Analysis Plan	**Statistical Analysis Plan**	**Rationale for Changes**
soluble sST2 levels in serum will be analysed.		The impact of injection site is of key interest (which will not be assessed in an ANCOVA analysis given the small numbers per cohort per injection site). The results for percent suppression from the summary tables will be reported in the CSR (and not from an analysis).

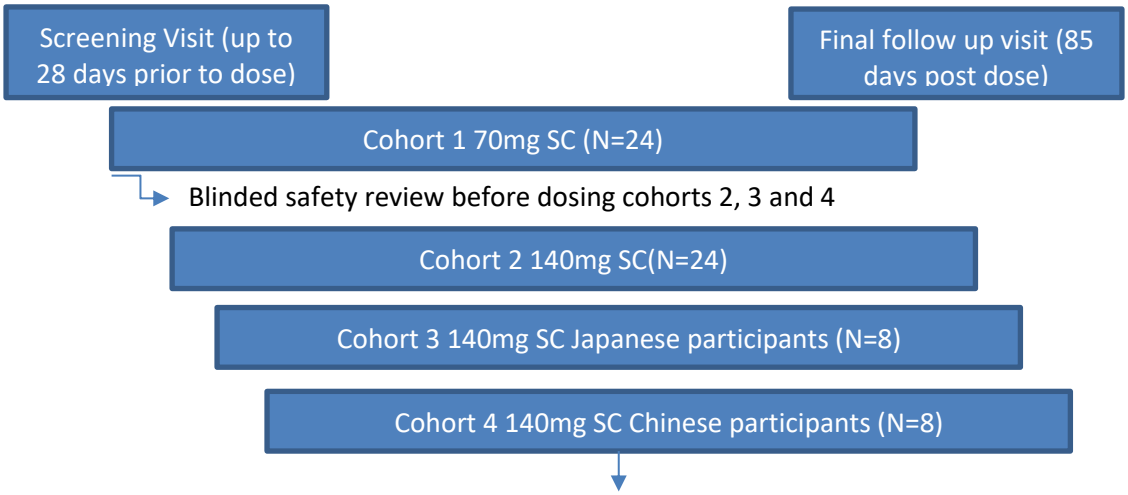
2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary	**Primary**
• To evaluate the safety and tolerability of a single dose of GSK3772847, compared with placebo administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants.	• Occurrence of adverse events (AEs) and serious adverse events (SAEs) (including injection site reactions)
• To assess the pharmacokinetics (PK) of a single dose of GSK3772847 administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants (Cohorts 1 and 2 also summarised by injection site)	• PK parameters, including but not limited to, Area under the plasma-concentration time curve (AUC), maximum plasma concentration (Cmax), time to Cmax (Tmax) and terminal half-life (t1/2) of GSK3772847 per cohort. (Cohorts 1 and 2 also summarised by injection site)
Secondary	**Secondary**
• To evaluate the pharmacodynamics (PD) of a single dose of GSK3772847 administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants.	• Maximal decrease from baseline in free soluble ST2 levels in serum up to a maximum of 85 days post dose • Maximal increase from baseline in total soluble ST2 levels in serum up to a maximum of 85 days post dose
• To assess the immunogenicity of a single dose of GSK3772847 administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants.	• Occurrence of anti-GSK3772847 antibodies
• To assess potential changes in Cytochrome P450 3A4 (CYP3A4) enzyme activity following a single dose of GSK3772847in healthy participants including cohorts of Japanese and Chinese participants.	• Plasma 4β-Hydroxycholesterol (4βOH) /cholesterol ratio as an endogenous marker for CYP3A4 activity pre-treatment and following a single dose of GSK3772847

Objectives	Endpoints
Other	**Other**
• To further assess the safety and tolerability of a single dose of GSK3772847, compared with placebo administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants.	• 12-lead electrocardiogram (ECG) measurements • Clinical chemistry laboratory tests • Vital signs
• To evaluate the pharmacodynamics (PD) of a single dose of GSK3772847 administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants.	• Free and total soluble ST2 levels in serum • Blood eosinophil levels
• To assess the pharmacokinetics (PK) of a single dose of GSK3772847 administered subcutaneously in healthy participants including cohorts of Japanese and Chinese participants	• GSK3772847 levels in serum

2.3. Study Design

Overview of Study Design and Key Features



Design Features	• This is a single centre, randomized, placebo-controlled, double-blind, ascending dose study in healthy participants.
Dosing	• Following a screening period (of up to 28 days), participants who meet the eligibility criteria will be assigned to one of four cohorts and will be randomly allocated within each cohort to receive a single dose of either GSK3772847 or placebo. All treatments will be administered subcutaneously by an HCP. The site of injection will be randomized to the upper arm, abdomen or thigh for cohorts 1 and 2 with cohorts 3 and 4 receiving injections in the upper arm only.
Time & Events	• Refer to 15.2 Appendix 2: Schedule of Activities
Treatment Assignment	• Cohort 1: Participants will be assigned to either 70mg SC of GSK3772847 or Placebo in a 3:1 ratio, participants will also be randomised to 1 of 3 injection sites (upper arm, thigh, or abdomen) in a 1:1:1 ratio. • Cohort 2: Participants will be assigned to either 140mg SC of GSK3772847 or Placebo in a 3:1 ratio, participants will also be randomised to 1 of 3 injection sites (upper arm, thigh, or abdomen) in a 1:1:1 ratio. • Cohort 3: Japanese participants will be assigned to either 140mg SC of GSK3772847 or Placebo in a 3:1 ratio. They will receive injections in the upper arm only. • Cohort 4: Chinese participants will be assigned to either 140mg SC of GSK3772847 or Placebo in a 3:1 ratio. They will receive injections in the upper arm only.

Cohort	Treatment Code	Treatment Description	Injection Site
1	A	70mg SC GSK3772847	Abdomen
1	B	70mg SC GSK3772847	Thigh
1	C	70mg SC GSK3772847	Upper Arm
2	D	140mg SC GSK3772847	Abdomen
2	E	140mg SC GSK3772847	Thigh
2,3 and 4	F	140mg SC GSK3772847	Upper Arm

Overview of Study Design and Key Features					
		1,2	G	Placebo SC	Abdomen
		1,2	H	Placebo SC	Thigh
		1,2,3 and 4	I	Placebo SC	Upper Arm

2.4. Statistical Hypotheses

The primary objective of this study is to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of GSK3772847 administered subcutaneously. There are no formal hypothesis tests associated with this objective and no formal significance tests. The information acquired from this study will be used to quantify the effects of GSK3772847 on safety and tolerability via the SC route where the main focus will be on injection site reactions and to assess the pharmacokinetics and pharmacodynamics across the 3 injection sites and doses. In addition, PK will be evaluated in Japanese and Chinese participants.

3. PLANNED ANALYSES

3.1. Instream Review and Interim Analyses

A dose escalation committee will review blinded summary safety data (including injection site data obtained up to 48 hours post-dose) of at least 20 participants from cohort 1.

The Dose Escalation charter will describe the procedures related to DEC operations in greater detail. The dose escalation committee (DEC), comprised of members from the GSK Study Team (namely safety and clinical) and the Investigator(s), will review blinded safety data (including injection site data obtained 48 hours post-dose) from at least 20 participants in cohort 1 before initiating dosing in cohorts 2, 3 and 4. Dose escalation may occur only after review of individual injection site data. The decision to proceed to dosing in cohorts 2, 3 and 4 will be made by the Dose Escalation Committee based on assessment of the injection site data at 70mg dose level. Data may be reviewed in an unblinded fashion by a subset of the DEC (namely safety and clinical) should a significant safety concern arise during the blinded review.

An interim analysis was originally planned to inform on the properties of GSK3772847 dosed via the subcutaneous route and allow the project to move forward to the next phase of development. Due to the termination of aIL33r clinical development, this interim analysis is no longer needed.

