A Phase 1a, randomized, double-blind placebo-controlled study to evaluate safety and tolerability and to characterize the pharmacokinetic profile of single ascending doses of fenretinide oral capsules in healthy adult volunteers

NCT06181760

SAP dated 07December2023

Statistical Analysis Plan

Sponsor: Island Pharmaceuticals Ltd

Protocol Number: ISLA101-P01-CT001

A Phase 1a, Randomized, Double-blind Placebo-controlled Study to Evaluate Safety and Tolerability and to Characterize the Pharmacokinetic Profile of Single Ascending Doses of Fenretinide Oral Capsules in Healthy Adult Volunteers

Version: Final Version 1.0
Date: 2023-12-07

Signature Page

Author:

DocuSigned by:
Ella Liu
Signer Name: Ella Liu
Signing Reason: I am the author of this document
Signing Time: 2023-12-07 | 2:03:20 PM AEDT
0C83B3EDF8A24B68B0BEA6F9B10AE82A

Name: Ella Liu
Title: Senior Biostatistician
Company: Resolutum Global

Approved by:

DocuSigned by:
Teresa M. Byrne
Signer Name: Teresa M. Byrne
Signing Reason: I approve this document
Signing Time: 2023-12-09 | 6:43:15 AM AEDT
992ABD575D8B4DF7A369F4B7AAFE9F75

Name: Teresa M. Byrne
Title: VP, Clinical Development
Company: Island Pharmaceuticals Ltd

Table of Contents

1. INTRODUCTION 5
1.1 Rationale 5

2. SUMMARY OF THE PROTOCOL 5
2.1 Study Objectives 5
2.1.1 Primary Objective 5
2.1.2 Secondary Objectives 5
2.1.3 Exploratory Objective 5
2.2 Study Endpoints 6
2.2.1 Primary Endpoints 6
2.2.2 Secondary Endpoints 6
2.2.3 Exploratory Endpoints 6
2.3 Study Design 6
2.4 Sample Size Determination 7
2.5 Schedule of Assessments 7

3. ANALYSIS POPULATIONS 10
3.1 Safety Population 10
3.2 Pharmacokinetic (PK) Population 10
3.3 Analysis of Subgroups 10

4. STUDY MEASURES 10
4.1 Safety Measures 10
4.1.1 Exposure to Study Drug 10
4.1.2 Adverse Events 11
4.1.3 Laboratory Evaluations 11
4.1.4 Vital Signs Evaluations 13
4.1.5 12-lead ECG Evaluations 13
4.1.6 Physical Examination 13
4.2 Pharmacokinetic Concentrations 14
4.3 Pharmacokinetic Parameters 15
4.4 Baseline Characteristics and Other Measures 16
4.4.1 Subject Disposition 16
4.4.2 Protocol Deviations and Eligibility 16
4.4.3 Demographics 17
4.4.4 Baseline Subject Characteristics 17
4.4.5 Medical and surgical History 17
4.4.6 Prior and Concomitant Medications 18
4.4.7 Assignment to Treatment 18

5. STATISTICAL METHODOLOGY 18
5.1 General Statistical Methods 18
5.1.1 Software 18
5.1.2 Definitions 18
5.1.3 Default Descriptive Statistics and Data Presentation Rules 19
5.1.4 Date and Time Display Conventions 19
5.1.5 General Display Conventions 20
5.2 Hypotheses and Decision Rules 21
5.3 Multiple Comparisons and Adjustments for Multiplicity 21
5.4 Covariates 21
5.5 Multi-Centre Data 21
5.6 Handling of Missing Data 21
5.6.1 Efficacy Endpoints 21
5.6.2 Safety Endpoints 21
5.7 Windowing Conventions 22
5.8 Interim Analyses 22

5.9 Clinical Data Interchange Standards Consortium (CDISC) Specifications 22

6. STATISTICAL ANALYSES 22
6.1 Subject Disposition and Analysis Sets 23
6.2 Protocol Deviations and Eligibility 23
6.3 Demographic 23
6.4 Baseline Subject Characteristics 23
6.5 Medical and Surgical History 23
6.6 Prior and Concomitant Medication 24
6.7 Efficacy Analyses 24
6.8 Safety Analyses 24
6.8.1 Exposure to Study Drug 24
6.8.2 Adverse Events 24
6.8.3 Laboratory Parameters 26
6.8.4 Vital Signs 26
6.8.5 12-lead ECG Evaluations 26
6.8.6 Physical Examination 27
6.9 Pharmacokinetic Analyses 27
6.9.1 Plasma Concentrations 27
6.9.2 Pharmacokinetic Parameters 27

7. CHANGES TO THE PLANNED ANALYSES 28
7.1 Changes to the Analyses Described in the Study Protocol and Protocol Amendments 28
7.2 Changes from the Statistical Analysis Plan Version x.x to Version x.x 28

8. REFERENCES 29

9. ATTACHMENTS AND APPENDICES 30
Appendix 1 Dose Proportionality Analysis SAS® Code 30
Appendix 2 Food Effect Analysis SAS® Code 31

ATTACHMENT 1 LIST OF TABLES, LISTINGS AND FIGURES 32

1. Introduction

The purpose of this statistical analysis plan (SAP) is to describe the methodology that will be followed in the analysis of the data that were collected for the Island Pharmaceuticals Ltd, ISLA101-P01-CT001 study.

This SAP is based on assessments and methods described in the study Protocol Amendment Version 1, dated 18 October 2023. The SAP contains a complete and detailed specification of the statistical analyses that will be performed.

All analyses described in this document will be conducted in accordance with Resolutum Global's standard operating procedures (SOPs).

1.1 Rationale

An estimated 3.9 billion people in more than 125 countries are at risk of dengue fever, with approximately 390 million infections occurring annually. These infections lead about 500,000 persons to require hospitalization due to dengue each year, and about 20,000 deaths occur due to severe dengue every year (WHO, 2018). Dengue is a mosquito-borne infection caused by the dengue virus (DENV) and is found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. The severe form of the disease is a leading cause of serious illness and death in some Asian and Latin American countries (WHO, 2021). Importantly, there is no specific treatment for dengue infection.

Dengue prevention and control is based on vector control measures, which require sustained community involvement and usually are not highly effective in preventing disease transmission. In view of the current situation, there is an unmet medical need for therapies focusing on the prophylaxis of dengue infection, aiming to minimize viral transmission in endemic areas. To answer to this need, Island Pharmaceuticals Ltd is developing the ISLA101 product, an immediate-release oral capsule of fenretinide (100 mg), for the prophylaxis of dengue fever. ISLA101 is an oral capsule formulation of fenretinide. Island plans to submit a New Drug Application (NDA) for ISLA101 for the prophylaxis of dengue fever via the 505(b)(2) regulatory pathway.

This study is a randomized, double-blind, placebo-controlled single ascending dose (SAD) study in healthy subjects and is considered appropriate to evaluate the safety, tolerability, and PK of ISLA101. Single ascending doses of ISLA or placebo will be administered under fasting conditions, and safety and tolerability data will be evaluated in each cohort to guide doses administered to future cohorts. The highest tolerated dose will also be administered under fed conditions to assess any potential food effect (in a crossover manner).

2. Summary of the Protocol

2.1 Study Objectives

2.1.1 Primary Objective

The primary objective of the study is to evaluate the safety and tolerability of single ascending doses (SAD) of ISLA101 in healthy adult volunteers (fasted).

2.1.2 Secondary Objectives

The secondary objective of the study is to characterize the pharmacokinetic (PK) profile (fasted) of fenretinide and its metabolites after administration of SAD of ISLA101 in healthy adult volunteers (fasted).

2.1.3 Exploratory Objective

The exploratory objective of the study is to assess the PK profile of fenretinide and its metabolites in healthy adult volunteers under fed conditions.

2.2 Study Endpoints

2.2.1 Primary Endpoints

The primary endpoints are:

- Vital Signs, clinical laboratory tests, changes from baseline in physical examinations, adverse events (AEs) and treatment-emergent adverse events (TEAEs).

2.2.2 Secondary Endpoints

The secondary endpoints are:

- Single dose PK parameters for fenretinide and its metabolites in plasma: Maximum plasma concentration (C_{max}), Time to C_{max} (t_{max}), Area under the curve from time 0 to infinity (AUC_{inf}), Area under the curve to the last concentration (AUC_{last}), Terminal half-life ($T_{½}$) and others as relevant.

2.2.3 Exploratory Endpoints

The exploratory endpoints are:

- Single dose PK parameters for fenretinide and its metabolites in plasma under fed conditions: Maximum plasma concentration (C_{max}), Time to C_{max} (t_{max}), Area under the curve from time 0 to infinity (AUC_{inf}), Area under the curve to the last concentration (AUC_{last}), Terminal half-life ($T_{½}$) and others as relevant.

2.3 Study Design

The study is a randomized, double-blind, placebo-controlled single ascending dose (SAD) study of ISLA101 (fenretinide oral capsules) to evaluate safety, tolerability, and pharmacokinetics in healthy human subjects. The study will consist of up to 4 cohorts that will evaluate dose levels of 300 mg/m^2 (fasted), 600 mg/m^2 (fasted), and 900 mg/m^2 (fasted). The highest tolerated dose level cohort will then be evaluated in a fed condition (in a crossover manner). Eight subjects will be enrolled per dose cohort, with 6 subjects receiving active drug and 2 subjects receiving placebo treatment in a blinded manner. Each subject will be allocated to 1 dose level only.

After completing screening activities, eligible subjects will enter the clinical research unit (CRU) on Day -1 for 5 days. Subjects will receive a single dose of study drug in the morning of Day 1 after an overnight fast of approximately 10 hours, followed by additional 4 hours fast after dose for PK sampling. Cohorts 1 through 3 will receive 300 mg/m^2, 600 mg/m^2, and 900 mg/m^2, respectively, under fasted conditions. After the safety review by the independent safety review committee (SRC), the dose level can be escalated to the planned or lower than planned dose level or de-escalated to an intermediate dose level. Decisions to proceed to the next cohort will be made by the Investigator, SRC, and Sponsor based on the safety data from previous cohort(s).

Safety data will be reviewed to identify the cohort that received the highest dose level under fasted condition. The subjects in this cohort will be recalled to evaluate the PK of ISLA101 under fed conditions (8 subjects; Cohort 4). In Cohort 4, subjects will fast for approximately 10 hours overnight and will consume a high-fat, high-calorie meal approximately 30 minutes prior to administration of study drug. No food consumption will be permitted for at least 4 hours post-dose.

For all cohorts, study drug will be taken with up to 240 mL of water. In fasted cohorts, water will be allowed ad libitum except the interval from 1 hour before to 1 hour after the dose. In the fed cohort, water will be allowed ad libitum except the interval from 10 minutes before to 1 hour after dose.

Subjects will be discharged from the clinic on Day 5. At the discretion of the Investigator or designee, the confinement time can be extended to ensure the safety of each subject. Subjects will have up to 3 days of follow up. For Cohort 4 (the food effect cohort), the confinement and follow-up visit will be repeated. Subjects who are dosed but withdrawn prior to study completion will participate in an Early Termination visit and may be replaced if needed to obtain sufficient information as possible based on the timing.

In all cohorts, safety will be assessed via vital signs, clinical laboratory tests, physical examinations, AEs, and TEAEs. Pharmacokinetic data will be collected and analyzed at the end of the study but will not be used for dose escalation decisions.

2.4 Sample Size Determination

No formal sample size calculation was performed. The study is considered exploratory with a sample size of 8 subjects per cohort (2 placebo + 6 active). This cohort size and active/placebo ratio are considered standard to evaluate safety profile and to provide sufficient PK information for future development of the compound.

2.5 Schedule of Assessments

Table 1 presents the schedule of study events.

Table 1 Study Procedures and Assessment to Dose Under Fasted (Cohort 1-3) and Fed Condition (Cohort 4)

Study Procedure		Cohorts 1-3								Cohort 4						
	Study Period	Screening	Clinic Check-in	Treatment Period					Follow-up/ET	Clinic Check-in	Treatment Period					Follow-up/ET
	Study Day	-28 to -2	-1	1	2	3	4	5	8	9[9]	10	11	12	13	14	17
	Visit Window (days)	N/A	Inpatient						+/-1	+/-3	Inpatient					+/-1
Informed Consent		X								X						
Inclusion/Exclusion Criteria		X	X							X						
Demographics		X														
Height and weight		X								X						
Medical History		X	X							X						
Vital Signs[1]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
12-lead electrocardiogram (ECG)[2]		X	X	X						X	X					
Full Physical Exam		X	X						X	X						X
Hep B, Hep C, HIV		X														
Safety laboratory tests (chemistry, hematology, coagulation, urinalysis)		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Pregnancy test[3]		X	X						X	X						X
FSH[4]		X														
Urine screen for drugs of abuse[5]		X								X						
Alcohol breath test		X	X							X						
Admission			X							X						

Study Procedure		Cohorts 1-3								Cohort 4						
	Study Period	**Screening**	**Clinic Check-in**	**Treatment Period**					**Follow-up/ET**	**Clinic Check-in**	**Treatment Period**					**Follow-up/ET**
	Study Day	-28 to -2	-1	1	2	3	4	5	8	9[9]	10	11	12	13	14	17
	Visit Window (days)	N/A	Inpatient						+/-1	+/-3	Inpatient					+/-1
Study drug administration				X							X[6]					
High-fat, high-calorie breakfast											X					
PK blood samples[7]				X	X	X	X	X			X	X	X	X	X	
Adverse events[8]		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Concomitant medication review		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Discharge								X							X	

ECG = electrocardiogram; ET = early termination; FSH = follicle-stimulating hormone; Hep = hepatitis; HIV =human immunodeficiency virus; PK = pharmacokinetic(s);

1 Vital signs include blood pressure, pulse, respiration and temperature.

2 12-lead ECG will be performed in triplicate at screening, and on Day -1 (check-in) to confirm eligibility, and on Day 1 at 5 hours (±15-minute) post dose. A single ECG will be performed on Day 9 (check-in) and on Day 10 at 5 hours (±15-minute) post dose.

3 A serum pregnancy test will be performed at screening and urine pregnancy test will be performed at check-in and at follow-up for all female subjects.

4 For all female subjects to confirm or refute postmenopausal status.

5 A nicotine urine or breath test may be utilized for tobacco use testing at site discretion.

6 Study drug will be administered approximately 30 minutes after start of a high-fat, high-calorie meal; 100% meal consumption is preferred.

7 PK sampling to assess the PK of fenretinide will be performed at the time points as specified in Table 2.

8 Monitoring for serious adverse events begins when the informed consent form is signed; and treatment-emergent adverse events begins after the first dose is administered.

9 Study day is relative to study drug administration for the subjects in Cohort 3.

3. Analysis Populations

Two (2) different analysis populations will be defined:

- Safety Population
- Pharmacokinetic (PK) Population

The criteria for exclusion from each analysis set will be described in the following sections.

3.1 Safety Population

This Safety Population will include all subjects who received at least 1 dose of study drug (active and placebo).

The following is reason for exclusion from the Safety Population:

- Subjects did not receive at least one dose of study drug.

The Safety Population will be used for all baseline characteristics, disposition and safety analyses and will be based on actual treatment received if different from randomized treatment.

3.2 Pharmacokinetic (PK) Population

The Pharmacokinetic (PK) Population will consist of all subjects in the safety population who received at least one dose of ISLA101 and have a pre-dose PK sample and at least 1 post-dose analyzable PK sample (quantifiable Plasma concentration).

The following are reasons for exclusion from the PK Population:

- Subjects did not receive at least one dose of the ISLA101.
- Subjects did not have at least one quantifiable plasma fenretinide concentration.

Subjects will be analyzed according to the treatment they actually receive if this differs from that to which the subject was randomized. Adverse events (e.g., vomiting within 2 hours of dose), protocol deviations or dosing or sampling issues which may potentially impact PK will be assessed on a subject-by-subject basis.

Subjects with sufficient PK concentrations of fenretinide to allow determination of at least 1 PK parameter from (C_{max} or AUC) will be included in the PK parameters evaluations.

3.3 Analysis of Subgroups

No subgroup analyses are planned for this study.

4. Study Measures

This section describes the measures that were collected and/or derived during the study at the time points specified in the Schedule of Assessments (Section 2.5).

4.1 Safety Measures

The safety endpoints described in this section will be analyzed according to the analysis methods described in Section 6.8.

4.1.1 Exposure to Study Drug

Study drug administration information, including treatment administered (Yes/No), the date/time of last meal, high fat meal taken before dosing (Yes/No), the date/time of high meal consumed, the date/time

of the first capsule consumed, the dosage, the capsule administration quantity, the completion of all administered (Yes/No), the subject fasting for at least 4 hours post-study drug administration (Yes/No) and the calculated body surface area (BSA), will be reported on the 'Study Drug Administration' eCRF.

4.1.2 Adverse Events

An AE is the development of an undesirable medical condition or the deterioration of a pre-existing medical condition, regardless of whether it is considered casually related to the study treatment.

Adverse events data will be collected and recorded on the 'Adverse Events' eCRF from the time that informed consent was given and throughout the duration of the study.

Missing and partial AE dates will be handled according to the rules specified in Sections 5.1.4 and 5.6.2.

4.1.2.1 Adverse Event Definitions

Treatment-emergent AEs (TEAEs) are defined as AEs occurring or worsening after the first administration of the study drug. If only partial information is available, the rules specified in Section 5.6.2 will be applied to determine treatment emergence.

Treatment-related AEs are defined as AEs where the relationship to study drug was reported as 'Possibly', 'Probably" or 'Definitely" Related or where the relationship is missing.

Serious AEs (SAEs) are defined as AEs where the events are reported as serious.

Severe AEs are defined as AEs where the event severity rating is reported as 'Severe'.

Adverse events leading to study drug discontinuation are defined as AEs where the action taken with study drug is reported as 'Drug Withdrawn'.

Adverse events leading to study discontinuation are defined as AEs where 'Other' action taken is reported as 'Withdrawn from study'.