3.2. Final Analyses

The final planned primary analyses will be performed according to IQVIA's procedures after the completion of the following sequential steps:

1. All participants have completed the study as defined in Section 4.4 of the protocol: A participant is considered to have completed the study if he/she has completed all phases of the study including the final follow up visit.
2. All required database cleaning activities have been completed and final soft lock), and final database lock) have been declared by Data Management. IQVIA final database lock is defined as no changes can be made to the data and the end of the study milestone has been reached with all data clean, SDV'd, frozen and locked.
3. All criteria for unblinding the randomization codes have been met.
4. Randomization codes have been distributed according to IQVIA procedures using SAS v9.4.
5. Final SDTM sent to GSK (defined as GSK final DBF)

4. ANALYSIS POPULATIONS

The following populations (as defined below), will include participants who are randomized and replaced because they withdraw prior to D29:

Population	Definition / Criteria	Analyses Evaluated
Enrolled	All participants who sign the ICF	• Study Population
Pharmacokinetic	The PK population consists of all randomized subjects who received at least one dose of study treatment, and for whom at least one post-randomisation pharmacokinetic sample was obtained, analyzed and was measurable. Displays will be based on the treatment and injection site which the participant actually received.	• PK outputs
Pharmacodynamic	The PD population consists of all randomized subjects who received at least one dose of study treatment, and for whom at least one pharmacodynamic sample was obtained, analyzed and was measurable. Displays will be based on the treatment and injection site which the participant actually received.	• PD outputs
Safety	All randomized participants who take at least 1 dose of study intervention. Participants will be analyzed according to the treatment they actually received.	• Study Population • Safety

Refer to 15.11 Appendix 11: List of Data Displays which details the population used for each display.

4.1. Protocol Deviations

Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, participant management or participant assessment) will be summarised and listed.

Protocol deviations will be tracked by the study team and IQVIA throughout the conduct of the study in accordance with the Protocol Deviation Management Plan.

- Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
- This dataset will be the basis for the summaries and listings of protocol deviations.

A separate listing of all inclusion/exclusion criteria deviations will also be provided. This output will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

Treatment Group Descriptions					
Treatment Description in randomisation			Data Displays for Reporting		
Code	Description	Injection Site	Description	Injection Site	Order in TLF
A	70mg SC GSK3772847 / Abdomen	Abdomen	70mg SC GSK3772847	Abdomen	2
B	70mg SC GSK3772847/ Thigh	Thigh	70mg SC GSK3772847	Thigh	3
C	70mg SC GSK3772847 / Upper Arm	Upper Arm	70mg SC GSK3772847	Upper Arm	4
D	140mg SC GSK3772847 / Abdomen	Abdomen	140mg SC GSK3772847	Abdomen	6
E	140mg SC GSK3772847 / Thigh	Thigh	140mg SC GSK3772847	Thigh	7
F	140mg SC GSK3772847 / Upper Arm	Upper Arm	140mg SC GSK3772847	Upper Arm	8
G[2]	Placebo SC / Abdomen	Abdomen	Placebo SC	Abdomen	NA
H[2]	Placebo SC / Thigh	Thigh	Placebo SC	Thigh	NA
I[2]	Placebo SC / Upper Arm	Upper Arm	Placebo SC	Upper Arm	NA
J[1]	70mg SC GSK3772847	Overall (Cohort 1)	70mg SC GSK3772847 Overall	Combined (Cohort 1)	5
K[1]	140mg SC GSK3772847	Overall (Cohort 2)	140mg SC GSK3772847 Overall	Combined (Cohort 2)	9
L	140mg SC GSK3772847/ Upper Arm	Upper Arm	Japanese 140mg SC GSK3772847	Upper Arm	11
M	140mg SC GSK3772847/ Upper Arm	Upper Arm	Chinese140mg SC GSK3772847	Upper Arm	12
N[1]	Placebo SC	Overall (Cohorts 1 and 2)	Placebo SC	Combined(Cohorts 1 &2)	1

Treatment Group Descriptions					
Treatment Description in randomisation			Data Displays for Reporting		
Code	Description	Injection Site	Description	Injection Site	Order in TLF
O[1]	Placebo SC	Overall (Cohorts 3 and 4)	Placebo SC	Combined(Cohorts 3&4)	10

[1]J, K, N and O will not be received in the randomisation file, and will be derived within the AdAM datasets.
[2]G, H are for cohorts 1 and 2 only and I is for cohorts 1,2, 3 and 4.
For summary tables, Cohorts 1 and 2 will be summarised overall (i.e. by treatment and across all injection sites), in addition to per injection site. Placebo data will be pooled across injection site for cohorts 1 and 2 and similarly across Japanese and Chinese participants for cohorts 3 and 4.

5.2. Baseline Definitions

For all endpoints (except as noted in baseline definitions) the baseline value will be the latest pre-dose assessment with a non-missing value, including those from unscheduled visits. If time is not collected, Day 1 assessments are assumed to be taken prior to first dose and used as baseline.

Parameter	Study Assessments Considered as Baseline			Baseline Used in Data Display
	Screening	Day 0	Day 1 (Pre-Dose)	
Safety				
Vital Signs	X	X	X	Day 1 (Pre-Dose)
12-lead Electrocardiogram (ECG) measurements	X		X	Day 1 (Pre-Dose)
Clinical laboratory tests (haematology and chemistry)	X		X	Day 1 (Pre-Dose)
Pharmacokinetic				
PK Blood samples			X	Day 1 (Pre-Dose)
Pharmacodynamic				
Free sST2 and total sST2 blood sample			X	Day 1 (Pre-Dose)
Biomarker				
Immunogenicity: Anti-GSK3772847 antibodies			X	Day 1 (Pre-Dose)
Plasma 4βOH cholesterol			X	Day 1 (Pre-Dose)

Unless otherwise stated, if baseline data is missing, the latest assessment pre-dose will be used.

5.3. Examination of Covariates, Other Strata and Subgroups

5.3.1. Strata

The list of strata may be used in descriptive summaries. Additional strata of clinical interest may also be considered.

Category	Details
Stratum	Injection site for all summary statistics.

5.4. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
15.3	Appendix 3: Assessment Windows
15.4	Appendix 4: Study Phases and Treatment Emergent Adverse Events
15.5	Appendix 5: Data Display Standards & Handling Conventions
15.6	Appendix 6: Derived and Transformed Data
15.7	Appendix 7: Reporting Standards for Missing Data
15.8	Appendix 8: Values of Potential Clinical Importance

6. STUDY POPULATION ANALYSES

The study population analyses will be based on the Safety population, unless otherwise specified. Study population analyses including analyses of participant's disposition, protocol deviations, demographic and baseline characteristics, prior and concomitant medications, and exposure and treatment compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 11: List of Data Displays.

7. EFFICACY ANALYSES

There are no efficacy analyses to be included in this study.

8. SAFETY ANALYSES

The safety analyses will be based on the Safety population, unless otherwise specified.

8.1. Adverse Events Analyses

The definition of an AE is detailed in Appendix 3 of the protocol.

Separate analyses of AEs will be conducted including those events that are captured during the on-treatment period as well as the post-treatment period defined in Section 15.4.

Adverse events analyses including the analysis of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 11: List of Data Displays.

8.2. Adverse Events of Special Interest Analyses

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event. Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team (SRT) agreements in place at the time of reporting. The updated GSK respiratory Adverse Events of Special Interest (AESIs) can be found in the following folder (aesi.sas7bdat):
\\uk1salx00175.corpnet2.com\arenv\arprod\respiratory\res_safety\aesi\refdata.

The details of the planned displays are provided in Appendix 11: List of Data Displays.

8.3. Clinical Laboratory Analyses

Laboratory evaluations including the analyses of Chemistry laboratory tests, Haematology laboratory tests (including blood eosinophil levels), Urinalysis, and Liver function tests will be based on GSK Core Data Standards. Clinical laboratory summaries will include all assessments post-baseline. The laboratory assessments for each category are displayed below (Table 4 in Section 10.2 of Appendix 2 of the protocol):

8.4. COVID-19 Displays

Due to the short duration and small size of the study, only listings will be produced for COVID-19 related data. The details of the planned COVID-19 displays are in Appendix 11: List of Data Displays.

Table 2 Protocol-Required Safety Laboratory Assessments

Laboratory Assessments	Parameters
Haematology	Platelet Count; ***RBC Indices***: RBC Count, Haemoglobin, Haematocrit; MCHC, MCV; ***WBC count with Differential (see footnote 3)***: WBC, Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils
Clinical Chemistry	BUN, Creatinine, Glucose; Potassium, Sodium, Calcium, Magnesium; AST (SGOT), ALT (SGPT), Alkaline phosphatase; Total and direct bilirubin, Total Protein, Albumin
Routine Urinalysis	• Specific gravity • pH, glucose, protein, blood and ketones by dipstick • Microscopic examination and UACR (if blood or protein is abnormal [evidence of microalbuminuria or haematuria of ≥ 1+])
Other tests	• hsCRP
Other Screening Tests	• HIV • Hepatitis B • Hepatitis C (Hep C antibody) • FSH and estradiol (as appropriate) • Alcohol, cotinine and drug screen (to include at minimum: amphetamines, barbiturates, cocaine, opiates, cannabinoids and benzodiazepines)

Abbreviations: ALT (SGPT) = alanine aminotransferase (serum glutamic pyruvic transaminase); AST (SGOT) = aspartate aminotransferase (serum glutamic oxaloacetic transaminase); BUN = blood urea nitrogen; FSH = follicle stimulating hormone; HBsAg = hepatitis B surface antigen; anti-HBc = hepatitis B core antibody; hsCRP = highly sensitive C-reactive protein; MCHC = mean corpuscular haemoglobin concentration; MCV = mean corpuscular volume; RBC = red blood cell; UACR = urinary albumin-creatinine ratio; WBC = white blood cell, pH= hydrogen ion concentration.

1. Details of liver chemistry stopping criteria and required actions and follow-up assessments after liver stopping or monitoring event are given in Section 7.1 and Appendix 6 (of the protocol). All events of ALT ≥3 × upper limit of normal (ULN) and bilirubin ≥2 × ULN (>35% direct bilirubin) or ALT ≥3 × ULN and international normalized ratio (INR) >1.5, if INR measured, which may indicate severe liver injury (possible Hy's Law), must be reported as an SAE (excluding studies of hepatic impairment or cirrhosis).
2. Local urine testing will be standard for the protocol unless serum testing is required by local regulation or IRB/IEC.
3. WBC differentials will be reviewed at screening only, in order to confirm participant eligibility. At all other times the site must order haematology test with blinded differentials.

9. PHARMACOKINETIC ANALYSES

9.1. Primary Pharmacokinetic Analyses

9.1.1. Endpoint / Variables

9.1.1.1. Drug Concentration Measures

Refer to Appendix 5: Data Display Standards & Handling Conventions (Section 15.5.3 Reporting Standards for Pharmacokinetic)

The pharmacokinetic (PK) analyses will be based on the "Pharmacokinetic (PK)" population, unless otherwise specified.

Plasma concentrations will be listed and summarised by cohort. Cohorts 1 and 2 will also be summarised by injection site. See Section 9.1.2 for details on the summary measures used.

Refer to the PK Guidance document, titled Non-Compartmental Analysis of Pharmacokinetic Data (GUI_51487) for more information regarding the treatment of concentrations below the assay's lower limit of quantification (NQ).

The details of the planned displays are presented in Appendix 11: List of Data Displays

9.1.1.2. Derived Pharmacokinetic Parameters

Pharmacokinetic parameters will be calculated by standard non-compartmental analysis according to current working practices and using the currently supported version of WinNonlin. All calculations of non-compartmental parameters will be based on actual sampling times. Pharmacokinetic parameters listed will be determined from the plasma concentration-time data, as data permits.

Parameter	Parameter Description
AUC(0-t)	• Area under the plasma-concentration time curve from time zero to the time of last quantifiable concentration (C(t)). • Calculated using the linear trapezoidal rule for each incremental trapezoid and the log trapezoidal rule for each decremental trapezoid.
AUC(0-∞)	• Area under the plasma-concentration time curve from time zero extrapolated to infinite time.
Cmax	• Maximum observed concentration. • Determined directly from the concentration-time data.
tmax	• Time to Cmax of GSK3772847
t1/2	• Terminal half-life of GSK3772847 will be calculated as • t1/2 = ln2 / lambda_z
%AUCext	The percentage of AUC(0-∞) obtained by extrapolation (%AUCex) will be calculated as: • [AUC(0-∞) – AUC(0-t)] / AUC(0-∞) x 100

Parameter	Parameter Description
Ct	The last observed quantifiable concentration
Tlast	Time of last quantifiable concentration
* associated parameters lambda_z, lambda_z_lower, lambda_x_upper, No_points_lambda_z to be listed. NOTES: Additional parameters may be included as required. Lambda_z is the terminal phase rate constant.	

9.1.2. Summary Measure

Descriptive statistics will be calculated by cohort for all PK concentrations over time and for the derived PK parameters. Additionally, for cohorts 1 and 2 parameters will be summarised per injection site.

- For each of the PK derived parameters AUC (0-inf), AUC (0-t), t1/2 and Cmax, the following summary statistics will be calculated and tabulated: N, n, Geometric Mean, %CV, Min, Median, Max.

  For tmax, the summary statistics shall include N, n, arithmetic mean, 95% confidence interval (CI) for the arithmetic mean, SD, median, minimum, maximum.

- For PK concentration data, the following summary statistics will be calculated and tabulated by treatment: N, n, arithmetic mean, 95% confidence interval (CI), SD, median, minimum, Q1. Q3, maximum

9.1.3. Population of Interest

The primary pharmacokinetic analyses will be based on the PK population, unless otherwise specified.

9.1.4. Strategy for Intercurrent (Post-Randomization) Events

No intercurrent events are defined for this study. All data collected for each participant in the relevant population will be included in the analysis.

- Missing and anomalous concentration data not due to intercurrent events will be handled by CPMS according to SOP_314000.

9.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 9.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

10. POPULATION PHARMACOKINETIC (POPPK) ANALYSES

Population PKPD analyses may be conducted using data from this study as part of a multi-study analyses to inform on the PK and PD properties of GSK3772847 and will not have any impact on the conduct or reporting of study 209635. These analyses will be conducted by CPMS, if conducted, and will be reported separately so will not be described in this RAP.

11. PHARMACODYNAMIC ANALYSES

11.1. Secondary Pharmacodynamic Analyses

11.1.1. Endpoint / Variables

- Maximal decrease from baseline in free soluble ST2 levels in serum
- Maximal increase from baseline in total soluble ST2 levels in serum

11.1.2. Summary Measure

Change from baseline in free and total soluble ST2 levels in serum will be calculated in the ADaM (Analysis Data Model) Datasets (see Section 15.6.4 for derivation)

Maximal decrease from baseline in free sST2 and maximal increase from baseline in total soluble sST2 levels in serum will be summarised and listed.

Descriptive statistics will be calculated by cohort for maximal decrease from baseline in free sST2 and maximal increase in total soluble sST2. Additionally, for cohorts 1 and 2 parameters will be summarised per injection site.

For maximal decrease from baseline in free sST2 and maximal increase in total soluble sST2 data, the following summary statistics will be calculated and tabulated: n, Geometric Mean, %CV, Min., Q1. Q3, Median, Max

11.1.3. Population of Interest

The secondary pharmacodynamics analyses will be based on the PD population, unless otherwise specified.

11.1.4. Strategy for Intercurrent (Post-Randomization) Events

No intercurrent events are defined for this study. All data collected for each participant in the relevant population will be included in the analysis.