4.1.2.2 Coding of Adverse Event Terms

Adverse event terms (Investigator terms) will be coded to a lowest level term (LLT), preferred term (PT), high level term (HLT), high level group term (HLGT) and a system organ class (SOC) according to the Medical Dictionary for Regulatory Activities (MedDRA) dictionary, Version 26.1 or later, depending on the latest version available during the study.

4.1.3 Laboratory Evaluations

Laboratory evaluations will be performed in accordance with the Schedule of Study Assessments (Section 2.5). Blood and urine samples will be collected and analyzed by a local laboratory and the results of urinalysis will be reported on the 'Dipstick Urinalysis and Microscopy' eCRF and the result of hematology, coagulation, chemistry and microscopy will be provided in electronic format from the analyzing laboratory.

If the results for a specific laboratory test are not required by the study protocol (for example, only one subject has data for a specific test that was performed in error) or for urine microscopy tests that were only required in the presence of abnormal urinalysis results, the results will not be included in the summary tables, but the data will be listed.

The test panels and parameters presented in Table 2 will be collected and analyzed.

Parameter names will be based on the Clinical Data Interchange Standards Consortium (CDISC) Study Data Tabulation Model (SDTM) Controlled Terminology terms. The mapping of the reported parameter names to the standardized names will be presented in the SDTM specifications. Parameters will be sorted alphabetically.

If the results for a parameter were reported in different units, the results (including the actual measurement and the normal range limits) will be converted to the Système International (S.I.) unit for the specific parameter and the standardized results/units will be reported. The specific conversion rules will be documented in the SDTM specifications.

Quantitative laboratory measurements reported as '< X', i.e., below the lower limit of quantification (BLQ), or '> X', i.e., above the upper limit of quantification (ULQ), will be converted to X for the purpose of quantitative summaries, but will be presented as recorded, i.e., as '<X' or '>X' in the listing. Any conversion rules that are applied will be highlighted in the footnotes of the affected tables and listings.

Where applicable, parameter names in the outputs will be comprised of the test name and the standardized unit of measure (if applicable), for example, 'Albumin (g/L)'. If a specific test is qualitative or unitless, the parameter name will be the test name only.

For all parameters where a normal range limit value was reported, the normal range will be derived based on the available lower and upper limit values and any reported mathematical symbols. If both a lower and upper limit value is available, the normal range will be presented as '(Lower, Upper)'. If the event that only one of the limit values exist, 'N/A' will be used to replace the 'missing' limit value (for example, '(N/A, Upper)'), unless a direction has been specified, in which case the normal range will be displayed as '(< or > Limit)'.

Quantitative parameter results will be classified as being 'Low' or 'High' depending on whether the result is below or above the normal range limits provided by the analyzing laboratory.

Baseline and change from baseline values will be derived for each parameter (as appropriate) in accordance with the methods defined in Section 5.1.2.

Table 2 Laboratory Assessments

Hematology:	**Clinical Chemistry:**	**Urinalysis (dipstick)**
Platelet count Red blood cell count (RBC) Hemoglobin Hematocrit White Blood Cell (WBC) count with Differential: Basophils (% and Absolute) Eosinophils (% and Absolute) Lymphocytes (% and Absolute) Monocytes (% and Absolute) Neutrophils (% and Absolute)	ALT (Alanine aminotransferase) Albumin ALP (Alkaline phosphatase) AST (Aspartate aminotransferase) Blood urea nitrogen (BUN) Calcium Carbon dioxide (CO_2) Chloride Creatinine Glucose Inorganic phosphorus Magnesium Potassium Sodium Total bilirubin Total Protein Uric acid	Specific gravity pH Clarity Color Glucose Protein Blood Leukocytes Esterase Bilirubin Ketones Nitrites
Coagulation		**Microscopy (if applicable)**
Prothrombin time (PT) International normalized ratio (INR)		Urinary sediment WBC (White blood cells) RBC (Red blood cells) Casts Crystals Epithelial cells Bacteria

4.1.4 Vital Signs Evaluations

Vital signs will be performed according to the schedule of assessment (Section 2.5).

The following parameters will be assessed, and measurements and findings will be reported on the 'Vital Signs' eCRF:

- Systolic blood pressure (SBP) (mmHg).
- Diastolic blood pressure (DBP) (mmHg).
- Pulse rate (beats/min).
- Respiratory Rate (breaths/min)
- Temperature (°C)
- Height (cm) (Screening only)
- Body Weight (kg) (Screening only)
- Body Mass Index (kg/m^2) (Screening only)
- Body Surface Area (BSA) (m^2)

Baseline and change from baseline values will be derived for each parameter (as appropriate) in accordance with the methods defined in Section 5.1.2

4.1.5 12-lead ECG Evaluations

Triplicate and single 12-lead ECG recordings will be performed according to the schedule of assessments (Section 2.5).

The following parameters will be assessed, and measurements and findings will be reported on the '12-lead Electrocardiogram' eCRF:

- Heart Rate (beats/min)
- RR Interval (msec)
- QTcF Interval (msec).
- PR Interval (msec).
- QRS Duration (msec).
- Overall Assessment ('Normal', 'Abnormal Not Clinically Significant [NCS]' or 'Abnormal Clinically Significant [CS]').

Baseline and change from baseline values will be derived for each parameter (as appropriate) in accordance with the methods defined in Section 5.1.2.

4.1.6 Physical Examination

Complete physical examinations will be performed in accordance with the schedule of assessments (Section 2.5).

The following body systems will be assessed as part of the physical examination findings and clinical significance as assessed by the investigator ('Normal', 'Abnormal NCS', 'Abnormal CS' including specification of any abnormalities observed) will be recorded on the 'Physical Examination' eCRF:

- General appearance
- Head, ears, eyes, nose, and throat

- Neck and thyroid
- Lymph nodes
- Cardiovascular system
- Respiratory System
- Gastrointestinal system
- Renal system
- Neurological system
- Musculoskeletal system
- Skin
- Other

4.2 Pharmacokinetic Concentrations

Plasma PK samples will be collected at the time points specified in the schedule of assessments (Section 2.5) and Table 3. The PK samples from pre-dose to 96 hours post dose will be considered. The actual sample collection dates and times will be reported on the 'PK Blood Sample Collection' eCRF.

Table 3 Study Schedule and Sampling Time Points for Pharmacokinetic Analysis

		Time Relative to Dose (hours)[a]	-1	0.5	0.75	1	1.5	2	3	4	5	6	8	10	12	24	36	48	72	96
		Assessment Window (minutes)[b]	+/-2				+/-5			+/-15					+/-30					
Study Day	Cohorts 1-3	1	X	X	X	X	X	X	X	X	X	X	X	X	X					
		2														X	X			
		3																X		
		4																	X	
		5																		X
	Cohort 4	10	X	X	X	X	X	X	X	X	X	X	X	X	X					
		11														X	X			
		12																X		
		13																	X	
		14																		X

a: Time from dose begins when first capsule is consumed

b: Vital signs should be assessed prior to PK samples taken

The actual elapsed time (hours) from the reference study drug administration will be calculated as the difference between the actual date time of the sample collection at the nominal time point and the date time of the study drug administration for the specific period.

The time deviation at each time point (minutes), defined as the difference between the nominal (planned) and actual collection times will be calculated as the difference between the nominal collection time point value (i.e., 2 hours post-dose will be 2 hours).

For pre-dose visit, the actual elapsed time from the reference study drug administration and the time deviation will be presented as '- '.

Deviations from the collection time points will be used to identify out of window samples that may be excluded from the PK analysis (and PK parameter derivation) if deemed to have a major impact on the overall analysis.

The plasma concentrations of fenretinide and its metabolites N-(4-methoxyphenyl) retinamide (MPR) and 4-oxo-N-(4-hydroxyphenyl) retinamide (oxo-HPR) will be determined using a validated analytical procedure. Specifics about the analytical method will be provided in the bioanalysis report. Concentrations data will be provided electronically by the analyzing laboratory.

Concentrations that are below limit of quantification (BLQ) prior to the first measurable concentration will be set to zero for all calculation and analyses. BLQ concentrations observed after the first measurable concentration will be treated as missing. In addition to statistical descriptors, number of BLQ concentrations will be presented in the summary for each treatment and time point.

4.3 Pharmacokinetic Parameters

The PK parameters described in this section will be derived based on the plasma concentration-time profiles of fenretinide, MPR and oxo-HPR as observed after the study drug administrations on Day 1 for Cohort 1-3 and Day 10 for Cohort 4 if the data permits using actual timepoints for PK samples. The parameters will be calculated separately for each cohort based on concentrations collected during the specific period.

The PK concentrations will be processed using standard noncompartmental analytical procedures to derive the required parameters. The software used for the analysis will be Phoenix™ WinNonlin® v8.4.0 or greater (Certara, Princeton NJ, USA). Extravascular plasma model with linear up log down trapezoidal rule will be utilized.

The PK parameters described in Table 4 will be derived for the analytes (fenretinide, MPR and oxo-HPR) provided that the required concentration data are available. Supporting PK parameters (used to derive or assess the validity of λ_z and associated parameters) which include Adjusted R^2, number of points for estimation of λ_z or K_{el} , $\%AUC_{extrap}$ and span (ratio of time interval to estimate λ_z to $t_{1/2}$) will only be listed and not included in the summary tables. $\%AUC_{extrap} < 20\%$ will be used to validate AUC_{inf} and parameters derived from AUC_{inf}.

Table 4 Plasma PK Parameters

Parameter	Definition
C_{max}	Maximum concentration which is directly determined from the plasma concentration-time profiles.
T_{max}	Time to maximum observed plasma concentration. If the same C_{max} concentration occurs at different time points, T_{max} is assigned to the first occurrence of C_{max}.
AUC_{inf}	The area under the plasma concentration-time curve from time 0 (time of dosing) extrapolated to infinity. AUC_{inf} is calculated as the sum of AUC_{last} plus the ratio of the last measurable plasma concentration (C_{last}) to the elimination rate constant (λ_z), calculated by 'the linear up and log down' method.
AUC_{last}	Area under the drug concentration-time curve, from time 0 (time of dosing) to the last measurable concentration.
AUC_{0-24}	The area under the plasma concentration-time curve, from time 0 (time of dosing) to 24 hours, calculated by 'the linear up and log down' method.
λz or kel	Apparent terminal elimination rate constant calculated by linear regression of the terminal linear portion of the log concentration vs. time curve.
$T_{1/2}$	Apparent plasma terminal half-life calculated as ln (2)/λ_z.
C_L/F	Apparent total plasma clearance, using the following formula: Dose/AUC_{inf} (Parent compound only).

Parameter	Definition
Vz/F	Apparent volume of distribution, using the formula: $C_L/F/\lambda_z$ (Parent compound only).
DN_C_{max}	Dose-normalised C_{max} will be calculated by dividing C_{max} by the total administered dose in mg (C_{max}/Dose).
DN_AUC_{inf}	Dose-normalised $AUC_{0\text{-}inf}$ will be calculated by dividing AUC_{inf} by the total administered dose in mg (AUC_{inf} /Dose).
DN_AUC_{last}	Dose-normalised $AUC_{0\text{-}last}$ will be calculated by dividing AUC_{last} by the total administered dose in mg (AUC_{last}/Dose).
Adjusted R^2 (*)	R-squared adjusted.
No. of Points (*)	Number of points for determination of λz.
Span(*)	Span = ($\lambda_{z\ upper} - \lambda_{z\ lower}$)/ $t_{1/2}$ (h).
AUC%extrap(*)	The percentage of the AUC that has been extrapolated beyond the last observed data point, using the following formula, calculated by 'the linear up and log down' method
Values for λ_z, $t_{½}$, AUC_{inf}, CL/F and V_z/F will not be reported for cases that do not exhibit an acceptable terminal log-linear phase in the concentration versus time profile. Additional pharmacokinetic parameters may be determined where appropriate. (*) Derived to determine $t_{1/2}$, results will only be listed.	

λz and $T_{1/2,}$ will only be included in the summary statistics if the following criteria are met:

- A minimum of 3 measurable concentration-time points is available during log-linear portion of the terminal elimination phase (excluding C_{max}), i.e., No. of Points is ≥ 3.
- Adjusted $R^2 > 0.80$.

AUC_{inf} , C_L/F and V_z/F will only be included in the summary statistics if the following criterion is met:

- $\%AUC_{extrap} < 20\%$.
- Span ≥ 2

4.4 Baseline Characteristics and Other Measures

4.4.1 Subject Disposition

Subject disposition data will be collected on the 'End of Study Participation' eCRF when a subject completed or early terminated the study.

The following data will also be presented in the disposition listing:

- Date of informed consent ('Informed Consent' eCRF),
- Date/time of the first study drug administrations ('Study Drug Administration' eCRF.)

The number of subjects included in the analysis sets defined in Section 3 will be summarized and presented as part of the subject disposition data.

4.4.2 Protocol Deviations and Eligibility

Protocol deviations will be reported on the 'Protocol Deviation' eCRF.

Protocol deviations will be grouped by deviation grade (minor/major), deviation term, assessment type, and a description of the deviation will also be noted.

Eligibility will be reported on the 'Eligibility Confirmation' eCRF.

The eligibility of all subjects for entry into the study will be assessed at Screening and Day -1 (For Cohort 1-3)/Day 9 (for Cohort 4). A subject should have met all the inclusion, and none of the exclusion criteria before entry into the study.

4.4.3 Demographics

Demographic information provides data about the subjects and is necessary to determine whether the individuals in the study are a representative sample of the target population.

The following demographic data will be collected on the 'Demography' eCRF at Screening.

- Year of birth
- Age (Years)
- Sex ('Male', 'Female')
- Childbearing Potential (Yes/No) -If yes, the menopausal status
- Ethnicity ('Hispanic or Latino', 'Not Hispanic or Latino', 'Not Reported', 'Unknown')
- Race:
    - 'White'
    - 'Black or African American'
    - 'Asian'
    - 'American Indian or Alaska Native'
    - 'Native Hawaiian or Other Pacific Islander'
    - 'Other'
    - 'Not Reported'
    - 'Unknown'

4.4.4 Baseline Subject Characteristics

Baseline subject characteristics include characteristics that subjects presented with prior to the administration of study drug.

The following subject characteristics will be collected on the 'Vital Signs' eCRF at Screening (for Cohort1-3) and on Day 9 (for Cohort 4):

- Height (cm)
- Body Weight (kg)
- Body Mass Index (BMI) (kg/m^2)

The following other baseline data will also be collected:

- Alcohol Breath Test ('Alcohol Breath Test' eCRF)
- Pregnancy Test ('Pregnancy Test' eCRF)
- Serology – hepatitis B surface antigen, hepatitis C antibody titer, and HIV ('Serology' eCRF)
- Urine Drug Screen ('Urine Drug Test' eCRF)

4.4.5 Medical and surgical History

Medical history is information about conditions that a subject might have suffered from prior to the administration of study drug, or conditions that were ongoing at the time of the administration of study drug.

Medical and surgical history data will be collected on the 'Medical and Surgical History' eCRF.

4.4.5.1 Coding of Medical History Terms

Medical and surgical history terms (Investigator terms) will be coded to a lowest level term (LLT), preferred term (PT), high level term (HLT), high level group term (HLGT) and a system organ class (SOC) according to the Medical Dictionary for Regulatory Activities (MedDRA) dictionary, Version 26 or later, depending on the latest version available during the study.

4.4.6 Prior and Concomitant Medications

Prior and concomitant medications/vaccinations data will be collected throughout the study on the 'Prior and Concomitant Medications' eCRF.

Missing and partial concomitant medications dates will be handled according to the rules specified in Sections 5.1.4 and 5.6.2.

4.4.6.1 Medication Definitions

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

Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of study drug. Medications stopping on the same day as the first study drug administration will be considered as concomitant medications.

4.4.6.2 Coding of Medication Terms

Prior and concomitant medication terms will be coded to an anatomical therapeutic chemical (ATC) class term (Level 2) and a preferred medication name based on the active drug substance using the World Health Organization-Drug Dictionary (WHO-DD), Version Global C3, Sep 2023.

4.4.7 Assignment to Treatment

Subjects will be randomized to a treatment and the randomization number will be reported on the 'Randomization' eCRF. The randomization information collected on the 'Randomization' eCRF will be listed.

5. Statistical Methodology

5.1 General Statistical Methods

5.1.1 Software

All analysis data sets and outputs will be produced by the Biostatistics Department of Resolutum Global using the SAS® Version 9.4 (SAS Institute, Cary, North Carolina, USA) or higher.

The pharmacokinetic concentrations will be processed using standard noncompartmental analytical procedures to derive the required parameters. The software used for the analysis will be Phoenix™ WinNonlin® v8.4.0 or greater (Certara, Princeton NJ, USA).

5.1.2 Definitions

The following definitions will be used:

- Date of the First Study Drug Administration: The date of the first study drug administration is defined as the earliest date on which study drug was administered as reported on the 'Study Drug Administration' eCRF.
- Baseline: The baseline value is defined as the last available valid assessment collected prior to the first study drug administration. Repeat and unscheduled assessments will be included in

the derivation of the baseline values. Results including, but not limited to, 'Not done', 'Not applicable', 'Unknown' will not be included in the baseline derivations.

Baseline calculation for the ECG parameters will be based on the mean value of the triplicate ECG reading at baseline visit for Cohort 1-3.

- Change from Baseline: The change from baseline value is defined as the difference between the result collected/derived at a post-baseline visit and the baseline value (for that specific period for changes from the baseline values).

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

  Change from Baseline Value = Result at Post-Baseline Visit – Baseline Value

  The change from baseline value will only be calculated if the specific post-baseline result and the baseline value for the parameter are both available and will be treated as missing otherwise. In the data listings, the change values will be set to '-' (not applicable) for pre-baseline assessments.

- Study Day: The study day of an event is defined as the relative day of the event starting with the date of the first study drug administration (reference date) as Day 1 (there will be no Day 0).

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

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

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

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

  Study days will only be calculated for events with complete dates and will be undefined otherwise.