11.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 11.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

12. BIOMARKER ANALYSES

12.1. Biomarker Analyses

12.1.1. Endpoint / Variables

Incidence and prevalence of anti-GSK3772847 antibodies and Plasma 4βOH /cholesterol ratio (pre-treatment and following dosing of GSK3772847).

12.1.2. Summary Measure

Summaries of the incidence of and titres of anti- GSK3772847 antibodies on Day 1 (pre-dose), 15, 29, 57, 85 will be produced.

The plasma 4βOH/cholesterol ratio will be calculated at each visit in the ADaM datasets. Change from baseline will be summarised as a ratio to the pre-treatment visit i.e using the following derivation: post-dosing of GSK3772847/ pre-treatment). Samples post-dose will be received on Days 5, 15, 29 and 85. Pre-treatment sample will be taken Day 1 pre-dose.

12.1.3. Population of Interest

The biomarker analyses will be based on the PD population, unless otherwise specified.

12.1.4. Strategy for Intercurrent (Post-Randomization) Events

No intercurrent events are defined for this study. All data collected for each participant in the relevant population will be included in the analysis.

12.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, endpoints / variables defined in Section 11.1.1 will be summarised using descriptive statistics, graphically presented (where appropriate) and listed.

13. OTHER ENDPOINTS

12-Lead ECGs, clinical laboratory safety tests, vital signs, blood eosinophil levels, free and total soluble sST2 levels in serum and GSK3772847 levels in the serum will be listed and summarised by cohort (and injection site for cohorts 1 and 2) over time.

13.1. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 11: List of Data Displays and will be based on GSK Data Standards and statistical principles.

Unless otherwise specified, blood eosinophil levels and free and total soluble sST2 levels in serum and GSK3772847 levels in the serum will be summarised using descriptive statistics (n, Geometric Mean, %CV, Min., Q1. Q3, Median, Max (95% CIs will be included for ratio to baseline) and Geometric mean and 95% CI graphically presented (where appropriate) and listed.

12-Lead ECGs, and vital signs will be summarised using descriptive statistics (n, Arithmetic Mean, SD, Median, Min and Max) and listed.

14. REFERENCES

GlaxoSmithKline Document Number 2020N427367_02, Protocol: A randomized, double-blind, single ascending dose study to determine the safety and tolerability, pharmacokinetics and pharmacodynamics of GSK3772847 administered subcutaneously in healthy participants [02/JUL/2020].

Protocol Deviation Management Plan (PDMP) [09/JUN/2020]

15. APPENDICES

15.1. Appendix 1: Exclusions from Per Protocol Population

Instream and final analysis population reviews as per SOP 130050 are not planned for this study because it does not include a Per-Protocol population.

However, protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan. Data will be reviewed prior to freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset. This dataset will be the basis for the summaries and listings of protocol deviations.

15.2. Appendix 2: Schedule of Activities

15.2.1. Protocol Defined Schedule of Events

Procedure	Day 0	Day 1 (Hours)					Day 2	Day 3	Day 4	Day 5	Day 6	Day 9	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85/Early withdrawal visit	Notes Time window for Outpatient visits: Day 9 ± 2, Day 15 ± 4 days, and Days 29, 43 and 57 ± 7 days, Days 71 and 85 ± 10 days
		Pre-dose	0	2	4	8													
Clinic Visits																			
Admission to clinic	X																		Participants may remain in the clinic until day 6 with visits at days 6-8 as outpatient, at the investigator's discretion
Inclusion/Exclusion criteria review	X																		
Discharge from clinic											X								
Out-patient visit												X	X	X	X	X	X	X	
Study Intervention																			
Randomisation		X																	
SC dosing			X																
Safety Assessments																			
Safety labs (haematology, clinical chemistry and urinalysis)		X					X		X			X		X	X			X	WBC differentials MUST be blinded (see Appendix 2 in protocol)

Procedure	Day 0	Day 1 (Hours)					Day 2	Day 3	Day 4	Day 5	Day 6	Day 9	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85/Early withdrawal visit	Notes Time window for Outpatient visits: Day 9 ± 2, Day 15 ± 4 days, and Days 29, 43 and 57 ± 7 days, Days 71 and 85 ± 10 days
		Pre-dose	0	2	4	8													To be taken in non-fasted state
Alcohol/drug screen	X																		
Urinary Cotinine Test	X																		
12-lead ECG		X				X		X		X				X		X		X	When scheduled at the same timepoint, ECG's should be taken as close as possible to PK samples
Vital signs	X	X				X	X	X	X	X	X			X		X		X	Supine blood pressure and heart rate
Concomitant medications	◄==========►																		
SAE/AE Review	◄==========►																		Including injection site reactions

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Procedure	Day 0	Day 1 (Hours)					Day 2	Day 3	Day 4	Day 5	Day 6	Day 9	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85/Early withdrawal visit	Notes Time window for Outpatient visits: Day 9 ± 2, Day 15 ± 4 days, and Days 29, 43 and 57 ± 7 days, Days 71 and 85 ± 10 days
		Pre-dose	0	2	4	8													
Local Injection site reaction evaluation					X		X	X											Targeted evaluation at 4 hours post-dose on Day 1 & 24 hours post-dose on Day 2 and 48 hours post-dose on Day 3. Spontaneous reporting at all other times.
Pregnancy test	X													X		X		X	Serum pregnancy test at screening and urine dipstick test at all other visits
Brief Physical Examination																		X	
Biomarker Collection																			
PK blood sample		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Day 1 samples +/- 1 hours. Days 2-6 +/- 2 hours relative to time of dosing

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Procedure	Day 0	Day 1 (Hours)					Day 2	Day 3	Day 4	Day 5	Day 6	Day 9	Day 15	Day 29	Day 43	Day 57	Day 71	Day 85/Early withdrawal visit	Notes Time window for Outpatient visits: Day 9 ± 2, Day 15 ± 4 days, and Days 29, 43 and 57 ± 7 days, Days 71 and 85 ± 10 days
		Pre-dose	0	2	4	8													
Free sSt2 and total sST2 blood sample		X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	Samples should be taken within ± 2 minutes of PK
Immunogenicity blood sample		X											X	X		X		X	Collect pre-dose on Day 1
4βOH cholesterol/cholesterol plasma sample		X								X			X	X				X	All samples should be in non-fasted state for comparison with baseline.
Pharmacogenetic (PGx) blood sample				X															May be taken at any time post-dose

- The timing and number of planned study assessments, including safety, pharmacokinetic, pharmacodynamic/biomarker or other assessments may be altered during the course of the study based on newly available data (e.g., to obtain data closer to the time of peak plasma concentrations) to ensure appropriate monitoring.
- Any changes in the timing or addition of time points for any planned study assessments as the result of emerging pharmacokinetic/pharmacodynamic data from this study must be documented and approved by the relevant study team member and then archived in the sponsor and site study files but will not constitute a protocol amendment. The Competent Authority (CA) and ethics committee (EC) will be informed of any safety issues that constitute a substantial amendment and require alteration of the safety monitoring scheme or amendment of the informed consent form (ICF). The changes will be approved by the CA and the EC before implementation.
- When scheduled at the same timepoints, vital signs should be conducted followed by ECG's prior to any blood draws.

15.3. Appendix 3: Assessment Windows

15.3.1. Definitions of Assessment Windows for Analyses

Dosing should occur up to 28 days after screening.

No assessment windows will be defined for Day 0, Day 1 (pre-dose), Day 1 2hrs, Day 1 4hrs, Day 1 8hrs, Day 2, Day 3, Day 4, Day 5 and Day 6 analyses. Summaries and analyses will be based on nominal visits as these are inpatient visits.

For the following outpatient visits, assessment windows are as follows:

- Day 9 ± 2 days
- Days 15 ± 4 days
- Days 29, 43, 57 ± 7 days
- Days, 71 and 85 ± 10 days.

If two visit dates overlap then the assessment that is closest to the scheduled visit is assigned as that visit assessment and the other visit would be assigned as an unscheduled visit e.g. if a subject has a day 9 visit outside the day 9 window but is in the window of the day 15 visit then the visit closest to day 15 gets assigned to day 15 and the other visit becomes an unscheduled visit.

Analysis will be performed on actual time (for adverse events) and nominal time for all other endpoints. No exclusion will be made to plasma samples taken outside the sample windows as long as there is time recorded. Any data falling outside of these assessment windows will be classified as unscheduled visits.

15.4. Appendix 4: Study Phases and Treatment Emergent Adverse Events

15.4.1. Study Phases

Assessments and events will be classified according to the time of occurrence relative to dose.

Study Phase	Definition
Pre-Treatment	Start Date ≤ Study Treatment Start Date
On-Treatment	Study Treatment Start Date < Date ≤ Study Treatment Stop Date + 28 days
Post-Treatment	Date > Study Treatment Stop Date + 28 days

15.4.1.1. Study Phases for Concomitant Medication

Study Phase	Definition **Note: All programming should use start and end dates where available, CMSTRF and CMENRF are only to be used where dates are unavailable to help determine the correct study phase.**
Pre-treatment	• Conmed Start Date < Study Treatment First Dose Date • Conmed End Date < Study Treatment First Dose Date • CMSTRF = ”BEFORE” • Randomisation date is missing i.e. subject was not randomised
On-treatment	• Study Treatment First Dose Date <= Conmed Start Date <= Study Treatment Last Dose Date + 28 • Study Treatment First Dose Date <= Conmed End Date <= Study Treatment Last Dose Date + 28 • (Conmed Start Date <= Study Treatment Last Dose Date + 28) and (Conmed End Date >= Study Treatment First Dose Date) • (Conmed Start Date <= Study Treatment Last Dose Date + 28) and (CMENRF =”DURING/AFTER” or CMENRF =”AFTER” or CMSTRF = “DURING”) • (CMSTRF = ”BEFORE” or CMSTRF = ”DURING” or CMENRF =”DURING/AFTER”) and (Conmed End Date >= Study Treatment First Dose Date) • (CMSTRF = ”BEFORE” or CMSTRF =”DURING”) and (CMENRF =”DURING/AFTER” or CMENRF =”AFTER”) • CMSTRF = ”DURING” • CMENRF = ”DURING/AFTER”
Post-treatment	• Conmed Start Date > Study Treatment Last Dose Date + 28 • Conmed End Date > Study Treatment Last Dose Date + 28 • CMENRF = ”AFTER” • CMENRF = ”DURING/AFTER”
All phases	• Conmed start date is missing and CMSTRF is missing and conmed end date is missing and CMENRF is missing

Study Phase	**Definition** **Note: All programming should use start and end dates where available, CMSTRF and CMENRF are only to be used where dates are unavailable to help determine the correct study phase.**

1. **NOTES:**

- The duration of a single concomitant medication can extend over multiple study phases
- Please refer to Appendix 7: Reporting Standards for Missing Data for handling of missing and partial dates for concomitant medication. Use the rules in this table if concomitant medication date is completely missing.

15.4.2. Treatment Emergent Flag for Adverse Events

Adverse Events will be flagged as Treatment Emergent as described in the table in Section 15.4.1, where the AE Start Date/Time will be considered. If the study treatment stop date is missing, then the AE will be considered to be on-treatment.

15.5. Appendix 5: Data Display Standards & Handling Conventions

15.5.1. Reporting Process

Software	
• The currently supported versions of SAS software will be used.	
Reporting Area	
HARP Server	: UK1SALX00175
HARP Compound	: the following directories will be used for the final analysis: : \arprod\gsk3772847\mid209635\final_01
Analysis Datasets	
• Analysis datasets will be created according to CDISC standards (SDTM Implementation Guide Version 3.2 & AdaM Implementation Guide Version 1.1 .	
Generation of RTF Files	
• RTF files will be generated for all tables in the final reporting effort for use in writing the CSR.	

15.5.2. Reporting Standards

General

• The current GSK Statistical Display Standards in the GSK Standards Library (IDSL) will be applied for reporting, unless otherwise stated (Library Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics
  • Do not include participant level listings in the main body of the GSK Clinical Study Report. All participant level listings should be located in the modular appendices as ICH or non-ICH listings

Formats
• GSK Statistical Display Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected, unless otherwise stated. • Numeric data will be reported at the precision collected on the eCRF. • The reported precision from non eCRF sources will follow the GSK Standard Statistical Display Principles but may be adjusted to a clinically interpretable number of DP's.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analyses:
  • Planned time relative to dosing will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
  • The impact of any major deviation from the planned assessment times and/or scheduled visit days on the analyses and interpretation of the results will be assessed as appropriate.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings (Refer to GSK Standard Statistical Display Principle 5.05.1).
  • Unscheduled or unplanned readings will be presented within the participant's listings.

Unscheduled Visits	
• Unscheduled visits will only be included in summary tables as part of 'minimum/maximum post baseline' and 'minimum/maximum change from baseline' summary. • Unscheduled visits will not be included in figures. • All unscheduled visits will be included in listings.	
Descriptive Summary Statistics	
Continuous Data	Refer to GSK Standard Statistical Display Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to GSK Standard Statistical Display Principals 7.01 to 7.13.	

15.5.3. Reporting Standards for Pharmacokinetic

Reporting of Pharmacokinetic Concentration Data	
Descriptive Summary Statistics	Refer to IDSL PK Display Standards. Refer to IDSL Statistical Principle 6.06.1. Note: Concentration values will be imputed as per GUI_51487 for descriptive summary statistics/analysis and summarized graphical displays only.
Reporting of Pharmacokinetic Parameters	
Descriptive Summary Statistics (Log Transformed)	N, n, geometric mean, and between geometric coefficient of variation (CVb (%)), Min, Median, Max will be reported. CV_b (%) = √ (exp(SD^2) - 1) * 100 (SD = SD of log transformed data)
Parameters Not Being Log Transformed	T_{max}, T_{last}, first point, last point, and number of points used in the determination of λz, %AUCex
Summary Tables	All provided PK parameters will be summarised except Lamz, lamzUL, LamzLL, LamzNP and AUC % extrapolated area , Rsq-adjusted (if calculated).
Listings	Additionally, include the first point, last point and number of points used in the determination of lambda_z for listings.

15.6. Appendix 6: Derived and Transformed Data

15.6.1. General

Multiple Measurements at One Analysis Time Point
• Mean of the measurements will be calculated and used in any derivation of summary statistics but if listed, all data will be presented. • If there are two values within a time window (as per Section 15.3.1) the value closest to the target day for that window will be used. If values are the same distance from the target, then the mean will be taken. • Participants having both High and Low values for Normal Ranges at any post-baseline visit for safety parameters will be counted in both the High and Low categories of "Any visit post-baseline" row of related summary tables. This will also be applicable to relevant Potential Clinical Importance summary tables.
Study Day

• Calculated as the number of days from First Dose Date:
  • Ref Date = Missing → Study Day = Missing
  • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date
  • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1

15.6.2. Study Population

Age
• Only year of birth will be collected on the CRF and birth date will be presented in listings as 'YYYY'. • GSK standard IDSL algorithms will be used for calculating age where birth date will be imputed as'30th June' and then calculated based on the dose date.