5.1.3 Default Descriptive Statistics and Data Presentation Rules

Unless otherwise stated, summary statistics including the number of subjects, mean, standard deviation, median, minimum, and maximum, will be presented for all continuous variables. Minimum and maximum values will be presented to the same decimal precision as the raw values, the mean and median values to one more and the standard deviation values to two more than the raw values. Derived values (including descriptive statistics) will be presented to a maximum of 4 significant decimals.

For categorical variables, per category, the absolute counts (n) and percentages (%) of subjects with data, and if appropriate, the number of subjects with missing data, will be presented. Unless specifically stated otherwise, denominator for all percentage calculations will be the number of subjects in the specific treatment group and analysis set. All percentages will be presented to one decimal place except for 100%. Where a count is zero, the percentage will not be shown (e.g., 0 (0.0%) will be displayed as 0).

If required, results will be rounded using the SAS® function ROUND. Values will be rounded after all calculations have been performed.

5.1.4 Date and Time Display Conventions

The following display conventions will be applied in all outputs where dates and/or times are displayed:

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

If only partial information is available, unknown components of the date or time will not be presented, for example if only the year is known, '2016'. Times will be reported using a 24-hour clock.

5.1.5 General Display Conventions

All data collected during the study (data originating from the eCRFs or electronic transfers), except for screen failure data, will be presented in the data listings. Event-based listings will be sorted by cohort, treatment group, subject number and event start and end dates. Assessment-based listings will be sorted by cohort, treatment group, subject number, parameter name (alphabetically unless specifically stated otherwise), visit and time point (if applicable).

Fields that are missing because they are not applicable for the subject/time point (for example change from baseline results at the baseline visit) will be presented as "-", unless otherwise specified. Missing data points will be presented as blank fields in the data listings.

All summary tables will be presented by the treatment group. Assessment-based tables will be sorted alphabetically by parameter (unless specifically stated otherwise) and chronologically by visits/time point within parameter. Only values collected at scheduled study visits/time points will be presented in summary tables. Event-based tables will be ordered as specified in Section 6.

Treatment groups will be presented based on increasing dose levels of ISLA101 followed by a pooled Placebo groups and an All-Subjects group (only for the baseline tables).

Tables 5,6, and 7 present the treatment group, and visit labels that will be used in the tables, listings, and figures (TLFs).

Table 5 Study Treatments – Tables and Figures

Cohort: Actual Treatment	Treatment Label
Cohort 1: ISLA101 300 mg Fasted	ISLA101 300 mg Fasted
Cohort 2: ISLA101 600 mg Fasted	ISLA101 600 mg Fasted
Cohort 3: ISLA101 900 mg Fasted	ISLA101 900 mg Fasted
Cohort 4: ISLA101 TBD* mg Fed	ISLA101 TBD* mg Fed
Cohort x/4: ISLA101 TBD* mg	ISLA101 TBD* mg Fasted/Fed
Cohort 1-3: Placebo	Pooled Placebo
Cohort 4: Placebo (Fasted)	Placebo (Fasted)
Cohort 4: Placebo (Fed)	Placebo (Fed)
Cohort 1-3	All Subjects
*One of the Cohort 1 to 3 Subjects (the highest tolerated dose-level cohort) will return for additional dose to determine the effect of food. Subjects participating in Cohort 4, the food effect cohort, will maintain the same treatment assignment from their fasted cohort.	

Table 6 Study Treatments – Listings

Cohort: Actual Treatment	Treatment Label
Cohort 1: ISLA101 300 mg Fasted	Cohort 1: ISLA101 300 mg Fasted
Cohort 1: Placebo	Cohort 1: Placebo Fasted
Cohort 2: ISLA101 600 mg Fasted	Cohort 2: ISLA101 600 mg Fasted
Cohort 2: Placebo	Cohort 2: Placebo Fasted
Cohort 3: ISLA101 900 mg Fasted	Cohort 3: ISLA101 900 mg Fasted
Cohort 3: Placebo	Cohort 3: Placebo Fasted
Cohort 4: ISLA101 TBD* mg Fed	Cohort 4: ISLA101 TBD* mg Fed
Cohort 4: Placebo	Cohort 4: Placebo Fed
*One of the Cohort 1 to 3 Subjects (the highest tolerated dose-level cohort) will return for additional dose to determine the effect of food.	

Table 7 Study Visits

Actual Visit	Summary Table Treatment Label	By-subject Listing Treatment Label
Screening		Screening
Day -1 – Clinic Check-In	Baseline	Day -1
Day 9 -Clinic Check-In		Day 9
Day 1	Day 1	Day 1
Day 10		Day 10
Day 2	Day 2	Day 2
Day 11		Day 11
Day 3	Day 3	Day 3
Day 12		Day 12
Day 4	Day 4	Day 4
Day 13		Day 13
Day 5 - Discharge	Day 5	Day 5
Day 14 - Discharge		Day 14
Day 8 – Follow Up/ET	Follow-up	Day 8 – Follow UP
Day 17 – Follow Up/ET		Day 17 – Follow Up
Unscheduled		Unscheduled
		Early Termination*
*If early termination occurred, the visit labels “Day 8 – Follow Up” and “Day 17 – Follow Up” will be marked as “Early Termination”.		

5.2 Hypotheses and Decision Rules

Not applicable for this study.

5.3 Multiple Comparisons and Adjustments for Multiplicity

Not applicable for this study.

5.4 Covariates

Not applicable for this study.

5.5 Multi-Centre Data

Not applicable for this study.

5.6 Handling of Missing Data

5.6.1 Efficacy Endpoints

Not applicable for this study.

5.6.2 Safety Endpoints

Missing start dates/times will be imputed to one minute after the study drug administration.

Partial start dates will be imputed to the last day of the month/year considering that the start date should not be after the stop date/time. Missing start times will be imputed to ‘23:59’. If the imputation results in the start date/time being after the stop date/time, the start date/time will be set to the stop/date time.

The imputation method will only be used to determine treatment emergence and to determine the time of the event relative to the first administration of study drug. If no clear determination can be made, the event will be deemed to have started at the same time as the study drug, i.e., the event will be analyzed as being treatment emergent.

Stop dates/times will not be imputed if the AE is ongoing.

A worst-case approach will be followed in the event of missing severity or causality data. If the severity is missing, 'Severe' will be imputed. If causality data are missing, 'Definitely Related' will be imputed.

Missing/partial concomitant medication dates will be handled in a similar fashion as described for the adverse event dates.

5.7 Windowing Conventions

Not applicable.

5.8 Interim Analyses

No interim analyses are planned for this study.

5.9 Clinical Data Interchange Standards Consortium (CDISC) Specifications

The study data will be converted into CDISC-compliant datasets based on the Study Data Tabulation Model Implementation Guide (SDTMIG) Version 3.3 and the Analysis Data Model Implementation Guide (ADaMIG) Version 1.1.

The SDTM data package will be based on raw data (clinical database and external data) and will include SAS® datasets and transport files (.XPT format) for each required SDTM domain, as well as the SDTM Case Report Tabulation Data Definition Specifications (CRT-DD) (define.xml Version 2.1) that describes the origin of the data and all the derivations and imputations that were applied, and includes an SDTM-annotated CRF and the Study Data Reviewer's Guide (SDRG).

The ADaM datasets will be based on the SDTM datasets and will be used for the analysis. The ADaM data package will include SAS® datasets and transport files (.XPT format) for each analysis dataset, as well as the ADaM CRT-DD (define.xml Version 2.1) and the Analysis Data Reviewer's Guide (ADRG).

The SDTM and ADaM data packages will be validated using Pinnacle 21 Community (531 Plymouth Road, Suite 508, Plymouth Meeting, PA 19462) and the validation reports will be included with the respective data packages.

All data conversions will be performed using SAS® Version 9.4 or higher (SAS Institute, Cary, North Carolina, USA) with program code prepared specifically for the study.

The output SAS® programs will generate rich-text-formatted (RTF) output with the ".RTF" extension using the SAS® Output Delivery System (ODS). Each output display will show the name of the SAS® program which was used to produce it.

6. Statistical Analyses

The baseline cohort 1 to 4 results will be presented in the same outputs. Furthermore, the results from the highest tolerated dose-level cohort (fasted results) in one of Cohort 1 to Cohort 3 will be presented with the results of Cohort 4 (fed results) (where appropriate).

Summary tables and analyses will be based on the specified analysis population in each section. Data listings will be based on the Safety Population unless specifically stated otherwise.

6.1 Subject Disposition and Analysis Sets

Summary tables will be based on the Safety Population.

The number and percentage of randomized subjects, subjects completing or discontinuing from the study as well as the primary reason for discontinuation will be presented by treatment group and for all subjects overall in the subject disposition table. The denominator for the reason for discontinuation from the study percentage calculations will be the number of subjects that discontinued from the study.

All subject disposition information (as described in Section 4.4.1) will be listed together with the date that the subjects provided informed consent and the date/time of the first study drug administration in the subject disposition listing.

The number of subjects included in the analysis populations defined in Section 3 will be summarized along with the reasons for exclusion from any analysis population by treatment group and for all subjects overall using frequencies and percentages.

In addition, the inclusion/exclusion of each subject into/from each of the defined analysis set will be listed.

The randomization information (where applicable) including the randomized treatment group will be listed.

6.2 Protocol Deviations and Eligibility

Summary tables will be based on the Safety Population.

The number and percentage of subjects with at least one protocol deviation, at least one major protocol deviation, and at least one minor protocol deviation, as well as the number and percentage of subjects with a deviation in each of the deviation categories will be presented by treatment groups in the protocol deviation table. Subjects will be counted once per category, but all deviations will be counted.

All protocol deviation information and all eligibility data will be listed.

6.3 Demographic

Summary tables will be based on the Safety Population.

Demographic data (as described in Section 4.4.3) will be summarized and presented by treatment group and for all subjects overall in the demography table. The homogeneity between treatments will be assessed based on the descriptive statistics only.

All collected and derived demographic data will be listed.

6.4 Baseline Subject Characteristics

Summary tables will be based on the Safety Population.

Baseline subject characteristics data (as described in Section 4.4.4) will be summarized and presented by treatment groups and for all subjects overall in the baseline characteristics table.

The vital sign parameters will be listed as part of the vital signs listing.

The listings of alcohol breath test results, serology test results, pregnancy test results and urine drug test results will include all available results (collected at scheduled and unscheduled visits) in the clinical database.

6.5 Medical and Surgical History

Summary tables will be based on the Safety Population.

Medical and surgical history conditions will be summarized by SOC and by PT within SOC by treatment group and for all subjects overall. Within each category, the number of subjects who experienced a condition (frequency and percentage) and the actual number of events (frequency only) will be presented by treatment group and for all subjects overall. Subjects who experienced the same condition on more than one occasion (based on the specific category) will only be counted once in each relevant category (SOC and PT), but all conditions will be included in the event frequencies. System organ class terms will be sorted alphabetically, and preferred terms will be sorted alphabetically within SOCs in the table.

In addition to the coded terms, the number of subjects with at least one medical and surgical history condition and the total number of events will be presented.

All information that was collected as well as the coded MedDRA terms will be included in the listing. Partial dates will not be imputed.

6.6 Prior and Concomitant Medication

Summary of concomitant medication table will be based on the Safety Population.

Concomitant mediations will be summarized by WHO-DD ATC Level 2 term and preferred medication name. Within each ATC term and preferred name, the number of subjects who used the medication (frequency and percentage) will be presented. Subjects who used the same medication on multiple occasions will only be counted once. ATC terms and preferred names with ATC term will be sorted alphabetically.

In addition to the summaries by the WHO-DD terms, the number of subjects who used at least one concomitant medication during the study will be presented.

All information as well as the WHO-DD terms, will be included in the relevant prior and concomitant medication listings. Furthermore, the relative medication starts, and end days (relative to the first study drug administration) will be presented where complete medication start and end dates are available.

6.7 Efficacy Analyses

Not applicable for this study.

6.8 Safety Analyses

Statistical methods for the safety analyses will be descriptive in nature and no formal statistical comparisons will be made. Endpoints will be summarized by the treatment group based on the methods described in Section 5.1.

Safety endpoints will be analyzed based on the Safety Population according to the actual treatment received.

All listings will be presented by treatment group.

6.8.1 Exposure to Study Drug

All collected study drug administration data (as described in section 4.1.1) will be listed.

6.8.2 Adverse Events

All tables will present the number of subjects who experienced an AE (count and percentage) and the actual number of AEs (count only) within each specific category by treatment group. Subjects who experienced multiple AEs will only be counted once in each relevant category (high-level summary, SOC, PT, severity rating or relationship to study drug category), but all events will be included in the event counts. Percentages will be based on the number of subjects in the Safety Population. Tables will only include treatment-emergent events.

The overall summary of TEAEs table will present the total number of subjects who experienced a TEAE and the total number of TEAEs in each of the following categories:

- At least one TEAE.
- At least one serious TEAE.
- At least one severe TEAE.
- At least one treatment-related TEAE.
- At least one TEAE leading to study discontinuation.
- At least one TEAE leading to study drug discontinuation.

The incidence of TEAEs table will include the number and percentage of subjects who experienced at least one TEAE and the corresponding number of events, and furthermore summarize the TEAE data by SOC and preferred term (PT) within SOCs. SOC/PT terms will be sorted alphabetically.

The incidence of serious TEAE table will include the number and percentage of subjects who experienced at least one serious TEAE and the corresponding number of events, and furthermore summarize the serious TEAE data by SOC and preferred term within SOCs. SOC/PT terms will be sorted alphabetically.

The incidence of treatment-related TEAEs table will include the number and percentage of subjects who experienced at least one treatment-related TEAE and the corresponding number of events, and furthermore summarize the treatment-related TEAE data by SOC and PT within SOCs. SOC/PT terms will be sorted alphabetically.

The incidence of TEAEs by severity rating table will include the number and percentage of subjects who experienced at least one TEAE, at least one TEAE within each severity rating (‘Mild’, ‘Moderate’, ‘Severe’) and the corresponding number of events for each severity rating. In addition, the TEAE data will be summarized by SOC, PT within SOCs, and severity rating within SOC and PT. SOC/PT terms will be sorted alphabetically, and severity ratings will be sorted in increasing order of severity (Mild to Severe) within SOCs and PTs in the table.

The incidence of TEAEs by relationship to study drug (causality) table will include the number and percentage of subjects who experienced at least one TEAE, at least one TEAE within each relationship to study drug category (‘Unrelated’, ‘Unlikely’, ‘Possibly’, ‘Probably’, Definitely’) and the corresponding number of events for each category. In addition, the TEAE data will be summarized by SOC, PT within SOCs, and relationship category within SOC and PT. SOC/PT terms will be sorted alphabetically, and relationship category will be sorted from the least to the strongest relationship to study drug (Unrelated to Definitely) within SOCs and PTs in the table.

The incidence of TEAEs leading to study drug discontinuation will include the number of subjects who experienced at least one TEAE that lead to study drug discontinuation and the corresponding number of events, and furthermore summarize the TEAE data by SOC and preferred term within SOCs. SOC/PT terms will be sorted alphabetically.

The incidence of TEAEs leading to study discontinuation will include the number of subjects who experienced at least one TEAE that lead to study discontinuation and the corresponding number of events, and furthermore summarize the TEAE data by SOC and preferred term within SOCs. SOC/PT terms will be sorted alphabetically.

The listing of AEs will include all AE data in the clinical database. The listing will present all the information (fields) collected on the ‘Adverse Event’ eCRF, as well as the SOC and preferred terms obtained from the MedDRA dictionary. In addition, the AE start and end days (relative to the first study drug administration) and a flag indicating whether the AE was treatment emergent will be presented. Non-TEAEs will not be assigned to any treatment. If the AE was ongoing at the end of the study,

'Ongoing' will be presented under the 'End Date Time/Study Day' heading. Partial dates/times will be presented as described in Section 5.1.4.

The subsets of SAEs, treatment-related AEs, AEs leading to the discontinuation of study drug will be listed separately and will include all the information presented in the main AE listing.

6.8.3 Laboratory Parameters

The laboratory parameters described in Section 4.1.3 will be summarized and listed.

The summary tables of hematology, coagulation and biochemistry results will present summary statistics for each laboratory parameter within the specific test panel by treatment group. For each parameter, summaries will be presented for the baseline and each scheduled post-baseline visit. In addition, summaries will be presented for the change from baseline values at each scheduled post-baseline visit. Refer to Section 4.1.3 for the handling of character results.

The summary of hematology, coagulation, and biochemistry shift tables will present summaries for the shifts in the result classifications ('Normal', 'Low', 'High') from the baseline to each of the scheduled post-baseline visit for each parameter with a defined reference range, within the specific test panel.

The listings of hematology, coagulation and biochemistry data will include all laboratory data (collected at scheduled and unscheduled visits) in the clinical database. The listings will present all the information (fields) that is available in the laboratory dataset. In addition, the observation that was used as the baseline records (values) for each parameter will be flagged, the change from baseline value and the derived result classification (based on the normal ranges where applicable) at each post-baseline visit will be presented.

The summary of urinalysis table will present the number and percentage of subjects for each or the result classifications (Normal, Abnormal NCS and Abnormal CS) for the baseline, each scheduled post-baseline per parameter.

The listing of urinalysis (including microscopy) data will include all laboratory data (collected at scheduled and unscheduled visits) in the clinical database. The listings will present all the information (fields) that is available in the laboratory dataset. In addition, the observation that was used as the baseline record (value) for each parameter will be flagged.

The FSH parameters will be listed as part of the pregnancy listing.

6.8.4 Vital Signs

The vital signs parameters described in Section 4.1.4 will be summarized and listed.

The summary tables of vital signs results will present summary statistics for results at the baseline and each scheduled post-baseline visit for each parameter by treatment group. In addition, summaries will be presented for the change from baseline values (baselines) at each scheduled post-baseline visit.

The listings of vital signs results will include all data (collected at scheduled and unscheduled visits) in the clinical database. The observations that were used as the baseline records for each parameter will be flagged and the change from baseline values at each post-baseline visit will be presented. Height, weight, derived BMI and BSA will be listed only.

6.8.5 12-lead ECG Evaluations

The 12-lead ECG parameters described in Section 4.1.5 will be summarized and listed.