15.6.3. Safety

ECG Parameters
Laboratory Parameters
If a laboratory value which is expected to have a numeric value for summary purposes, has a nondetectable level reported in the database, where the numeric value is missing, but typically a character value starting with '<x' or '>x' (or indicated as less than x or greater than x in the comment field) is present, the number of significant digits in the observed values will be used to determine how much to add or subtract in order to impute the corresponding numeric value. • Example 1: 2 Significant Digits →'< x'becomes x –0.01 • Example 2: 1 Significant Digit →'> x' becomes x + 0.1 • Example 3: 0 Significant Digits →'< x' becomes x –1

15.6.4. Pharmacodynamic and Biomarker

Free and Soluble ST2
Maximal decrease in free/Maximal Increase in total Soluble ST2 from baseline
Change from baseline in free soluble ST2 levels in serum will be calculated in the ADaM (Analysis Data Model) Datasets as follows for each individual for all assessments: Free soluble ST2 in serum assessment at Timepoint X – Baseline For all timepoints (X) post dose where a free soluble ST2 in serum assessment has been taken and Baseline is defined in Section 5.2. Maximal decrease from baseline is then the largest decrease calculated across all timepoints post dose. Maximum increase from baseline in total soluble ST2 level will be calculated in a similar manner albeit as the largest increase from baseline.
Plasma 4βOH /cholesterol ratio
The plasma 4βOH /cholesterol ratio will be calculated for each visit in the ADaM datasets. Change from baseline will be summarised as a ratio to the pre-treatment visit i.e. using the following derivation: post-dosing of GSK3772847/ pre-treatment). Samples post-dose will be received on Days 5, 15, 29 and 85. Pre-treatment sample will be taken Day 1 pre-dose. See also Section 12.1.1

15.7. Appendix 7: Reporting Standards for Missing Data

15.7.1. Premature Withdrawals

Element	Reporting Detail
General	• For the final analysis, participant study completion (i.e. as specified in the protocol) is defined as having completed all phases of the study including the final follow up visit. • Participants who withdraw prior to D29 will be replaced in the study. Replacement participants will be dosed with the planned treatment of the withdrawn participant. • All available data from participants including those who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified. • The Withdrawal visit will be slotted as per Appendix 3: Assessment Windows or will be summarised as the withdrawal visit.

15.7.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument ○ These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. ○ Answers such as "Not applicable" and "Not evaluable" are not considered to be missing data and should be displayed as such. ○ No manual imputation will be made for any missing numerical data. ○ Missing data will generally not be considered in the calculation of percentages (i.e., the denominator will not include subjects who have missing data at a given time point).
Outliers	• Any participants excluded from the summaries will be documented along with the reason for exclusion in the clinical study report.

15.7.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	• Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: ○ Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 4: Study Phases and Treatment Emergent Adverse Events. ○ Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

Element	Reporting Detail

Concomitant Medications/ Medical History	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention:
	  ○ If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month
	  ○ If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month.
	• The recorded partial date will be displayed in listings.

15.8. Appendix 8: Values of Potential Clinical Importance

Values of potential clinical importance will not be used in this study, instead normal reference ranges of “Low”, “Normal” and “High” will be used.

15.9. Appendix 9: Population Pharmacokinetic (PopPK) Analyses

Population PKPD analyses may be conducted using data from this study as part of a multi-study analyses to inform on the PK and PD properties of GSK3772847 and will not have any impact on study 209635. These analyses will be conducted by CPMS and will be reported separately so will not be described in this RAP.

15.10. Appendix 10: Abbreviations & Trademarks

15.10.1. Abbreviations

Abbreviation	Description
ADaM	Analysis Data Model
AE	Adverse Event
AIC	Akaike's Information Criteria
A&R	Analysis and Reporting
AUC(0-∞)	Area under the plasma concentration-time curve, from time zero to infinity
AUC(0-t)	Area under the plasma concentration-time curve, from time zero to the time of the last quantifiable concentration
CDISC	Clinical Data Interchange Standards Consortium
CI	Confidence Interval
CPMS	Clinical Pharmacology Modelling & Simulation
CS	Clinical Statistics
CSR	Clinical Study Report
CTR	Clinical Trial Register
CV_b / CV_w	Coefficient of Variation (Between) / Coefficient of Variation (Within)
DBF	Database Freeze
DBR	Database Release
DOB	Date of Birth
DP	Decimal Places
eCRF	Electronic Case Record Form
EMA	European Medicines Agency
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Clinical Results Disclosure Requirements
GSK	GlaxoSmithKline
IA	Interim Analysis
ICH	International Conference on Harmonization
IDMC	Independent Data Monitoring Committee
IDSL	Integrated Data Standards Library (GSK Standards Library)
IMMS	International Modules Management System
IP	Investigational Product
ITT	Intent-To-Treat
MMRM	Mixed Model Repeated Measures
PCI	Potential Clinical Importance
PD	Pharmacodynamic
PDMP	Protocol Deviation Management Plan
PK	Pharmacokinetic
PP	Per Protocol
PopPK	Population PK
QC	Quality Control
QTcF	Frederica's QT Interval Corrected for Heart Rate
QTcB	Bazett's QT Interval Corrected for Heart Rate
RAP	Reporting & Analysis Plan

Abbreviation	Description
RAMOS	Randomization & Medication Ordering System
SAC	Statistical Analysis Complete
SDSP	Study Data Standardization Plan
SDTM	Study Data Tabulation Model
SDV	Source Data Verification
SOP	Standard Operation Procedure
TA	Therapeutic Area
TFL	Tables, Figures & Listings
Tmax	Time to Cmax
t1/2	Apparent terminal phase half-life

15.10.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
NONE

Trademarks not owned by the GlaxoSmithKline Group of Companies
IQVIA
NONMEM
SAS
WinNonlin

15.11. Appendix 11: List of Data Displays

All displays (Tables, Figures & Listings) will use the term 'Subjects' instead of "Participants".

15.11.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.1 to 1.n	1.1 to 1.n
Safety	2.1 to 2.n	2.1 to 2.n
Pharmacokinetic	3.1 to 3.n	3.1 to 3.n
Pharmacodynamic	4.1 to 4.n	4.1 to 4.n
Biomarker	5.1 to 5.n	5.1 to 5.n
Section	**Listings**	
ICH Listings	1 to x	
Other Listings	y to z	

15.11.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 12: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln
Pharmacokinetic	PK_Fn	PK_Tn	PK_Ln
Pharmacodynamic or Biomarker	PD_Fn	PD_Tn	PD_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

15.11.3. Deliverables

Delivery [Priority]	Description
Final SAC	Final Statistical Analysis Complete

15.11.4. Study Population Tables

Study Population Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Subject Disposition						
1.1.	Safety	ES8	Summary of Subject Status and Reason for Study Withdrawal	ICH E3, FDAAA, EudraCT	Final SAC	Prog
1.2.	ASE	ES6	Summary of Screening Status and Reasons for Screen Failure	Journal Requirements Note that the reasons for rescreen of subjects who initially failed but subsequently entered the study are not included in the display. This will be footnoted.	Final SAC	Prog
Population Analysed						
1.3.	ASE	SP1	Summary of Study Populations	IDSL	Final SAC	Prog
Demographic and Baseline Characteristics						
1.4.	Safety	DM1	Summary of Demographic Characteristics	ICH E3, FDAAA, EudraCT	Final SAC	Prog
1.5.	ASE	DM11	Summary of Age Ranges	EudraCT	Final SAC	Prog
1.6.	Safety	DM5	Summary of Race and Racial Combinations	ICH E3, FDA, FDAAA, EudraCT	Final SAC	Prog

Study Population Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Prior and Concomitant Medications						
1.7.	Safety	MH4	Summary of Current Medical Conditions at Screening	ICH E3	Final SAC	Prog
1.8.	Safety	SU1	Summary of Smoking History at Screening		Final SAC	Prog

15.11.5. Safety Tables

Safety: Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Adverse Events (AEs)						
2.1.	Safety	SAFE_T01	Overview of On-treatment Adverse Events During the Study	See 3.01 /arenv/arprod/gsk3772847/mid207597/final_02/output for example Include footnote defining "On-treatment"	Final SAC	Prog
2.2	Safety	SAFE_T01	Overview of Post-treatment Adverse Events During the Study	Include footnote defining "Post-treatment"	Final SAC	Prog
2.3	Safety	AE1	Summary of All On-treatment Adverse Events by System Organ Class and Preferred Term	ICH E3. Include footnote defining "On-treatment" See 3.02 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.4	Safety	AE1	Summary of All Post-treatment Adverse Events by System Organ Class and Preferred Term	ICH E3. Include footnote defining "Post-treatment" See 3.02 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.5	Safety	AE1	Summary of All On-treatment Adverse Events Leading to Withdrawal from Study by System Organ Class and Preferred Term	ICH E3. Include footnote defining "On-treatment"	Final SAC	Prog

Safety: Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
2.6	Safety	AE1	Summary of All On-treatment Fatal Adverse Events by System Organ Class and Preferred Term	ICH E3. Include footnote defining "On-treatment" See 3.07 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.7	Safety	AE3	Summary of All On-treatment Common (>=1%) Adverse Events by Overall Frequency	ICH E3. Include footnote defining "On-treatment" See 3.08 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.8	Safety	AE1	Summary of On-treatment Drug-Related Adverse Events by System Organ Class and Preferred Term	ICH E3 See 3.09 /arenv/arprod/gsk3772847/mid207597/final_02/output for example. Include footnote defining "On-treatment"	Final SAC	Prog
2.9	Safety	AE15	Summary of All On-treatment Common (>=1%) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Participant and Occurrences)	FDAAA, EudraCT. Include footnote defining "On-treatment" See 3.10 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog

Safety: Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
2.10	Safety	AE1	Summary of All On-treatment Serious Adverse Events by System Organ Class and Preferred Term	Include footnote defining "On-treatment" See 3.11 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.11	Safety	AE16	Summary of All On-treatment Serious Adverse Events by System Organ Class and Preferred Term (Number of Participants and Occurrences)	FDAAA, EudraCT. Include footnote defining "On-treatment" See 3.13 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.13	Safety	AE1	Summary of All On-treatment Serious Adverse Events Leading to Withdrawal from Study by System Organ Class and Preferred Term	IDSL. Include footnote defining "On-treatment" See 3.15 /arenv/arprod/gsk3772847/mid207597/final_02/output for example	Final SAC	Prog
2.14	Safety	AE1	Summary of On-treatment Injection Site Reactions	A subset of 3.03 where we display the injection site reactions only. Include footnote defining "On-treatment"	Final SAC	Prog
Adverse Events of Special Interest (AESIs)						
2.15	Safety	AE1	Summary of On-treatment Adverse Events of Special Interest	IDSL	Final SAC	Prog
2.16	Safety	LB1	Summary of Clinical Chemistry	ICH E3	Final SAC	Prog

Safety: Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
2.17	Safety	LB1	Summary of Change from Baseline in Clinical Chemistry	ICH E3	Final SAC	Prog
2.18	Safety	LB1	Summary of Hematology	ICH E3	Final SAC	Prog
2.19	Safety	LB1	Summary of Changes from Baseline in Hematology	ICH E3	Final SAC	Prog
2.20	Safety	LIVER1	Summary of Liver Monitoring/Stopping Event Reporting	IDSL	Final SAC	Prog
2.21	Safety	EG1	Summary of ECG Findings	IDSL	Final SAC	Prog
2.22	Safety	VS1	Summary of Vital Signs	ICH E3	Final SAC	Prog
2.23	Safety	VS1	Summary of Change from Baseline in Vital Signs	ICH E3	Final SAC	Prog

15.11.6. Pharmacokinetic Tables

Pharmacokinetic: Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Secondary: Pharmacokinetic						
3.1	PK	PK01	Summary of GSK3772847 Serum Concentration-Time Data (ug/ml) by Cohort, and Injection Site	The display will be summarised by the following: • 70 mg dose abdomen injection site • 70 mg dose thigh injection site • 70 mg dose arm injection site • Cohort 1 • 140 mg dose abdomen injection site • 140 mg dose thigh injection site • 140 mg dose arm injection • Cohort 2 • Cohort 3 140 mg Japanese population • Cohort 4 140 mg Chinese population	Final SAC	Prog
3.2	PK	PK04	Summary of Derived GSK3772847 Pharmacokinetic Parameters by Cohort, and Injection Site		Final SAC	Prog

15.11.7. Pharmacodynamic Tables

Pharmacodynamic Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Secondary Pharmacodynamic: Free and Total SST2						
4.1	PD	Table 6.01 CSR: 2019N414678_00207597	Summary of Raw and Change from Baseline in Free Soluble ST2 concentration (ng/mL) by Cohort and Injection Site	The display will be summarised by the following treatment groups: • 70 mg dose abdomen injection site • 70 mg dose thigh injection site • 70 mg dose arm injection site • Cohort 1 • 140 mg dose abdomen injection site • 140 mg dose thigh injection site • 140 mg dose arm injection • Cohort 2 • Cohort 3 140 mg Japanese population • Cohort 4 140 mg Chinese population • Placebo (pooled Cohorts 1+2) • Placebo (pooled Cohorts 3+4) • Include a line for maximum increase from baseline (for all treatments)	Final SAC	Prog
4.2	PD	Table 6.09 CSR: 2019N414678_00207597	Summary of Raw and Change from Baseline in Total Soluble ST2 concentration (ng/mL) by Cohort and Injection Site	The display will be summarised by the following treatment groups below • 70 mg dose abdomen injection site • 70 mg dose thigh injection site • 70 mg dose arm injection site • Cohort 1 • 140 mg dose abdomen injection site • 140 mg dose thigh injection site	Final SAC	Prog

Pharmacodynamic Tables						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
				• 140 mg dose arm injection • Cohort 2 • Cohort 3 140 mg Japanese population • Cohort 4 140 mg Chinese population • Placebo (pooled Cohorts 1+2) Placebo (pooled Cohorts 3+4) Include a line for maximum decrease from baseline (for all treatments)		
4.3	PD		Summary of Observed Results and Change from baseline in Plasma 4β hydroxycholesterol /cholesterol ratio	See t_4_06(002).pdf in med_ds_proj/\Projects\Respiratory & Inflammation\GSK3772847 (IL33)\209635\RAP\TFLs	Final SAC	
4.4	PD		Summary of Incidence and Titres of Anti-GSK3772847 Antibodies	See Table 4.02 'arenv/arprod/gsk3772847/207597/final_02/output'	Final SAC	

15.11.8. Pharmacokinetic: Figures

Pharmacokinetic Figures						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Secondary: Pharmacokinetic						
3.1	PK		Serum Concentrations of GSK3772847 over Time by Dose and Injection Site	Plot median and range PK concentration over time. There will be 2 plots. One for cohort 1 (70mg) and one for cohort 2 (140mg). Each plot will have 3 groups of different line type differentiating between the injection sites • Cohort dose abdomen injection site • Cohort dose thigh injection site • Cohort dose arm injection site Plot on normal and logarithmic (base10) scales.	Final SAC	Prog
3.2	PK		Serum Concentrations of GSK3772847 over Time by Ethnicity for 140 mg SC Dose	Plot median and range PK concentration over time. There will be 3 groups of different line type. • Cohort 2 (upper arm injection site) • Cohort 3 (Japanese population) • Cohort 4 (Chinese population) Plot on normal and logarithmic (base10) scales.	Final SAC	Prog

Pharmacokinetic Figures						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
3.3	PK		Serum Concentrations of GSK3772847 over Time by Dose	Plot median and range PK concentration over time. There will be 2 groups of different line type. One for cohort 1 (70mg) and one for cohort 2 (140mg). Plot on normal and logarithmic (base10) scales.	Final SAC	Prog

15.11.9. Pharmacodynamic Figures

Pharmacodynamic: Figures						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
Secondary: Pharmacodynamic						
4.1	PD		Free Soluble ST2 levels by Dose, Injection Site and Placebo	Plot median and range free sst2 over time. There will be 2 plots. One for cohort 1 (70mg) and one for cohort 2 (140mg). Each plot will have 4 groups of different line type differentiating between the injection sites • Cohort dose abdomen injection site • Cohort dose thigh injection site • Cohort dose arm injection site • Placebo (pooled Cohorts 1+2) Plot on normal and logarithmic (base10) scales.	Final SAC	Prog
4.2	PD		Free Soluble ST2 levels by Ethnicity and Placebo for 140 mg SC Dose	Plot median and range free sst2 over time. There will be 5 groups of different line type. • Cohort 2 (upper arm injection site) • Cohort 3 (Japanese population) • Cohort 4 (Chinese population) • Placebo (pooled Cohorts 1+2) • Placebo (pooled Cohorts 3+4) Plot on normal and logarithmic (base10) scales.	Final SAC	Prog