The summary of ECG results tables will present summary statistics for results at the baseline and each scheduled post-baseline visit for each parameter by treatment group. In addition, summaries will be presented for the change from baseline values at each scheduled post-baseline visit.

The summary of ECG overall assessment table will present summaries for the baseline and each scheduled post-baseline visit for the overall result (Normal, Abnormal not clinically significant and Abnormal clinically significant).

If multiple tracings are conducted as part of one assessment, the mean of the three tracings per parameter and the worst clinical interpretation per timepoint will be summarized for each subject. All values will be listed including the mean value per parameter and the worst clinical interpretation. Changes from baseline will be calculated based on the mean values of the triplicates where appropriate.

The listings of ECG results will include all data (collected at scheduled and unscheduled visits) in the clinical database. The observations that were used as the baseline records for each parameter will be flagged and the change from baseline values at each post-baseline visit will be presented.

6.8.6 Physical Examination

The physical examination assessment data described in Section 4.1.6 will be listed.

6.9 Pharmacokinetic Analyses

6.9.1 Plasma Concentrations

The analysis of the PK concentration data will be based on the PK population. The PK analysis will be conducted separately for fenretinide and its metabolism (MPR and oxo-HPR) based on the available concentrations data (data permitting). Results will be presented by treatment group and study visit/ time point.

The plasma concentrations data for Fenretinide, MPR and oxo-HPR will be summarized by treatment group and nominal collection time points using the statistics described in Section 5.1.3. Below the lower limit of quantification (BLQ) concentration that occurred prior to the first quantifiable concentration will be set to 0 and treated as missing otherwise, for the calculation of summary statistics. The number of BLQ concentrations per treatment group per time point will be included in the summary of concentrations. Zero values will be excluded from the calculation of the geometric statistics. Missing values will be omitted from the calculation of descriptive statistics.

For Cohort 1 to 3, figures of the individual plasma concentrations vs. actual time profiles (all subjects within a treatment group on the same plot) will be presented on a linear and a log-linear scale for 3 analytes (Fenretinide, MPR and oxo-HPR). For the food effect cohort (Cohort 4 and one of the Cohort 1 to 3), the individual fasting and fed (fasted and fed results for all subjects in separate plots, and plots showing each subject's fasting and fed results in the same plot) plasma concentrations vs. actual time profiles will be presented on linear and log-linear scales. BLQ concentrations that occurred prior to the first quantifiable concentration will be set to 0 and treated as missing otherwise in the linear plots. BLQ concentrations will be set to missing in the log-linear plots.

Mean concentration with error bars for standard deviations vs. nominal time curves will be presented on a linear and log-linear scale for 3 analytes (Fenretinide, MPR and oxo-HPR). All treatment groups will be presented on the same plot. Standard deviation bars will also be presented.

All plasma concentration data will be listed, and the listing will include the calculated elapsed time since the study drug administration in the specific period and the time deviations between the actual and planned sample collection times.

6.9.2 Pharmacokinetic Parameters

The calculated plasma PK parameters described in Section 4.3 will be summarized by treatment group using the statistics described in Section 5.1.3. For T_{max} and $T_{1/2}$, only n, median, minimum, and maximum will be presented. The summary tables will be based on the PK population. The food effect analysis will be analyzed separately based on the food effect cohorts.

The dose proportionality of fenretinide will be evaluated across Cohort 1 to Cohort 3 under fasted condition based on the AUC_{inf}, AUC_{last} and C_{max} values, using a power model and a graphical evaluation of the results.

The power model will be used to estimate the slope parameters and the 90% confidence interval (CI) for the slope. The power model is a linear regression model constructed with the natural log transformed dose as the independent variable and the natural log-transformed PK parameter as the dependent variable. The resulting estimated slope (β) is a measure of dose proportionality, i.e., the relationship is dose proportional when β=1. Associated 90% confidence intervals (CIs) will be presented. Refer to Appendix 1 for the SAS® code that will be used for the analysis. Scatter plots with the power model regression line will be prepared with the natural log-transformed PK parameter results as the values on the y-axis, and the natural log-transformed dose level as the values on the x-axis. The plot will also include the mean parameters values and standard error bars.

The food effect analysis of fenretinide (for cohort 1 to Cohort 3, the highest tolerated dose level cohort will then be evaluated in a fed condition) will be conducted to evaluate the effect of food on fenretinide based on the parameters AUC_{inf}, AUC_{last} and C_{max}. The natural log-transformed parameters will be analyzed separately using a mixed effect model (data permitting) with the food effect (with and without food) as fixed effect and subjects as a random effect. The geometric means (exponentiated least-squares means) for each food effect and the geometric mean ratio (exponentiated difference between the fed cohort least-square mean as test and the fasted cohort least-squares mean as reference) and the associated 90% confidence interval (CI) will be presented. The geometric mean rations and the associated confidence intervals will be expressed as percentages. Refer to Appendix 2 for the SAS® code that will be used for the food effect analysis.

The parameters AUC_{inf}, AUC_{last}, and C_{max} on fenretinide will also be presented graphically by means of box and whisker plots. The results for all treatment groups will be presented on the same plot. The dose-normalized results for each parameter will also be plotted separately.

All parameter results will be listed based on the PK population and any results that may have been excluded from the summary tables will be flagged.

7. Changes to the Planned Analyses

7.1 Changes to the Analyses Described in the Study Protocol and Protocol Amendments

Not applicable.

7.2 Changes from the Statistical Analysis Plan Version x.x to Version x.x

Not applicable.

8. References

- WHO. Dengue vaccines: WHO position paper. World Health Organization. https://www.who.int/immunization/policy/position_papers/who_pp_dengue_2018_summary.pdf. 2018.
- WHO. Dengue and severe dengue. World Health Organization. https://www.who.int/newsroom/fact-sheets/detail/dengue-and-severe-dengue. 2021.

9. Attachments and Appendices

Appendix 1 Dose Proportionality Analysis SAS® Code

The following SAS® code will be used for the dose proportionality analysis of fenretinide for the comparison:

```
ODS Output estimates=estimates;
ODS Output diffs=diffs;

PROC MIXED DATA = pk;

   BY param;

   MODEL log_aval = log_dose / ddfm = kr;

   ESTIMATE 'ESTIMATED SLOPE' log_dose 1/cl alpha=0.1;

   ESTIMATE 'INTERCEPT' INTERCEPT 1/cl alpha=0.1;

run;
```

Appendix 2 Food Effect Analysis SAS® Code

The following SAS® code will be used for the food effect analysis:

```
ODS Output lsmeans=lsmeans;
ODS Output diffs=diffs;

PROC MIXED DATA = pk;

   BY param;

   CLASS subjid trt;

   MODEL log_aval = trt / ddfm = kr;

   RANDOM subjid / subject =subjid type=un;

   LSMEANS trt/pdiff=control('Fasted') CL ALPHA=0.1;

RUN;
```

If the unstructured covariance structure results in invalid (i.e., not non-negative definite) results use TYPE=FA0(2) and then TYPE=CSH. If the model still produces invalid results or does not converge use the default covariance structure.

ATTACHMENT 1 LIST OF TABLES, LISTINGS AND FIGURES

Tables

Table 14.1.1.1 Summary of Analysis Population (Safety Population)
Table 14.1.2.1 Summary of Subject Disposition (Safety Population)
Table 14.1.3.1 Summary of Protocol Deviations (Safety Population)
Table 14.1.3.2 Summary of Protocol Deviations - Fasted and Fed Cohorts (Safety Population)
Table 14.1.4.1 Summary of Demography (Safety Population)
Table 14.1.5.1 Summary of Subject Baseline Characteristics (Safety Population)
Table 14.1.6.1 Summary of Medical and Surgical History (Safety Population)
Table 14.1.7.1 Summary of concomitant Medication (Safety Population)
Table 14.1.7.2 Summary of concomitant Medication – Fasted and Fed Cohorts (Safety Population)
Table 14.2.1.1 Summary of Plasma Pharmacokinetic Concentrations (Pharmacokinetic Population)
Table 14.2.1.2 Summary of Plasma Pharmacokinetic Concentrations – Fasted and Fed Cohorts (Pharmacokinetic Population)
Table 14.2.2.1 Summary of Plasma Pharmacokinetic Parameters (Pharmacokinetic Population)
Table 14.2.2.2 Summary of Plasma Pharmacokinetic Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population)
Table 14.2.3 Analysis of Dose Proportionality of Plasma Pharmacokinetic Parameters of Fenretinide (Pharmacokinetic Population)
Table 14.2.4 Analysis of Food Effect on Plasma Pharmacokinetic Parameters of Fenretinide (Pharmacokinetic Population)
Table 14.3.1.1.1 Overall Summary of Adverse Events (Safety Population)
Table 14.3.1.1.2 Overall Summary of Adverse Events – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.2.1 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.2.2 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.3.1 Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.3.2 Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.4.1 Summary of Treatment-Related Adverse Events by System Organ Class and Preferred Term (Safety Population)

Table 14.3.1.4.2 Summary of Treatment-Related Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.5.1 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity Rating (Safety Population)
Table 14.3.1.5.2 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity Rating – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.6.1 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug (Safety Population)
Table 14.3.1.6.2 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.7.1 Summary of Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.7.2 Summary of Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)
Table 14.3.1.8.1 Part A SAD: Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Safety Population)
Table 14.3.1.8.2 Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)
Listing 14.3.2.1. Serious Adverse Events (Safety Population)
Listing 14.3.2.2 Adverse Events Leading to Study Discontinuation (Safety Population)
Listing 14.3.2.3 Adverse Events Leading to Study Drug Discontinuation (Safety Population)
Table 14.3.4.1.1.1 Summary of Hematology Results (Safety Population)
Table 14.3.4.1.1.2 Summary of Hematology Results – Fasted and Fed Cohorts (Safety Population)
Table 14.3.4.1.2.1 Summary of Shifts from Baseline in Hematology Laboratory Range Indicator Categories (Safety Population)
Table 14.3.4.1.2.2 Summary of Shifts from Baseline in Hematology Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population)
Table 14.3.4.2.1.1 Summary of Biochemistry Results (Safety Population)
Table 14.3.4.2.1.2 Summary of Biochemistry Results – Fasted and Fed Cohorts (Safety Population)
Table 14.3.4.2.2.1 Summary of Shifts from Baseline in Biochemistry Laboratory Range Indicator Categories (Safety Population)
Table 14.3.4.2.2.2 Summary of Shifts from Baseline in Biochemistry Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population)
Table 14.3.4.3.1.1 Summary of Coagulation Results (Safety Population)
Table 14.3.4.3.1.2 Summary of coagulation Results – Fasted and Fed Cohorts (Safety Population)
Table 14.3.4.3.2.1 Summary of Shifts from Baseline in Coagulation Laboratory Range Indicator Categories (Safety Population)

Table 14.3.4.3.2.2 Summary of Shifts from Baseline in Coagulation Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population)
Table 14.3.4.4.1.1 Summary of Dipstick Urinalysis Results (Safety Population)
Table 14.3.4.4.1.2 Summary of Dipstick Urinalysis Results – Fasted and Fed Cohorts (Safety Population)
Table 14.3.5.1 Summary of Vital Signs Results (Safety Population)
Table 14.3.5.2 Summary of Vital Signs Results – Fasted and Fed Cohorts (Safety Population)
Table 14.3.6.1.1 Summary of 12-Lead ECG Results (Safety Population)
Table 14.3.6.1.2 Summary of 12-Lead ECG Results – Fasted and Fed Cohorts (Safety Population)
Table 14.3.6.2.1 Summary of 12-Lead ECG Overall Assessment (Safety Population)
Table 14.3.6.2.2 Summary of 12-Lead ECG Overall Assessment - Fasted and Fed Cohorts (Safety Population)

Listings

Listing 16.2.1.1 Analysis Sets (Safety Population)
Listing 16.2.1.2 Subject Disposition (Safety Population)
Listing 16.2.2.1 Protocol Deviations (Safety Population)
Listing 16.2.2.2 Subject Eligibility (Safety Population)
Listing 16.2.3 Randomization (Safety Population)
Listing 16.2.4.1 Demography (Safety Population)
Listing 16.2.4.2 Medical and Surgical History (Safety Population)
Listing 16.2.4.3 Alcohol Breath Test Results (Safety Population)
Listing 16.2.4.4 Urine Drug Test Results (Safety Population)
Listing 16.2.4.5 Pregnancy Test Results (Safety Population)
Listing 16.2.4.6 Serology Results (Safety Population)
Listing 16.2.4.7.1 Prior Medications (Safety Population)
Listing 16.2.4.7.2 Concomitant Medications (Safety Population)
Listing 16.2.5.1 Study Drug Administration (Safety Population)
Listing 16.2.6.1 Plasma Pharmacokinetic Concentrations (Pharmacokinetic Population)
Listing 16.2.6.2 Plasma Pharmacokinetic Parameters (Pharmacokinetic Population)
Listing 16.2.7.1 Adverse Events (Safety Population)
Listing 16.2.7.2 Treatment-Related Adverse Events (Safety Population)
Listing 16.2.8.1 Hematology Results (Safety Population)
Listing 16.2.8.2 Biochemistry Results (Safety Population)
Listing 16.2.8.3 Coagulation Results (Safety Population)
Listing 16.2.8.4 Urinalysis Results Including Microscopy (Safety Population)
Listing 16.2.9.1 Vital Signs Results (Safety Population)
Listing 16.2.9.2.1 12-Lead ECG Results (Safety Population)
Listing 16.2.9.2.2 12-Lead ECG Overall Assessment (Safety Population)

Listing 16.2.9.3 Physical Examination Findings (Safety Population)

Figures

Figure 14.2.1.1.1 Individual Plasma PK Concentrations over Time (Linear) (Pharmacokinetic Population)
Figure 14.2.1.1.2 Individual Plasma PK Concentrations over Time (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.1.1.3 Individual Plasma PK Concentrations over Time by Subject (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.1.2.1 Individual Plasma PK Concentrations over Time (Log-Linear) (Pharmacokinetic Population)
Figure 14.2.1.2.2 Individual Plasma PK Concentrations over Time (Log-Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.1.2.3 Individual Plasma PK Concentrations over Time by Subject (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.2.1.1 Mean Plasma PK Concentrations over Time (Linear) (Pharmacokinetic Population)
Figure 14.2.2.1.2 Mean Plasma PK Concentrations over Time (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.2.2.1 Mean Plasma PK Concentrations over Time (Log-Linear) (Pharmacokinetic Population)
Figure 14.2.2.2.2 Mean Plasma PK Concentrations over Time (Log-Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.3.1.1 Box Plots of Plasma PK Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.4.1.1 Box-Whisker Plots of Dose-Normalized Plasma PK Parameters (Pharmacokinetic Population)
Figure 14.2.4.1.2 Box-Whisker Plots of Dose-Normalized Plasma PK Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population)
Figure 14.2.5.1 Scatterplots of Natural Log-Transformed Plasma PK Parameters (Pharmacokinetic Analysis Set)

Attachment 1 of the Statistical Analysis Plan

Tables, Listings, and Figures

Sponsor: Island Pharmaceuticals Ltd

Protocol Number: ISLA101-P01-CT001

A Phase 1a, randomized, double-blind placebo-controlled study to evaluate safety and tolerability and to characterize the pharmacokinetic profile of single ascending doses of fenretinide oral capsules in healthy adult volunteers.

Version: Final Version 1.0
Date: 2023-12-07

List of Tables, Listings and Figures

1 General Statistical Methods 5
Table 14.1.1.1 Summary of Analysis Population (Safety Population) 6
Table 14.1.2.1 Summary of Subject Disposition (Safety Population) 7
Table 14.1.3.1 Summary of Protocol Deviations (Safety Population) 8
Table 14.1.3.2 Summary of Protocol Deviations - Fasted and Fed Cohorts (Safety Population) 9
Table 14.1.4.1 Summary of Demography (Safety Population) 10
Table 14.1.5.1 Summary of Subject Baseline Characteristics (Safety Population) 11
Table 14.1.6.1 Summary of Medical and Surgical History (Safety Population) 12
Table 14.1.7.1 Summary of concomitant Medication (Safety Population) 13
Table 14.1.7.2 Summary of concomitant Medication – Fasted and Fed Cohorts (Safety Population) 14
Table 14.2.1.1 Summary of Plasma Pharmacokinetic Concentrations (Pharmacokinetic Population) 15
Table 14.2.1.2 Summary of Plasma Pharmacokinetic Concentrations – Fasted and Fed Cohorts (Pharmacokinetic Population) 16
Table 14.2.2.1 Summary of Plasma Pharmacokinetic Parameters (Pharmacokinetic Population) 17
Table 14.2.2.2 Summary of Plasma Pharmacokinetic Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population) 18
Table 14.2.3 Analysis of Dose Proportionality of Plasma Pharmacokinetic Parameters of Fenretinide (Pharmacokinetic Population) 19
Table 14.2.4 Analysis of Food Effect on Plasma Pharmacokinetic Parameters of Fenretinide (Pharmacokinetic Population) 20
Table 14.3.1.1.1 Overall Summary of Adverse Events (Safety Population) 21
Table 14.3.1.1.2 Overall Summary of Adverse Events – Fasted and Fed Cohorts (Safety Population) 22
Table 14.3.1.2.1 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population) 23
Table 14.3.1.2.2 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population) 24
Table 14.3.1.3.1 Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population) 25
Table 14.3.1.3.2 Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population) 26
Table 14.3.1.4.1 Summary of Treatment-Related Adverse Events by System Organ Class and Preferred Term (Safety Population) 27
Table 14.3.1.4.2 Summary of Treatment-Related Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population) 28
Table 14.3.1.5.1 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity Rating (Safety Population) 29
Table 14.3.1.5.2 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity Rating – Fasted and Fed Cohorts (Safety Population) 30
Table 14.3.1.6.1 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug (Safety Population) 31
Table 14.3.1.6.2 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug – Fasted and Fed Cohorts (Safety Population) 32
Table 14.3.1.7.1 Summary of Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term (Safety Population) 33
Table 14.3.1.7.2 Summary of Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population) 34
Table 14.3.1.8.1 Part A SAD: Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Safety Population) 35
Table 14.3.1.8.2 Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population) 36

Listing 14.3.2.1. Serious Adverse Events (Safety Population) 37
Listing 14.3.2.2 Adverse Events Leading to Study Discontinuation (Safety Population) 38
Listing 14.3.2.3 Adverse Events Leading to Study Drug Discontinuation (Safety Population) 39
Table 14.3.4.1.1.1 Summary of Hematology Results (Safety Population) 40
Table 14.3.4.1.1.2 Summary of Hematology Results – Fasted and Fed Cohorts (Safety Population) 41
Table 14.3.4.1.2.1 Summary of Shifts from Baseline in Hematology Laboratory Range Indicator Categories (Safety Population) 42
Table 14.3.4.1.2.2 Summary of Shifts from Baseline in Hematology Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population) 43
Table 14.3.4.2.1.1 Summary of Biochemistry Results (Safety Population) 44
Table 14.3.4.2.1.2 Summary of Biochemistry Results – Fasted and Fed Cohorts (Safety Population) 45
Table 14.3.4.2.2.1 Summary of Shifts from Baseline in Biochemistry Laboratory Range Indicator Categories (Safety Population) 46
Table 14.3.4.2.2.2 Summary of Shifts from Baseline in Biochemistry Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population) 47
Table 14.3.4.3.1.1 Summary of Coagulation Results (Safety Population) 48
Table 14.3.4.3.1.2 Summary of coagulation Results – Fasted and Fed Cohorts (Safety Population) 49
Table 14.3.4.3.2.1 Summary of Shifts from Baseline in Coagulation Laboratory Range Indicator Categories (Safety Population) 50
Table 14.3.4.3.2.2 Summary of Shifts from Baseline in Coagulation Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population) 51
Table 14.3.4.4.1.1 Summary of Dipstick Urinalysis Results (Safety Population) 52
Table 14.3.4.4.1.2 Summary of Dipstick Urinalysis Results – Fasted and Fed Cohorts (Safety Population) 53
Table 14.3.5.1 Summary of Vital Signs Results (Safety Population) 54
Table 14.3.5.2 Summary of Vital Signs Results – Fasted and Fed Cohorts (Safety Population) 56
Table 14.3.6.1.1 Summary of 12-Lead ECG Results (Safety Population) 57
Table 14.3.6.1.2 Summary of 12-Lead ECG Results – Fasted and Fed Cohorts (Safety Population) 58
Table 14.3.6.2.1 Summary of 12-Lead ECG Overall Assessment (Safety Population) 59
Table 14.3.6.2.2 Summary of 12-Lead ECG Overall Assessment - Fasted and Fed Cohorts (Safety Population) 60
Listing 16.2.1.1 Analysis Sets (Safety Population) 61
Listing 16.2.1.2 Subject Disposition (Safety Population) 62
Listing 16.2.2.1 Protocol Deviations (Safety Population) 63
Listing 16.2.2.2 Subject Eligibility (Safety Population) 64
Listing 16.2.3 Randomization (Safety Population) 65
Listing 16.2.4.1 Demography (Safety Population) 66
Listing 16.2.4.2 Medical and Surgical History (Safety Population) 67
Listing 16.2.4.3 Alcohol Breath Test Results (Safety Population) 68
Listing 16.2.4.4 Urine Drug Test Results (Safety Population) 69
Listing 16.2.4.5 Pregnancy Test Results (Safety Population) 70
Listing 16.2.4.6 Serology Results (Safety Population) 71
Listing 16.2.4.7.1 Prior Medications (Safety Population) 72
Listing 16.2.4.7.2 Concomitant Medications (Safety Population) 73
Listing 16.2.5.1 Study Drug Administration (Safety Population) 74
Listing 16.2.6.1 Plasma Pharmacokinetic Concentrations (Pharmacokinetic Population) 75
Listing 16.2.6.2 Plasma Pharmacokinetic Parameters (Pharmacokinetic Population) 76
Listing 16.2.7.1 Adverse Events (Safety Population) 77
Listing 16.2.7.2 Treatment-Related Adverse Events (Safety Population) 78
Listing 16.2.8.1 Hematology Results (Safety Population) 79
Listing 16.2.8.2 Biochemistry Results (Safety Population) 80

Listing 16.2.8.3 Coagulation Results (Safety Population) 81
Listing 16.2.8.4 Urinalysis Results Including Microscopy (Safety Population) 82
Listing 16.2.9.1 Vital Signs Results (Safety Population) 83
Listing 16.2.9.2.1 12-Lead ECG Results (Safety Population) 84
Listing 16.2.9.2.2 12-Lead ECG Overall Assessment (Safety Population) 85
Listing 16.2.9.3 Physical Examination Findings (Safety Population) 86
Figure 14.2.1 1.1 Individual Plasma PK Concentrations over Time (Linear) (Pharmacokinetic Population) 87
Figure 14.2.1.1.2 Individual Plasma PK Concentrations over Time (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population) 88
Figure 14.2.1.1.3 Individual Plasma PK Concentrations over Time by Subject (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population) 89
Figure 14.2.1.2.1 Individual Plasma PK Concentrations over Time (Log-Linear) (Pharmacokinetic Population) 90
Figure 14.2.1.2.2 Individual Plasma PK Concentrations over Time (Log-Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population) 91
Figure 14.2.1.2.3 Individual Plasma PK Concentrations over Time by Subject (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population) 92
Figure 14.2.2.1.1 Mean Plasma PK Concentrations over Time (Linear) (Pharmacokinetic Population) 93
Figure 14.2.2.1.2 Mean Plasma PK Concentrations over Time (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population) 94
Figure 14.2.2.2.1 Mean Plasma PK Concentrations over Time (Log-Linear) (Pharmacokinetic Population) 95
Figure 14.2.2.2.2 Mean Plasma PK Concentrations over Time (Log-Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population) 96
Figure 14.2.3.1.1 Box Plots of Plasma PK Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population) 97
Figure 14.2.4.1.1 Box-Whisker Plots of Dose-Normalized Plasma PK Parameters (Pharmacokinetic Population) 98
Figure 14.2.4.1.2 Box-Whisker Plots of Dose-Normalized Plasma PK Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population) 99
Figure 14.2.5.1 Scatterplots of Natural Log-Transformed Plasma PK Parameters (Pharmacokinetic Analysis Set) 100

1 General Statistical Methods

Courier New will be used as font for all output produced in SAS®. The font size for all output will be 8p.

Results presented in table columns will be positioned as follows:

- Alphanumeric values will be left aligned.
- Integer numbers (e.g., counts) will be right aligned.
- Numbers containing fractional portions will be decimal aligned.

In all titles and analysis population names, coordinating conjunctions (and, or), articles (a, an, the) or prepositions will not be capitalized. All other words will be capitalized as well as the first and last words of the title or name.

The footnotes must make provision for the name of the SAS® program used to produce the output and the date and time that the output was created.

Words followed by a designator will be capitalized, for example, Day 1, Subject 3046, Day 10 etc.

Page numbers will be indicated as “Page x of y” at the bottom of each page.

Individual subject listings will be produced for all raw data and a selection of the derived data.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.1.1 Summary of Analysis Population (Safety Population)

	ISLA101 300 mg Fasted (N=xx) n (%)	ISLA101 600 mg Fasted (N=xx) n (%)	ISLA101 900 mg Fasted/Fed (N=xx) n (%)	Pooled Placebo (N=xx) n (%)	All Subjects (N=xx) n (%)
Safety Population					
Number of Subjects Included	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of Subjects Excluded	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Reasons for Exclusion					
Reasons for Exclusion 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Pharmacokinetic Population					
Number of Subjects Included	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of Subjects Excluded	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Reasons for Exclusion					
Reasons for Exclusion 1	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

The Safety Population will include all subjects who received at least one dose of the study drug (ISLA101 or Placebo).
The Pharmacokinetic Population will consist of all subjects in the safety population who have a pre-dose PK sample and at least one post dose analyzable PK sample and at least 1 post-dose analyzable PK sample (quantifiable Plasma concentration).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Percentage (%) of subjects (n) for the reason for exclusion categories are calculated based on the number of subjects that were excluded from the specific analysis population.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:

In the final analysis, the group "ISLA101 900 mg Fasted/Fed" will be replaced by the highest tolerated dose-level cohort. For the "Pooled Placebo" group, the placebo fasted and Fed subjects will be counted once only. Therefore, the number of subjects (N) in Pooled Placebo basically should be 6.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.2.1 Summary of Subject Disposition (Safety Population)

	ISLA101 300 mg Fasted (N=xx) n (%)	ISLA101 600 mg Fasted (N=xx) n (%)	ISLA101 900 mg Fasted/Fed (N=xx) n (%)	Pooled Placebo (N=xx) n (%)	All Subjects (N=xx) n (%)
Number of Subjects who Completed the Study	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Number of Subjects who did not Complete the Study	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Primary Reason for Early Study Discontinuation					
Adverse Event	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Withdrawal of Consent	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Physician Decision	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Pregnancy	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Protocol Deviation	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Lost to Follow-up	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Sponsor Request	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Other	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Percentages (%) of subjects (n) for the reason of early study termination categories are based on the number of subjects who early terminated the study.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
In the final analysis, the group "ISLA101 900 mg Fasted/Fed" will be replaced by the highest tolerated dose-level cohort. For the "Pooled Placebo" group, the placebo fasted and Fed subjects will be counted once only. Therefore, the number of subjects (N) in Pooled Placebo basically should be 6.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.3.1 Summary of Protocol Deviations (Safety Population)

	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
At least one Protocol deviation	xx	xx	xx	xx
At least one Major Protocol deviation	xx	xx	xx	xx
At least one Minor Protocol deviation	xx	xx	xx	xx
Major Protocol Deviation				
Missed Procedure/Assessment	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Procedures/Assessments Outside Protocol Window	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Order of Procedure/Assessments	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Missed Visit	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Eligibility	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Incorrect Randomization	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Informed Consent Error	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Study Drug Administration Error	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Incomplete Documentation	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Other	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Minor Protocol Deviation				
Missed Procedure/Assessment	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Procedures/Assessments Outside Protocol Window	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Order of Procedure/Assessments	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Etc.	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Subjects who experienced multiple deviations within a category are counted only once in the specific category (n), however each instance of the deviation is counted (E).
Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
The " Pooled Placebo" group means the placebo fasted subjects. Therefore, the number of subjects (N) in Pooled Placebo basically should be 6.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.3.2 Summary of Protocol Deviations - Fasted and Fed Cohorts (Safety Population)

	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
At least one Protocol deviation	xx	xx	xx	xx
At least one Major Protocol deviation	xx	xx	xx	xx
At least one Minor Protocol deviation	xx	xx	xx	xx
Major Protocol Deviation				
Missed Procedure/Assessment	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Procedures/Assessments Outside Protocol Window	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Order of Procedure/Assessments	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Missed Visit	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Eligibility	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Incorrect Randomization	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Informed Consent Error	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Study Drug Administration Error	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Incomplete Documentation	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Other	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Minor Protocol Deviation				
Missed Procedure/Assessment	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Procedures/Assessments Outside Protocol Window	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Order of Procedure/Assessments	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Etc.	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Subjects who experienced multiple deviations within a category are counted only once in the specific category (n), however each instance of the deviation is counted (E).
Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.4.1 Summary of Demography (Safety Population)

	Statistic	ISLA101 300 mg Fasted (N=xx) n (%)	ISLA101 600 mg Fasted (N=xx) n (%)	ISLA101 900 mg Fasted/Fed (N=xx) n (%)	Pooled Placebo (N=xx) n (%)	All Subjects (N=xx) n (%)
Age (Years)	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Minimum	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx
Sex	n	xx	xx	xx	xx	xx
Male	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Female	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Childbearing Potential	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Ethnicity	n	xx	xx	xx	xx	xx
Hispanic or Latino	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Not Hispanic or Latino	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Race	n	xx	xx	xx	xx	xx
White	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Black or African American	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Asian	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
American Indian or Alaskan Native	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Native Hawaiian or Other Pacific Islander	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)
Other	n (%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)	xx (xx%)

SD: Standard deviation.
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Percentages (%) of subjects (n) of childbearing potential are based on the number of female subjects.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x
Programmer Note:
In the final analysis, the group "ISLA101 900 mg Fasted/Fed" will be replaced by the highest tolerated dose-level cohort. For the "Pooled Placebo" group, the placebo fasted and Fed subjects will be counted once only. Therefore, the number of subjects (N) in Pooled Placebo basically should be 6.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.5.1 Summary of Subject Baseline Characteristics (Safety Population)

	Statistic	ISLA101 300 mg Fasted (N=xx)	ISLA101 600 mg Fasted (N=xx)	ISLA101 900 mg Fasted/Fed (N=xx)	Pooled Placebo (N=xx)	All Subjects (N=xx)
Height (cm) at Screening	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx
Weight (kg) at Screening	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx
Body Mass Index (kg/m^2) at Screening	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx
Body Surface Area (m^2) at Screening	n	xx	xx	xx	xx	xx
	Mean	xx.x	xx.x	xx.x	xx.x	xx.x
	SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Minimum	xx	xx	xx	xx	xx
	Maximum	xx	xx	xx	xx	xx

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.6.1 Summary of Medical and Surgical History (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted/Fed (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E	All Subjects (N=xx) n (%) E
Number of Subjects With at Least One Medical History	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
System Organ Class 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Term 4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Medical history terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer Note:
In the final analysis, the group "ISLA101 900 mg Fasted/Fed" will be replaced by the highest tolerated dose-level cohort.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.7.1 Summary of concomitant Medication (Safety Population)

ATC Class Level 2 Preferred Name	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Number of Subjects With at Least One Concomitant Medication	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
ATC Class Level 2 Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
ATC Class Level 2 Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

ATC: Anatomical Therapeutic Chemical.
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Subjects who used the same medication on multiple occasions are counted only once in the specific category (n), however each instance of the medication is counted (E).
Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of study drug.
Medication terms were coded using the World Health Organization – Drug Dictionary (WHO-DD) Version Global C3, September 2023.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer Note:
Sort preferred names alphabetically.
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.1.7.2 Summary of concomitant Medication – Fasted and Fed Cohorts (Safety Population)

ATC Class Level 2 Preferred Name	ISLA101 XXX mg Fasted (N=xx) n (%) E	ISLA101 XXX mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Number of Subjects With at Least One Concomitant Medication	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
ATC Class Level 2 Term 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
ATC Class Level 2 Term 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 1	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 2	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 3	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx
Preferred Name 4	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx	xx (xx.x%) xx

ATC: Anatomical Therapeutic Chemical.

Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Subjects who used the same medication on multiple occasions are counted only once in the specific category (n), however each instance of the medication is counted (E).
Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of study drug.

Medication terms were coded using the World Health Organization – Drug Dictionary (WHO-DD) Version Global C3, September 2023.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
Sort preferred names alphabetically.
In the final analysis, the dosage for the food effect cohorts will be replaced by the highest tolerated dose-level cohort from Cohort 1 to 3.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.2.1.1 Summary of Plasma Pharmacokinetic Concentrations (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]

Treatment Group Time Point (hours)	Statistics									
	n	n BLQ	Mean	SD	CV (%)	Median	Minimum	Maximum	Geometric Mean	Geometric CV (%)
ISLA101 300 mg Fasted (N=x)										
Pre-dose	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
0.5 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
0.75 hour	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
1 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
1.5 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
2 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
3 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
4 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
5 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
6 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
8 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
10 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
12 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
24 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
36 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
Etc.										

BLQ: Below the LLOQ; CV: Coefficient of Variation; LLOQ: Lower Limit of Quantification;
n BLQ: Number of BLQ Concentrations; SD: Standard Deviation.
BLQ concentrations observed prior to the first measurable concentration were set to zero for the calculation of the summary statistics and other BLQ concentrations were treated as missing. Zero concentrations were set to missing for the calculation of the geometric statistics.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer Note:
Repeat for analyte = MPR and oxo-HPR
The treatment group will be displayed as the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted and ISLA101 900 mg Fasted.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.2.1.2 Summary of Plasma Pharmacokinetic Concentrations – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]

Treatment Group Time Point (hours)	Statistics									
	n	n BLQ	Mean	SD	CV (%)	Median	Minimum	Maximum	Geometric Mean	Geometric CV (%)
ISLA101 XXX mg Fasted (N=x)										
Pre-dose	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
0.5 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
0.75 hour	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
1 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
1.5 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
2 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
3 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
4 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
5 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
6 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
8 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
10 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
12 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
24 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
36 hours	X	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
Etc.										

BLQ: Below the LLOQ; CV: Coefficient of Variation; LLOQ: Lower Limit of Quantification;
n BLQ: Number of BLQ Concentrations; SD: Standard Deviation.
BLQ concentrations observed prior to the first measurable concentration were set to zero for the calculation of the summary statistics and other BLQ concentrations were treated as missing. Zero concentrations were set to missing for the calculation of the geometric statistics.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
Repeat for analyte = MPR and oxo-HPR
The treatment group will be displayed as the following: ISLA101 XXX mg Fasted, and ISLA101 XXX mg Fed.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.2.2.1 Summary of Plasma Pharmacokinetic Parameters (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]

Treatment Group Time Point (hours)	Statistics								
	n	Mean	SD	CV (%)	Median	Minimum	Maximum	Geometric Mean	Geometric CV (%)
ISLA101 300 mg Fasted (N=x)									
C_{max} (ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
T_{max} (h)	X	-	-	-	XXXX.XXX	XXXX	XXXX	-	-
AUC_{last} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
AUC_{0-24} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
AUC_{inf} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
λ_z (1/h)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
$t_{1/2}$ (h)	X	-	-	-	XXXX.XXX	XXXX	XXXX	-	-
CL/F (L/h)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
Vz/F (L)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
DN_C_{max} (ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
DN_AUC_{inf} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
DN_AUC_{last} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
…									

DN: Dose normalized; AUC: Area Under the Curve; CV: Coefficient of Variation; -: Not Applicable; SD: Standard Deviation.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
The treatment group will be displayed as the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fed, and ISLA101 900 mg.
Repeat for analyte = MPR and oxo-HPR
The treatment group will be displayed as the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted and ISLA101 900 mg Fasted.
Results for λ_z, $t_{1/2}$, will only be included in the summary statistics if the following criteria are met:

- A minimum of 3 measurable concentrations-time points is available during log-linear portion of the terminal elimination phase (excluding C_{max}), i.e., No. of Points is ≥ 3.
- Adjusted R^2 > 0.80.