Pharmacodynamic: Figures						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
4.3	PD		Free Soluble ST2 levels by Dose and Placebo	Plot median and range free sST2 over time. There will be 3 groups of different line type: • cohort 1 (70mg) • cohort 2 (140mg) • placebo (pooled Cohorts 1+2). Plot on normal and logarithmic (base10) scales.	Final SAC	Prog
4.4	PD		Total Soluble ST2 levels by Dose, Injection Site and Placebo	Plot median and range total sst2 over time. There will be 2 plots. One for cohort 1 (70mg) and one for cohort 2 (140mg). Each plot will have 4 groups of different line type differentiating between the injection sites • Cohort dose abdomen injection site • Cohort dose thigh injection site • Cohort dose arm injection site • Placebo (pooled Cohorts 1+2) Plot on normal and logarithmic (base10) scales.	Final SAC	Prog

Pharmacodynamic: Figures						
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**	**Stats or Prog**
4.5	PD		Total Soluble ST2 levels by Ethnicity and Placebo for 140 mg SC Dose	Plot median and range total sst2 over time. There will be 5 groups of different line type. • Cohort 2 (upper arm injection site) • Cohort 3 (Japanese population) • Cohort 4 (Chinese population) • Placebo (pooled Cohorts 1+2) • Placebo (pooled Cohorts 3+4) Plot on normal and logarithmic (base10) scales.	Final SAC	Prog
4.6	PD		Total Soluble ST2 levels by Dose and Placebo	Plot median and range total sST2 over time. There will be 3 groups of different line type: • cohort 1 (70mg) • cohort 2 (140mg) • placebo (pooled Cohorts 1+2). Plot on normal and logarithmic (base10) scales.	Final SAC	Prog

15.11.10. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
1.	Screened	ES7	Listing of Reasons for Screen and Run-in Failure	Journal Guidelines	Final SAC
2.	Safety	ES2 / ES3	Listing of Reasons for Study Withdrawal	ICH E3	Final SAC
3.	Safety	BL1 / BL2	Listing of Participants for Whom the Treatment Blind was Broken	ICH E3	Final SAC
4.	Safety	TA1 / CP_RD1x	Listing of Planned and Actual Treatments	IDSL	Final SAC
Protocol Deviations					
5.	Safety	DV2	Listing of Important Protocol Deviations	ICH E3	Final SAC
6.	Safety	IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations	ICH E3	Final SAC
Demographic and Baseline Characteristics					
7.	Safety	DM2	Listing of Demographic Characteristics	ICH E3	Final SAC
8.	Safety	DM9	Listing of Race	ICH E3	Final SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Prior and Concomitant Medications					
9.	Safety	CP_CM3	Listing of Concomitant Medications	IDSL	Final SAC
Exposure and Treatment Compliance					
10.	Safety	EX3	Listing of Exposure Data	ICH E3	Final SAC
Adverse Events					
11.	Safety	AE8	Listing of All Adverse Events	ICH E3	Final SAC
12.	Safety	AE7	Listing of Subject Numbers for Individual Adverse Events	ICH E3	Final SAC
13.	Safety	AE8	Listing of Adverse Events Leading to Withdrawal from Study	ICH E3	Final SAC
14.	Safety	AE2	Listing of Relationship Between Adverse Event System Organ Classes, Preferred Terms, and Verbatim Text	IDSL	Final SAC
Serious and Other Significant Adverse Events					
15.	Safety	AE8	Listing of Fatal Serious Adverse Events	ICH E3	Final SAC
16.	Safety	AE8	Listing of Non-Fatal Serious Adverse Events	ICH E3	Final SAC
17.	Safety	AE14	Listing of Reasons for Considering as a Serious Adverse Event	ICH E3	Final SAC
18.	Safety	AE8	Listing of Serious Adverse Events Leading to Withdrawal from Study	ICH E3	Final SAC
19.	Safety	AE8	Listing of Adverse Events of Special Interest	ICH E3	Final SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Hepatobiliary (Liver)					
20.	Safety	MH2	Listing of Medical Conditions for Participants with Liver Stopping Events	IDSL	Final SAC
21.	Safety	SU2	Listing of Substance Use for Participants with Liver Stopping Events	IDSL	Final SAC
All Laboratory					
22.	Safety	LB5 / LB6	Listing of All Laboratory Data for Participants with Any Value Outside Normal Range	ICH E3	Final SAC
23.	Safety	LB14	Listing of Laboratory Data with Character Results	ICH E3	Final SAC
ECG					
24.	Safety	EG5	Listing of All ECG Findings for Participants with an Abnormal ECG Finding	IDSL	Final SAC
25.	Safety	EG5	Listing of Abnormal ECG Findings	IDSL	Final SAC
Vital Signs					
26.	Safety	VS4	Listing of All Vital Signs Data	IDSL	Final SAC

15.11.11. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events					
27.	Safety	ESI8	Listing of AE Terms of Special Interest	IDSL	Final SAC
Liver Events: Note only produced if there is a Liver Event					
28.	Safety	LIVER5	Listing of Liver Events		Final SAC
29.	Safety	LIVER6	Listing of Liver Event Information for RUCAM Score		Final SAC
30.	Safety	LIVER7	Listing of Liver Biopsy		Final SAC
31.	Safety	LIVER8	Listing of Liver Imaging Details		Final SAC
Cardiovascular Events: Note only produced if there is a Cardiovascular Event					
32.	Safety	Patient Profile	Listing of Myocardial infarction/unstable angina		Final SAC
33.	Safety	Patient Profile	Listing of Congestive heart failure		Final SAC
34.	Safety	Patient Profile	Listing of Arrhythmias		Final SAC
35.	Safety	Patient Profile	Listing of Valvulopathy		Final SAC
36.	Safety	Patient Profile	Listing of Pulmonary hypertension		Final SAC
37.	Safety	Patient Profile	Listing of Cerebrovascular events/stroke and transient ischemic attack		Final SAC
38.	Safety	Patient Profile	Listing of Peripheral arterial thromboembolism		Final SAC
39.	Safety	Patient Profile	Listing of Deep venous thrombosis/pulmonary embolism		Final SAC
40.	Safety	Patient Profile	Listing of Revascularisation		Final SAC
41.	Safety	Patient Profile	Listing of Deaths		Final SAC

Pharmockinetics					
42.	PK		Listing of GSK3772847 Plasma Pharmacokinetic Concentration – Time Data		Final SAC
43.	PK		Listing of Derived GSK3772847 Plasma Pharmacokinetic Parameters		Final SAC
Pharmacodynamics					
44.	PD		Listing of Free and Total Soluble ST2 Concentrations		Final SAC
45.	PD		Listing of Maximum decrease from baseline in Free and Maximum increase from baseline in Total Soluble ST2 Concentrations		Final SAC
46.	PD		Listing of Plasma 4β hydroxycholesterol/cholesterol ratio		Final SAC
47.	PD		Listing of Anti-GSK3772847 Antibodies		Final SAC
48.	PD		Listing of Blood Eosinophil Data		Final SAC
Covid-19					
49.	Safety	PAN7	Listing of All Subjects with Visits and Assessments Impacted by COVID-19 Pandemic		Final SAC
50.	Safety	PAN12	Listing of COVID-19 Assessments and Symptom Assessments for Subjects with COVID-19 Adverse Events		Final SAC
51.	Safety	DV2	Listing of Non-Important COVID-19 related Protocol Deviations		Final SAC

15.12. Appendix 12: Example Mock Shells for Data Displays

Data Display Specification will be made available on Request

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