AUC_{inf}, C_L/F and V_z/F will only be included in the summary statistics if the following criterion is met:

- $\%AUC_{extrap}$ < 20%.
- Span >=2

Cz/F and Vz/F will be displayed for the parent compound only.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.2.2.2 Summary of Plasma Pharmacokinetic Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]

Treatment Group Time Point (hours)	Statistics								
	n	Mean	SD	CV (%)	Median	Minimum	Maximum	Geometric Mean	Geometric CV (%)
ISLA101 xx mg Fasted (N=x)									
C_{max} (ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
T_{max} (h)	X	-	-	-	XXXX.XXX	XXXX	XXXX	-	-
AUC_{last} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
AUC_{0-24} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
AUC_{inf} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
λ_z (1/h)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
$t_{1/2}$ (h)	X	-	-	-	XXXX.XXX	XXXX	XXXX	-	-
CL/F (L/h)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
Vz/F (L)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
DN_C_{max} (ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
DN_AUC_{inf} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
DN_AUC_{last} (h*ng/ml)	X	XXX.XXX	XXX.XXXX	XX.X	XXXX.XXX	XXXX	XXXX	XXX.XXX	XX.X
…									

DN: Dose normalized; AUC: Area Under the Curve; CV: Coefficient of Variation; -: Not Applicable; SD: Standard Deviation.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
The treatment group will be displayed as the following: ISLA101 XXX mg Fasted, and ISLA101 XXX mg Fed.
Repeat for analyte = MPR and oxo-HPR
Repeat for the treatment groups: ISLA101 xxx mg Fed.
Results for λ_z, $t_{1/2}$, will only be included in the summary statistics if the following criteria are met:

- A minimum of 3 measurable concentrations-time points is available during log-linear portion of the terminal elimination phase (excluding C_{max}), i.e., No. of Points is ≥ 3.
- Adjusted R^2 > 0.80.

AUC_{inf}, C_L/F and V_z/F will only be included in the summary statistics if the following criterion is met:

- $\%AUC_{extrap}$ < 20%.
- Span >=2

Cz/F and Vz/F will be displayed for the parent compound only.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.2.3 Analysis of Dose Proportionality of Plasma Pharmacokinetic Parameters of Fenretinide (Pharmacokinetic Population)

		Power Model		
Parameter (Unit)	n	Model Coefficient	Estimates (SE)	90% Confidence Interval
C_{max} (ng/mL)	xx	Slope (β)	xx.x (xx.xx)	(xx.x, xx.x)
		Intercept (α)	xx.x (xx.xx)	(xx.x, xx.x)
AUC_{inf} (h*ng/ml)	xx	Slope (β)	xx.x (xx.xx)	(xx.x, xx.x)
		Intercept (α)	xx.x (xx.xx)	(xx.x, xx.x)
AUC_{last} (h*ng/ml)	xx	Slope (β)	xx.x (xx.xx)	(xx.x, xx.x)
		Intercept (α)	xx.x (xx.xx)	(xx.x, xx.x)

AUC: Area Under the Curve; SE: Standard Error.
A power model was used to assess dose proportionality: Natural log-transformed (PK Parameter Result) = α + β * Natural Log-transformed(Dose).

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programming note:
Include cohort 1 to 3 (fasted cohorts)in this analysis only.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.2.4 Analysis of Food Effect on Plasma Pharmacokinetic Parameters of Fenretinide (Pharmacokinetic Population)

Parameter (Unit)	Treatment	n	Geometric Least Squares Means	Ratio of Geometric Least Squares Means (Fed : Fasted)	90% CI for the Ratio (Fed : Fasted) Lower	Upper
AUC_{inf} (h*ng/mL)	ISLA101 xxx mg (Fed)	xx	xx.xx	xx.xx	xx.xx	xx.xx
	ISLA101 xxx mg (Fasted)	xx	xx.xx			
AUC_{last} (h*ng/mL)	ISLA101 xxx mg (Fed)	xx	xx.xx	xx.xx	xx.xx	xx.xx
	ISLA101 xxx mg (Fasted)	xx	xx.xx			
C_{max} (ng/mL)	ISLA101 xxx mg (Fed)	xx	xx.xx	xx.xx	xx.xx	xx.xx
	ISLA101 xxx mg (Fasted)	xx	xx.xx			

AUC: Area Under the Curve
An analysis of variance model with fasting status as fixed effect was fitted to the natural log-transformed pharmacokinetic parameters.
The geometric least squares mean and geometric mean ratios and confidence intervals were derived by back transforming the point estimates and confidence intervals from the model.
The point estimates and the associated confidence intervals are expressed as percentages.
If will be concluded that there is a food effect on the rate and extent of absorption of ISLA101 if the point estimates for the AUC_{inf}, AUC_{last} and C_{max} ratios lie outside of the range of 80 to 125%.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.1.1 Overall Summary of Adverse Events (Safety Population)

	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at Least One Serious TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at Least One Severe TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at Least One Treatment-Related TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at least one TEAE leading to study discontinuation.	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at least one TEAE leading to study drug discontinuation.	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Severe adverse events are defined as adverse events where the event severity is reported as 'Severe'.
Treatment-related adverse events are defined as adverse events where the relationship to study drug is reported as 'Possibly', 'Probably" or 'Definitely" Related or where the relationship is missing.
Adverse events leading to study drug discontinuation are defined as AEs where action taken is reported as 'Drug Withdrawn'.
Adverse events leading to study discontinuation are defined as AEs where 'Other' action taken is reported as 'Withdrawn from study'.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentages (%) are calculated based on the number of subjects in the analysis set (N).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis set (N).

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer Note:
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.1.2 Overall Summary of Adverse Events – Fasted and Fed Cohorts (Safety Population)

	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at Least One Serious TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at Least One Severe TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at Least One Treatment-Related TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at least one TEAE leading to study discontinuation.	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Subjects with at least one TEAE leading to study drug discontinuation.	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Severe adverse events are defined as adverse events where the event severity is reported as 'Severe'.
Treatment-related adverse events are defined as adverse events where the relationship to study drug is reported as 'Possibly', 'Probably" or 'Definitely" Related or where the relationship is missing.
Adverse events leading to study drug discontinuation are defined as AEs where action taken is reported as 'Drug Withdrawn'.
Adverse events leading to study discontinuation are defined as AEs where 'Other' action taken is reported as 'Withdrawn from study'.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentages (%) are calculated based on the number of subjects in the analysis population (N).

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.2.1 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.2.2 Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.3.1 Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One Serious TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.3.2 Summary of Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One Serious TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.4.1 Summary of Treatment-Related Adverse Events by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One Treatment-Related AE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events.
Treatment-related adverse events are defined as adverse events where the relationship to study drug is reported as 'Possibly', 'Probably" or 'Definitely" Related or where the relationship is missing.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wrap onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.4.2 Summary of Treatment-Related Adverse Events by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One Treatment-Related AE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events.
Treatment-related adverse events are defined as adverse events where the relationship to study drug is reported as 'Possibly', 'Probably" or 'Definitely" Related or where the relationship is missing.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.5.1 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity Rating
(Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Mild	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Moderate	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Severe	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Mild	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Moderate	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Severe	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Mild	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Moderate	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Severe	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.
For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.5.2 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Severity Rating – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Mild	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Moderate	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Severe	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Mild	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Moderate	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Severe	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Mild	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Moderate	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Severe	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.6.1 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug (Safety Population)

System Organ Class (SOC) Preferred Term (PT) Relationship to Study Drug	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unrelated	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unlikely	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Possibly	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Probably	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Definitely	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unrelated	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unlikely	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Possibly	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Probably	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Definitely	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unrelated	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unlikely	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Possibly	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Probably	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Definitely	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term. For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.6.2 Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT) Relationship to Study Drug	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One TEAE	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unrelated	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Possibly Related	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Related	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
				xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unrelated	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Possibly Related	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Related	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
				xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Unrelated	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Possibly Related	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Related	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.7.1 Summary of Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One TEAE Leading to Study Discontinuation	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
				xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Adverse events leading to study discontinuation are defined as AEs where 'Other' action taken is reported as 'Withdrawn from study'.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term. For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.7.2 Summary of Treatment-Emergent Adverse Events Leading to Study Discontinuation by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One TEAE Leading to Study Discontinuation	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
				xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Adverse events leading to study discontinuation are defined as AEs where 'Other' action taken is reported as 'Withdrawn from study'.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.8.1 Part A SAD: Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 300 mg Fasted (N=xx) n (%) E	ISLA101 600 mg Fasted (N=xx) n (%) E	ISLA101 900 mg Fasted (N=xx) n (%) E	Pooled Placebo (N=xx) n (%) E
Subjects with at Least One TEAE Leading to Study Drug Discontinuation	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Adverse events leading to study drug discontinuation are defined as AEs where action taken is reported as 'Drug Withdrawn'.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E).
Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with ' (Continued)' appended to the term. For this "Pooled Placebo" group, only the placebo subjects under the fasted condition will be included.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.1.8.2 Summary of Treatment-Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term – Fasted and Fed Cohorts (Safety Population)

System Organ Class (SOC) Preferred Term (PT)	ISLA101 xxx mg Fasted (N=xx) n (%) E	ISLA101 xxx mg Fed (N=xx) n (%) E	Placebo (Fasted) (N=xx) n (%) E	Placebo (Fed) (N=xx) n (%) E
Subjects with at Least One TEAE Leading to Study Drug Discontinuation	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
System Organ Class 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
				xx (xx%) xx
System Organ Class 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 1	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 2	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 3	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx
Preferred Term 4	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx	xx (xx%) xx

n: Number of subjects, E: Number of adverse events, TEAE: Treatment-emergent adverse event.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Adverse events leading to study drug discontinuation are defined as AEs where action taken is reported as 'Drug Withdrawn'.
Subjects who experienced multiple events within a category are counted only once in the specific category (n), however each instance of the event is counted (E). Percentage (%) of subjects (n) in each category are calculated based on the number of subjects in the analysis population (N).
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Results will be sorted by alphabetically.
If PT terms within a SOC wraps onto a second page, the SOC term will be repeated on the second page with '(Continued)' appended to the term.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 14.3.2.1. Serious Adverse Events (Safety Population)

Cohort 1: ISLA101 300 mg Fasted
Subject Number: xxx-xxx

AE No.	System Organ Class (SOC)/ Preferred Term (PT)/ Verbatim Term	Start Date Time/ Study Day/ TEAE	End Date Time/ Study Day/ Ongoing	SAE/ AESI/DL_AE	Signs of Drug Toxicity	Outcome	Severity	Relationship to Study Drug	Action Taken	Other Action Taken
1	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM/ XX/ Yes	YYYY-MM-DD HH:MM/ XX	Yes/Yes/Yes	Xxxxx	Recovered/ Resolved	Mild	Probably	Unknown	None
2	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM / XX/ Yes	YYYY-MM-DD HH:MM/ Ongoing	Yes/No/No	-	Recovering/ Resolving	Severe	Definitely	Dose not Changed	None None

AE No.: Adverse Event Number, SAE: Serious adverse event, TEAE: Treatment-emergent adverse event, -: Not Applicable.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Only serious adverse events are presented.
Study days are calculated relative to the date of the treatment group first study drug administration.

Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all AEs that a subject experienced and repeat for all treatment groups.
Add code list for Other Action Taken if results cannot be fitted onto a single page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 14.3.2.2 Adverse Events Leading to Study Discontinuation (Safety Population)

Cohort 1: ISLA101 300 mg Fasted
Subject Number: xxx-xxx

AE No.	System Organ Class (SOC)/ Preferred Term (PT)/ Verbatim Term	Start Date Time/ Study Day/ TEAE	End Date Time/ Study Day/ Ongoing	SAE/ AESI/DL_AE	Signs of Drug Toxicity	Outcome	Severity	Relationship to Study Drug	Action Taken	Other Action Taken
1	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM/ XX/ Yes	YYYY-MM-DD HH:MM/ XX	Yes/Yes/Yes	Xxxxx	Recovered/ Resolved	Mild	Probably	Unknown	None
2	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM / XX/ Yes	YYYY-MM-DD HH:MM/ Ongoing	No/No/No	-	Recovering/ Resolving	Severe	Definitely	Dose not Changed	None None

AE No.: Adverse Event Number, SAE: Serious adverse event, TEAE: Treatment-emergent adverse event, -: Not Applicable.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Adverse events leading to study discontinuation are defined as AEs where 'Other' action taken is reported as 'Withdrawn from study'.
Study days are calculated relative to the date of the treatment group first study drug administration.
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all AEs that a subject experienced and repeat for all treatment groups.
Add code list for Other Action Taken if results cannot be fitted onto a single page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 14.3.2.3 Adverse Events Leading to Study Drug Discontinuation (Safety Population)

Cohort 1: ISLA101 300 mg Fasted
Subject Number: xxx-xxx

AE No.	System Organ Class (SOC)/ Preferred Term (PT)/ Verbatim Term	Start Date Time/ Study Day/ TEAE	End Date/ Study Day/ Ongoing	Outcome	SAE	Severity	Relationship to Study Drug	Action Taken	Other Action Taken
1	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM/ XX/ Yes	YYYY-MM-DD/ XX	Recovered/ Resolved	Yes	Grade 1 (Mild)	Unrelated	-	Withdrawn from Study
2	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM / XX/ Yes	YYYY-MM-DD/ Ongoing	Recovering/ Resolving	No	Grade 3 (Severe)	Related	None/ Dose not Changed	Withdrawn from Study

AE No.: Adverse Event Number, SAE: Serious adverse event, TEAE: Treatment-emergent adverse event, -: Not Applicable.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Adverse events leading to study drug discontinuation are defined as AEs where action taken is reported as 'Drug Withdrawn'.
Study days are calculated relative to the date of the treatment group first study drug administration.
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all AEs that a subject experienced and repeat for all treatment groups.
Add code list for Other Action Taken if results cannot be fitted onto a single page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.1.1.1 Summary of Hematology Results (Safety Population)

Parameter (Unit)

Treatment Group / Visit	Actual Values n	Actual Values Mean	Actual Values SD	Actual Values Median	Actual Values Minimum	Actual Values Maximum	Change from Baseline[1] n	Change from Baseline[1] Mean	Change from Baseline[1] SD	Change from Baseline[1] Median	Change from Baseline[1] Minimum	Change from Baseline[1] Maximum
ISLA101 300 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 600 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
….	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 900 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
….	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Pooled Placebo (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.1.1.2 Summary of Hematology Results – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit)

Treatment Group / Visit	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fasted) (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fed) (N=xx)_												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note:
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.1.2.1 Summary of Shifts from Baseline in Hematology Laboratory Range Indicator Categories (Safety Population)

Parameter (Unit)

Treatment Group Post-Baseline Visit	Post-Baseline Range Indicator	Baseline[1] Range Indicator Low n (%)	 Normal n (%)	 High n (%)	 Total n (%)
ISLA101 300 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…< repeat for Day 3,4,5 and follow up visit>					
ISLA101 600 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					
ISLA101 900 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pooled Placebo (N=xx)					
…Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Range Indicators (result classifications) are based on the laboratory defined normal ranges for the specific parameter.
Percentage (%) are based on the number of participants (n) in the analysis population (N) with assessments available at baseline and the relevant post-baseline visit. Only parameters with a defined reference range are included in the table.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x
Programmer Note:
Start each new parameter on a new page.
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.1.2.2 Summary of Shifts from Baseline in Hematology Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit)

Treatment Group Post-Baseline Visit	Post-Baseline Range Indicator	Baseline[1] Range Indicator Low n (%)	 Normal n (%)	 High n (%)	Total n (%)
ISLA101 xx mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…< repeat for Day 3,4,5 and follow up visit>					
…					
ISLA101 xx mg Fed (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					
Placebo (Fasted) (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Placebo (Fed) (N=xx)					
…Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					

[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Range Indicators (result classifications) are based on the laboratory defined normal ranges for the specific parameter.
Percentage (%) are based on the number of participants (n) in the analysis set (N) with assessments available at baseline and the relevant post-baseline visit. Only parameters with a defined reference range are included in the table.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note: Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.2.1.1 Summary of Biochemistry Results (Safety Population)

Parameter (Unit):xxx

Treatment Group / Visit	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 300 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 600 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
….	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 900 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
….	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Pooled Placebo (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programming note:
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.2.1.2 Summary of Biochemistry Results – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit):

Treatment Group / Visit	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fasted) (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fed) (N=xx)_												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.2.2.1 Summary of Shifts from Baseline in Biochemistry Laboratory Range Indicator Categories (Safety Population)

Parameter (Unit)

Treatment Group Post-Baseline Visit	Post-Baseline Range Indicator	Baseline[1] Range Indicator Low n (%)	 Normal n (%)	 High n (%)	 Total n (%)
ISLA101 300 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…< repeat for Day 3,4,5 and follow up visit>					
ISLA101 600 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					
ISLA101 900 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pooled Placebo (N=xx)					
…Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Range Indicators (result classifications) are based on the laboratory defined normal ranges for the specific parameter.
Percentage (%) are based on the number of participants (n) in the analysis population (N) with assessments available at baseline and the relevant post-baseline visit. Only parameters with a defined reference range are included in the table.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x
Programmer Note:
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.2.2.2 Summary of Shifts from Baseline in Biochemistry Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit)

Treatment Group Post-Baseline Visit	Post-Baseline Range Indicator	Baseline[1] Range Indicator Low n (%)	 Normal n (%)	 High n (%)	Total n (%)
ISLA101 xx mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…< repeat for Day 3,4,5 and follow up visit>					
…					
ISLA101 xx mg Fed (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					
Placebo (Fasted) (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Placebo (Fed) (N=xx)					
…Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					

[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Range Indicators (result classifications) are based on the laboratory defined normal ranges for the specific parameter.
Percentage (%) are based on the number of participants (n) in the analysis set (N) with assessments available at baseline and the relevant post-baseline visit. Only parameters with a defined reference range are included in the table.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note: Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.3.1.1 Summary of Coagulation Results (Safety Population)

Parameter (Unit):xxx

Treatment Group / Visit	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 300 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 600 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
….	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 900 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
….	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Pooled Placebo (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programming note:
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.3.1.2 Summary of coagulation Results – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit):

Treatment Group / Visit	Actual Values n	Mean	SD	Median	Minimum	Maximum	Change from Baseline[1] n	Mean	SD	Median	Minimum	Maximum
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fasted) (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fed) (N=xx)_												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.3.2.1 Summary of Shifts from Baseline in Coagulation Laboratory Range Indicator Categories (Safety Population)

Parameter (Unit)

Treatment Group Post-Baseline Visit	Post-Baseline Range Indicator	Baseline[1] Range Indicator Low n (%)	 Normal n (%)	 High n (%)	Total n (%)
ISLA101 300 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…< repeat for Day 3,4,5 and follow up visit>					
ISLA101 600 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					
ISLA101 900 mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Pooled Placebo (N=xx)					
…Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Range Indicators (result classifications) are based on the laboratory defined normal ranges for the specific parameter.
Percentage (%) are based on the number of participants (n) in the analysis population (N) with assessments available at baseline and the relevant post-baseline visit. Only parameters with a defined reference range are included in the table.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x
Programmer Note:
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.3.2.2 Summary of Shifts from Baseline in Coagulation Laboratory Range Indicator Categories – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit)

Treatment Group Post-Baseline Visit	Post-Baseline Range Indicator	Baseline[1] Range Indicator Low n (%)	 Normal n (%)	 High n (%)	Total n (%)
ISLA101 xx mg Fasted (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Day 2	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…< repeat for Day 3,4,5 and follow up visit>					
…					
ISLA101 xx mg Fed (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					
Placebo (Fasted) (N=xx)					
Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Normal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	High	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Total	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Placebo (Fed) (N=xx)					
…Day 1	Low	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
……< repeat for Day 3,4,5 and follow up visit>					

[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Range Indicators (result classifications) are based on the laboratory defined normal ranges for the specific parameter.
Percentage (%) are based on the number of participants (n) in the analysis set (N) with assessments available at baseline and the relevant post-baseline visit. Only parameters with a defined reference range are included in the table.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer Note: Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.4.1.1 Summary of Dipstick Urinalysis Results (Safety Population)

Parameter (unit):

Treatment Group Visit	Result Classification			
	n	Normal n (%)	Abnormal NCS n (%)	Abnormal CS n (%)
ISLA101 300 mg Fasted (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 1	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 2	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 3	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
<repeat for Day 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ISLA101 600 mg Fasted (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
… <repeat for Day1,2,3 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ISLA101 900 mg Fasted (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…<repeat for Day1,2,3 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Pooled Placebo (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…<repeat for Day1,2,3 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] The baseline value is defined as the last available valid, non-missing observation prior to the first study drug administration.
CS: Clinically significant; NCS: Not clinically Significant.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM Page 1 of x

Programming Note:
Start each new parameter on a new page.
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.4.4.1.2 Summary of Dipstick Urinalysis Results – Fasted and Fed Cohorts (Safety Population)

Parameter (unit):

Treatment Group Visit	Result Classification			
	n	Normal n (%)	Abnormal NCS n (%)	Abnormal CS n (%)
ISLA101 xxx mg Fasted (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 1	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 2	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Day 3	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
<repeat for Day 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ISLA101 xxx mg Fed (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
… <repeat for Day1,2,3 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Placebo (Fasted) (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…<repeat for Day1,2,3 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Placebo (Fed) (N=X)				
Baseline[1]	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
…<repeat for Day1,2,3 4,5, follow-up visit>	xx	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

[1] The baseline value is defined as the last available valid, non-missing observation prior to the first study drug administration.
CS: Clinically significant; NCS: Not clinically Significant.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM Page 1 of x

Programming Note:
Start each new parameter on a new page.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.5.1 Summary of Vital Signs Results (Safety Population)

Parameter (Unit)

Treatment Group Visit: Time Point	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 300 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 600 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
……	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 900 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Pooled Placebo (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Start each new parameter on a new page.
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.

Present the results in the following order:

- SBP.
- DBP.
- Pulse Rate.
- Respiratory Rate.
- Temperature.
- BSA.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.5.2 Summary of Vital Signs Results – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit)

	Actual Values						Change from Baseline[1]					
Treatment Group Visit: Time Point	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 xx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 2	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 3	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 4	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Day 5	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Follow-up	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 xx mg Fed (N=xx)	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
…..	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fasted) (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo (Fed) (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
…	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.6.1.1 Summary of 12-Lead ECG Results (Safety Population)

Parameter (Unit)

Treatment Group Visit: Time Point	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 300 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 600 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 900 mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Pooled Placebo (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to study drug administration in that period.
Where triplicate measurements were taken, summaries were based on the mean of the triplicate measurements at each visit/time point.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Start each new parameter on a new page.
Present the results in the following order:

- Heart Rate.
- RR Interval.
- QTcF Interval.
- PR Duration.
- QRS Interval.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.6.1.2 Summary of 12-Lead ECG Results – Fasted and Fed Cohorts (Safety Population)

Parameter (Unit)

Treatment Group Visit: Time Point	Actual Values						Change from Baseline[1]					
	n	Mean	SD	Median	Minimum	Maximum	n	Mean	SD	Median	Minimum	Maximum
ISLA101 xxx mg Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
ISLA101 xx mg Fed (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo Fasted (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x
Placebo Fed (N=xx)												
Baseline[1]	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	-					
Day 1- 5 hours post dose	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xxx	xx.xx	xx.x	xx.x

SD: Standard deviation, - : Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to study drug administration in that period.
Where triplicate measurements were taken, summaries were based on the mean of the triplicate measurements at each visit/time point.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.6.2.1 Summary of 12-Lead ECG Overall Assessment (Safety Population)

Treatment Group Visit: Time Point		Overall Assessment		
	n	Normal n (%)	Abnormal NCS n (%)	Abnormal CS n (%)
ISLA101 300 mg Fasted (N=xx)				
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
ISLA101 600 mg Fasted (N=xx)	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
ISLA101 900 mg Fasted (N=xx)				
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Pooled Placebo (N=xx)				
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
…				

CS: Clinically Significant, NCS: Not Clinically Significant
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Percentage (%) are based on the number of participants (n) with assessments available at the relevant post-baseline visit.
Where triplicate measurements were taken, summaries were based on the worst overall interpretation of the triplicate measurements at each visit/time point.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
The treatment groups will be displayed for the following: ISLA101 300 mg Fasted, ISLA101 600 mg Fasted, ISLA101 900 mg Fasted, Pooled Placebo.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Table 14.3.6.2.2 Summary of 12-Lead ECG Overall Assessment - Fasted and Fed Cohorts (Safety Population)

Treatment Group Visit: Time Point	Overall Assessment n	Normal n (%)	Abnormal NCS n (%)	Abnormal CS n (%)
ISLA101 xxx mg Fasted (N=xx)				
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
ISLA101 xxx mg Fed (N=xx)	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Placebo Fasted (N=xx)				
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Placebo Fed (N=xx)				
Baseline[1]	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
Day 1- 5 hours post dose	xx	xx (xx.xx%)	xx (xx.xx%)	xx (xx.xx%)
…				

CS: Clinically Significant, NCS: Not Clinically Significant
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Percentage (%) are based on the number of participants (n) with assessments available at the relevant post-baseline visit.
Where triplicate measurements were taken, summaries were based on the worst overall interpretation of the triplicate measurements at each visit/time point.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.1.1 Analysis Sets (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Analysis Set	Included in Analysis Set	Reason if Excluded from Analysis set
xxx-xxx	Safety Population	Yes	
	Pharmacokinetic Population	Yes	
xxx-xxx	Safety Population		
	Pharmacokinetic Population	Yes	
		Yes	
…			

This Safety Population will include all subjects who received at least 1 dose of the study drug (ISLA101 or Placebo).
The PK Population will consist of all subjects in the safety population who have a pre-dose PK sample and at least 1 post-dose analyzable PK sample and at least 1 post-dose analyzable PK sample (quantifiable Plasma concentration).

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.1.2 Subject Disposition (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Date of Informed Consent	Date Time of First Study Drug Administration	Subject Completed the Study / If No, Reason	End of Study Date/ Study Day
xxx-xxx	YYYY-MM-DD	YYYY-MM-DD HH:MM	Yes	YYYY-MM-DD/ XX
xxx-xxx	YYYY-MM-DD	YYYY-MM-DD HH:MM	No - AE No.	YYYY-MM-DD/ XX
xxx-xxx	YYYY-MM-DD	YYYY-MM-DD HH:MM	No - PD No.	YYYY-MM-DD/ XX
xxx-xxx	YYYY-MM-DD	YYYY-MM-DD HH:MM	Yes	YYYY-MM-DD/ XX

Study days are calculated relative to the date of the study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.2.1 Protocol Deviations (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Deviation Number	Start Date of Deviation	Deviation Category	Deviation Type	Assessment Type	Deviation Description	Reported to HREC/If Yes, Date	Reason for Not Reported to HREC
xxx-xxx	xx	YYYY-MM-DD	Minor	Missed Procedure/Assessments	12-lead ECG	XXXXXXXXXXXXXXXXXXXXXXXX	No	XXXXXXX
			Major	XXXXXXXXXX	Vital Sign	XXXXXXXXXXXXXXXXXXXXXXXX	Yes/ YYYY-MM-DD	
				XXXXXXXXXXX	Xxxx	XXXXXXXXXXXXXXXXXXXXXXXX	NA	
				XXXXXXXXXXX	xxxx	XXXXXXXXXXXXXXXXXXXXXXXX	No	
				Other		X		

NA: Not Applicable; HREC: Human Research Ethics Committees.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.2.2 Subject Eligibility (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Protocol Date/Version	Eligibility Assessment Date	Did the Subject Meet All Eligibility Criteria	Category Failed (Inclusion/ Exclusion)	Inclusion Criterion not met/ Exclusion Criterion met
xxx-xxx	Screening	ISLA101-P01-CT001, 18-Sep-2023,V1.1	YYYY-MM-DD	No	Inclusion and Exclusion	Exclusion: xx, xx; Inclusion xx, xx
	Day -1		YYYY-MM-DD	Yes		

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups. List all screening failures at the beginning of the listing.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.3 Randomization (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Date of Randomization	Replacement Subject	Randomization Number/Replacement Randomization Number
xxx-xxx	YYYY-MM-DD HH:MM	No	xxxxxxxx
xxx-xxx	YYYY-MM-DD HH:MM	Yes	xxxxxxxx

Programmer note:
Repeat for all subjects within the treatment group, and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.1 Demography (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Year of Birth	Age (Years)	Sex	Childbearing Potential, No - Specify	Ethnicity	Race
xxx-xxx	YYYY	xx	Female	Yes	Hispanic or Latino	White
xxx-xxx	YYYY	xx	Male	-	Hispanic or Latino	Other - XXXXXXXXXXXXX
xxx-xxx	YYYY	xx	Female	No - Postmenopausal	Not Hispanic or Latino	Asian
xxx-xxx	YYYY	xx	Female	No - Perimenopausal	Not Hispanic or Latino	Asian

-: Not applicable.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.2 Medical and Surgical History (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	MH No.	Subcategory	System Organ Class/ Preferred Term/ Medical Name	Start Date/ Study Day	End Date / Study Day	Ongoing
xxx-xxx	1	Surgery	XXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD/ -XXX	YYYY-MM	No
	2	Endocrine	XXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD/ -XXX	YYYY-MM-DD/ -XXX	No
	3	Other	XXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXX/ XXXXXXXXXXXXXXXXXXXXX	YYYY-MM-DD/ -XXX		Yes

MH = Medical History.
Study days are calculated relative to the date of the first study drug administration.

Medical history terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.
Sort terms by start and end date, then alphabetically within subject.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.3 Alcohol Breath Test Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Assessment Date	Alcohol Breath Test Results	Specify Equivocal/Unevaluable
xxx-xxx	Screening	YYYY-MM-DD	Negative	-
	Day -1	YYYY-MM-DD	Equivocal/Unevaluable	xxxxxxxxxxxxxxxxxxxxxx

-: Not applicable.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects/visits/drugs or test within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.4 Urine Drug Test Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Sample Collected Date	Test	Urine Drug Test Results	Drugs Tested Positive	Specify Equivocal/Unevaluable
xxx-xxx	Screening	YYYY-MM-DD	Urine Drug	Positive	Amphetamines Barbiturates Benzodiazepines	-
			Cotinine	Negative	-	-
	Day -1	YYYY-MM-DD	Urine Drug	Negative	-	-
			Cotinine	Negative	-	-

-: Not applicable.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all subjects/visits/drugs or test within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.5 Pregnancy Test Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Sample Collection Date	Specimen type	Result	Specify Equivocal/Unevaluable
xxx-xxx	Screening	YYYY-MM-DD	Urine	Negative	-
	Day-1	YYYY-MM-DD	Serum	Equivocal/Unevaluable	xxxxxxxxxxx

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.6 Serology Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Sample Collection Date Time	Parameter	Result
xxx-xxx	Screening	YYYY-MM-DD HH: MM	HBsAg	Negative
			Hepatitis C Virus	Negative
			HIV 1/2	Negative

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.7.1 Prior Medications (Safety Population)

Cohort 1: ISLA101 300 mg Fasted
Subject Number: xxx-xxx

CM No.	WHO-DD ATC Class Level 2 Term/ WHO-DD Preferred Name/ Verbatim Term	Indication	Category	Dose	Unit	Frequency	Route	Start Date/ Study Day	End Date/ Study Day
1	ZZZZZZZZZZZZZZZZZZZ/ XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYY	XXXXXXX	Medical History: MH No.	xx.x	XXX	XXXXXXXX	XXXXXX	YYYY-MM-DD/ XX	YYYY-MM-DD/ XX
2	ZZZZZZZZZZZZZZZZZZZ/ XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYY	XXXXXX	Adverse Event: AE No.	xx.x	XXX	XXXXXXXX	XXXXXX	YYYY-MM-DD/ XX	YYYY-MM-DD/ XX

CM No.: Medication Number.
Prior medications are defined as any medication where the use was stopped prior to the first administration of study drug.
Only prior medications are presented.
Study days are calculated relative to the date of the first study drug administration.

Medication terms were coded using the World Health Organisation - Drug Dictionary Version Global (WHO-DD) C3, September 2023.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.4.7.2 Concomitant Medications (Safety Population)

Cohort 1: ISLA101 100 mg Fasted
Subject Number: xxx-xxx

CM No.	WHO-DD ATC Class Level 2 Term/ WHO-DD Preferred Name/ Verbatim Term	Indication	Category	Dose	Unit	Frequency	Route	Start Date/ Study Day	End Date/ Study Day
1	ZZZZZZZZZZZZZZZZZZZ/ XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYY	Xxxxxx	Medical History - Headache	xx.x	XXX	XXXXXXXX	XXXXXX	YYYY-MM-DD/ XX	YYYY-MM-DD/ XX
2	ZZZZZZZZZZZZZZZZZZZ/ XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYY	xxxxxxx	Adverse Event - XXXXXXXXXXX	xx.x	XXX	XXXXXXXX	XXXXXX	YYYY-MM-DD/ XX	YYYY-MM-DD/ Ongoing

CM No.: Medication Number.
Concomitant medications are defined as any medication (other than the study drug) that was used at least once after the first administration of study drug. Medications stopping on the same day as the first study drug administration will be considered as concomitant medications.
Only concomitant medications are presented.
Study days are calculated relative to the date of the first study drug administration.

Medication terms were coded using the World Health Organisation - Drug Dictionary Version Global (WHO-DD) C3, September 2023.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.5.1 Study Drug Administration (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Date Time of Last Meal (Before Fasting)	Take High Fat Meal Before Dosing/ Date time of High Fat Meal consumed	Date Time of First Capsule consumed/ Dose	How Many Dispensed Capsules Administered	All Capsules consumed/ If No, Capsules consumed	Fasting at Least 4 Hours After Study Drug Administration/ If No, hours (Fasted)
xxx-xxx	Day 1	YYYY-MM-DD HH:MM	No	YYYY-MM-DD HH:MM/ 300 mg/m^2	xx	Yes	No/ xx hrs
xxx-xxx	Day 1	YYYY-MM-DD HH:MM	Yes/ YYYY-MM-DD HH:MM	YYYY-MM-DD HH:MM/ 300 mg/m^2	Xx	No/ xx	Yes
xxx-xxx	Day 1	YYYY-MM-DD HH:MM	No				

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.6.1 Plasma Pharmacokinetic Concentrations (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Cohort 1: ISLA101 300 mg Fasted

Subject Number	Time Point	Sample Collection Date Time	Elapsed Time Since Study Drug Administration (Hours)	Time Deviation (Minutes)	Concentration (ng/mL)
xxx-xxx	Pre-dose	YYYY-MM-DD HH:MM	-	-	BLQ
	0.5 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	0.75 hour	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	1 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	1.5 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	2 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	3 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	4 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	5 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	6 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	8 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	10 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	12 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	24 hours	YYYY-MM-DD HH:MM	xx.xx	xx	XX.XX
	36 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	48 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	72 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx
	96 hours	YYYY-MM-DD HH:MM	xx.xx	xx	xx.xx

BLQ: Below the LLOQ; LLOQ: Lower Limit of Quantification;
Elapsed Time Since Study Drug Administration is calculated as the difference between the Date Time of the sample collection and the Date Time of the study drug administration for the specific period.
Time Deviation is calculated as the difference between the Elapsed Time Since Study Drug Administration and the nominal visit or time point in the specific period.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer Note:
Repeat for all treatment groups.
Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.6.2 Plasma Pharmacokinetic Parameters (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Cohort 1: ISLA101 300 mg Fasted

Subject Number	C_{max} (ng/ml)	DN_C_{max} (ng/ml)	T_{max} (h)	AUC_{0-24} (h*ng/ml)	AUC_{last} (h*ng/ml)	DN_AUC_{last} (h*ng/ml)	AUC_{inf} (h*ng/ml)	DN_AUC_{inf} (h*ng/ml)	CL/F (L/h)	V_z/F (L)	Adjusted R^2	No. of Points	Span	λ_z (1/h)	$t_{1/2}$ (h)	$\%AUC_{extrap}$ (%)
xx-xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
xx-xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
xx-xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
xx-xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
xx-xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx

DN: Dose Normalized; AUC: Area Under the Curve.
*Result excluded from the summaries and analyses.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM   Page 1 of x

Programmers note:
Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.7.1 Adverse Events (Safety Population)

Cohort 1: ISLA101 300 mg Fasted
Subject Number: xxx-xxx

AE No.	System Organ Class (SOC)/ Preferred Term (PT)/ Verbatim Term	Start Date Time/ Study Day/ TEAE	End Date Time/ Study Day/ Ongoing	SAE/ AESI/DL_AE	Signs of Drug Toxicity	Outcome	Severity	Relationship to Study Drug	Action Taken	Other Action Taken
1	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM/ XX/ Yes	YYYY-MM-DD HH:MM/ XX	Yes/Yes/Yes	Xxxxx	Recovered/ Resolved	Mild	Probably	Unknown	None
2	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM / XX/ Yes	YYYY-MM-DD HH:MM/ Ongoing	No/No/No	-	Recovering/ Resolving	Severe	Definitely	Dose not Changed	None None

AE No.: Adverse Event Number, SAE: Serious adverse event, TEAE: Treatment-emergent adverse event, AESI: Adverse event of special interest, DL: Dose-Limiting, -: Not Applicable.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Study days are calculated relative to the date of the treatment group first study drug administration.

Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all AEs that a subject experienced and repeat for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.7.2 Treatment-Related Adverse Events (Safety Population)

Cohort 1: ISLA101 300 mg Fasted
Subject Number: xxx-xxx

AE No.	System Organ Class (SOC)/ Preferred Term (PT)/ Verbatim Term	Start Date Time/ Study Day/ TEAE	End Date Time/ Study Day/ Ongoing	SAE/ AESI/DL_AE	Signs of Drug Toxicity	Outcome	Severity	Relationship to Study Drug	Action Taken	Other Action Taken
1	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM/ XX/ Yes	YYYY-MM-DD HH:MM/ XX	Yes/Yes/Yes	Xxxxx	Recovered/ Resolved	Mild	Probably	Unknown	None
2	XXXXXXXXXXXXXXXXXXX/ YYYYYYYYYYYYYYYYYYY/ ZZZZZZZZZZZZZZZZZZZ	YYYY-MM-DD HH:MM / XX/ Yes	YYYY-MM-DD HH:MM/ Ongoing	No/No/No	-	Recovering/ Resolving	Severe	Definitely	Dose not Changed	None None

AE No.: Adverse Event Number, SAE: Serious adverse event, TEAE: Treatment-emergent adverse event, AESI: Adverse event of special interest, DL: Dose-Limiting, -: Not Applicable.
Treatment-emergent adverse events are defined as adverse events that commenced or worsened on or after the first study drug administration.
Study days are calculated relative to the date of the treatment group first study drug administration.
Only treatment related AE will be presented.
Adverse event terms were coded using Medical Dictionary for Regulatory Activities (MedDRA) Version 26.1.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all AEs that a subject experienced and repeat for all treatment groups.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.8.1 Hematology Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Parameter (Unit)	Visit	Sample Collection Date Time	Result	Change from Baseline[1]	Reference Range (Low, High)	Reference Range Indicator
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day -1[1]	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	Low
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 3	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 4	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	Low
	…	Day 5	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 8 – Follow Up	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day -1 [1]	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Early Termination	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	High

-: Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Reference range indicators (result classifications) are based on the laboratory defined reference ranges for the specific parameter.

Program Name: xxx.sas, Creation Date and Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all treatment groups. Repeat for all parameters/subjects within a treatment group.
Present 'Early Termination' or 'Day 8 - Follow up' or 'Day 17 - Follow Up' depending on whether the subjects complete the study or not.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.8.2 Biochemistry Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Parameter (Unit)	Visit	Sample Collection Date Time	Result	Change from Baseline[1]	Reference Range (Low, High)	Reference Range Indicator
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day -1[1]	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	Low
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 3	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 4	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	Low
	…	Day 5	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 8 – Follow Up	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day -1 [1]	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Early Termination	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	High

-: Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Reference range indicators (result classifications) are based on the laboratory defined reference ranges for the specific parameter.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all treatment groups. Repeat for all parameters/subjects within a treatment group.
Present 'Early Termination' or 'Day 8 - Follow up' or 'Day 17 - Follow Up' depending on whether the subjects complete the study or not.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.8.3 Coagulation Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Parameter (Unit)	Visit	Sample Collection Date Time	Result	Change from Baseline[1]	Reference Range (Low, High)	Reference Range Indicator
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day -1[1]	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	Low
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 3	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 4	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	Low
	…	Day 5	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 8 - Follow Up	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day -1 [1]	YYYY-MM-DD HH:MM	XXX	-	(XXX, XXX)	
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	
		Early Termination	YYYY-MM-DD HH:MM	XXX	XXX	(XXX, XXX)	High

-: Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.
Reference range indicators (result classifications) are based on the laboratory defined reference ranges for the specific parameter.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Programmer note:
Repeat for all treatment groups. Repeat for all parameters/subjects within a treatment group.
Present 'Early Termination' or 'Day 8 - Follow up' or 'Day 17 - Follow Up' depending on whether the subjects complete the study or not.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.8.4 Urinalysis Results Including Microscopy (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Parameter (Unit)	Visit	Sample Collection Date Time	Result	Result Evaluation
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	Normal
		Day -1[1]	YYYY-MM-DD HH:MM	XXX	Normal
		Day 1	YYYY-MM-DD HH:MM	XXX	NCS
		Day 2	YYYY-MM-DD HH:MM	XXX	NCS
		Day 3	YYYY-MM-DD HH:MM	XXX	CS
		Day 4	YYYY-MM-DD HH:MM	XXX	Normal
	…	Day 5	YYYY-MM-DD HH:MM	XXX	Normal
		Day 8 – Follow Up	YYYY-MM-DD HH:MM	XXX	Normal
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	Normal
		Day -1 [1]	YYYY-MM-DD HH:MM	XXX	Normal
		Day 1	YYYY-MM-DD HH:MM	XXX	Normal
		Day 2	YYYY-MM-DD HH:MM	XXX	Normal
		Early Termination	YYYY-MM-DD HH:MM	XXX	Normal

-: Not applicable, CS: Clinically significant, NCS Not clinically significant.
[1] The baseline value is defined as the last available valid assessment collected prior to first study drug administration.

Clinical significance flags as reported by the Investigator.

Programmer note:
Repeat for all treatment groups. Repeat for all parameters/subjects within a treatment group.
Present 'Early Termination' or 'Day 8 - Follow up' or 'Day 17 - Follow Up' depending on whether the subject complete the study or not.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.9.1 Vital Signs Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Parameter (Unit)	Visit	Assessment Date Time	Result	Change from Baseline[1]
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-
		Day -1 [1]	YYYY-MM-DD HH:MM	XXX	-
		Day 1	YYYY-MM-DD HH:MM	XXX	XXX
		Day 2	YYYY-MM-DD HH:MM	XXX	XXX
		Day 3	YYYY-MM-DD HH:MM	XXX	XXX
		Day 4	YYYY-MM-DD HH:MM	XXX	XXX
		Day 5	YYYY-MM-DD HH:MM	XXX	XXX
		Day 8 - Follow Up	YYYY-MM-DD HH:MM	XXX	XXX
xxx-xxx	XXXXXX (XX)	Screening	YYYY-MM-DD HH:MM	XXX	-
		Day -1 [1]	YYYY-MM-DD HH:MM	XXX	-
		Early Termination	YYYY-MM-DD HH:MM	XXX	XXX

-: Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to the first study drug administration.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all treatment groups. Repeat for all parameters/subjects within a treatment group.
Present 'Early Termination' or 'Day 8 - Follow up' or 'Day 17 - Follow Up' depending on whether the subjects complete the study or not.
Present the results in the following order:
SBP, DBP, Pulse Rate, Respiratory Rate, Temperature, Height, Body Weight, BMI, BSA.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.9.2.1 12-Lead ECG Results (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Parameter (Unit)	Visit	Trace Reading	Assessment Date Time	Result	Change from Baseline[1]
xxx-xxx	XXXXX	Screening	1	YYYY-MM-DD HH:MM	XXX	-
			2	YYYY-MM-DD HH:MM	XXX	-
			3	YYYY-MM-DD HH:MM	XXX	-
			Mean		XXX.X	-
		Day -1 [1]	1	YYYY-MM-DD HH:MM	XXX	-
			2	YYYY-MM-DD HH:MM	XXX	-
			3	YYYY-MM-DD HH:MM	XXX	-
			Mean		XXX.X	-
		Day 1 - 5 hours Post Dose	1	YYYY-MM-DD HH:MM	XXX	
			2	YYYY-MM-DD HH:MM	XXX	
			3	YYYY-MM-DD HH:MM	XXX	
			Mean		XXX.X	XXX.X

-: Not applicable.
[1] The baseline value is defined as the last available valid assessment collected prior to the first study drug administration.
Where triplicate measurements were taken, continuous results were based on the mean of the triplicate measurements and overall interpretation was based on the worst overall interpretation of the triplicate measurements at each visit/time point.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM Page 1 of x

Present the results in the following order:

- Heart Rate.
- RR Interval.
- PR Interval.
- QRS Duration.
- QTcF Interval.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.9.2.2 12-Lead ECG Overall Assessment (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Trace Reading	Assessment Date Time	Result	Comments
xxx-xxx	Screening	1	YYYY-MM-DD HH:MM	Normal	
		2	YYYY-MM-DD HH:MM	Normal	
		3	YYYY-MM-DD HH:MM	Abnormal NCS	XXXXXXXXXX
		Worst		Abnormal NCS	XXXXXXXXXX
	Day -1	1	YYYY-MM-DD HH:MM	Normal	
		2	YYYY-MM-DD HH:MM	Normal	
		3	YYYY-MM-DD HH:MM	Normal	
		Worst		Normal	
	Day 1 – 5 Hours Post Dose	1	YYYY-MM-DD HH:MM	Normal	
		2	YYYY-MM-DD HH:MM	Normal	
		3	YYYY-MM-DD HH:MM	Normal	
		Worst		Normal	

-: Not applicable, -: Not applicable, CS: Clinically Significant, NCS: Not Clinically Significant.
[1] The baseline value is defined as the last available valid assessment collected prior to the first study drug administration.
Where triplicate measurements were taken, continuous results were based on the mean of the triplicate measurements and overall interpretation was based on the worst overall interpretation of the triplicate measurements at each visit/time point.

Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Listing 16.2.9.3 Physical Examination Findings (Safety Population)

Cohort 1: ISLA101 300 mg Fasted

Subject Number	Visit	Assessment Date Time	Body System	Examination Status	Abnormal Finding
xxx-xxx	Screening	YYYY-MM-DD HH:MM	General Appearance	Abnormal NCS	XXXXXXX
			Head, Ears, Eyes, Nose and Throat	Normal	
			Neck and Thyroid	Normal	
			Lymph Nodes	Normal	
			Cardiovascular system	Normal	
			Respiratory System	Normal	
			Gastrointestinal system	Normal	
			Renal system	Normal	
			Neurological system	Normal	
			Musculoskeletal system	Normal	
			Skin	Normal	
			Other: XXXXXXXX	Normal	
	Day -1	YYYY-MM-DD HH:MM	General appearance	Normal	

-: Not applicable, CS: clinically Significant, NCS Not clinically Significant

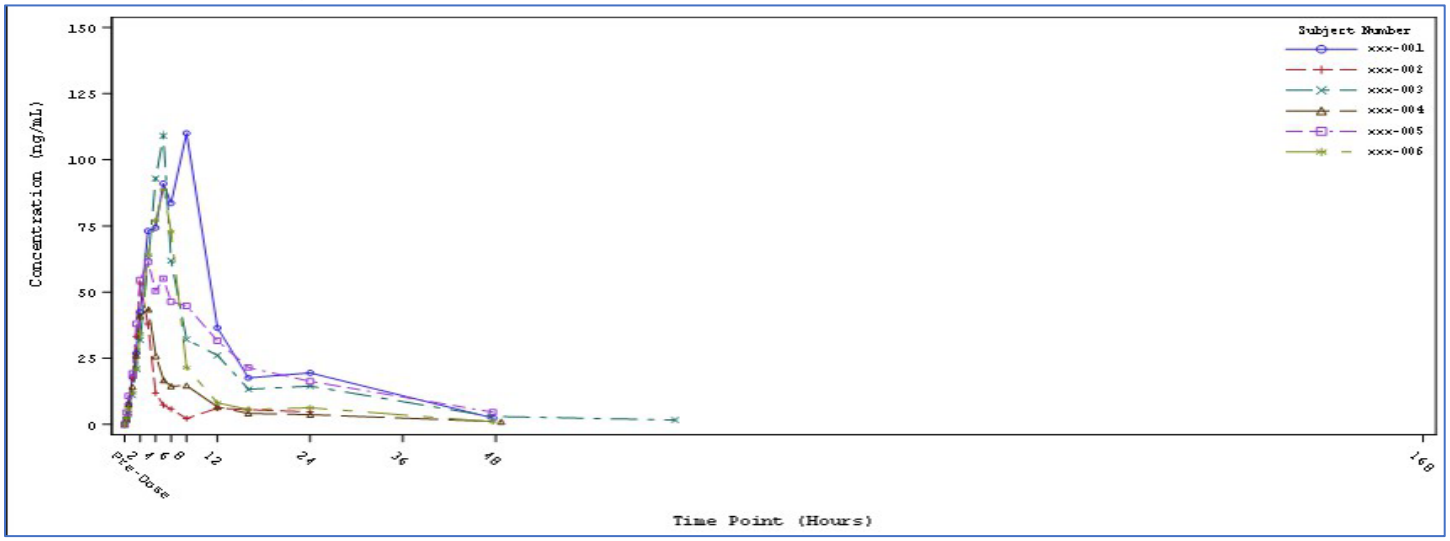
Program Name: xxx.sas, Creation Date Time: YYYY-MM-DD HH:MM

Programmer note:
Repeat for all subjects within the treatment group and for all treatment groups and all time points.
Present 'Early Termination' or 'Day 8 - Follow up' or 'Day 17 - Follow Up' depending on whether the subjects complete the study or not.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.1.1.1 Individual Plasma PK Concentrations over Time (Linear) (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Cohort 1: ISLA101 300 mg Fasted



BLQ: Below the Lower Limit of Quantitation.
BLQ concentrations observed prior to the first quantificationse concentration were set to zero and other BLQ concentrations were treated as missing.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

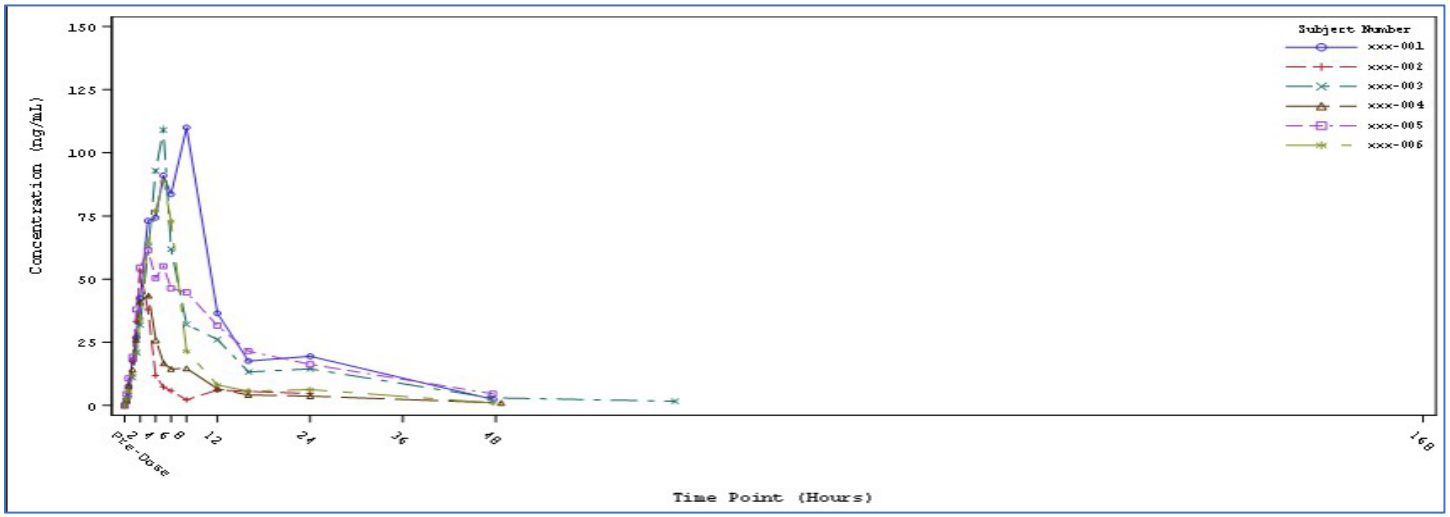
Programming Note:

- x-axis will represent the actual study time in hours.
- Y-axis: Use the analyte name/unit as the axis label. Adjust tick marks based on the actual concentrations for the specific analyte across all the treatment groups to ensure that the y-axis range is the same across all plots. The y-axis should be presented on a linear scale.
- Legend: Subject Number.
- Present each subject with a different line type/color and present each treatment group in a separate plot.
- Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.1.1.2 Individual Plasma PK Concentrations over Time (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Treatment: ISLA101 xxx mg Fasted (n=xx)



BLQ: Below the Lower Limit of Quantitation.
BLQ concentrations observed prior to the first quantificationse concentration were set to zero and other BLQ concentrations were treated as missing.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM Page 1 of x

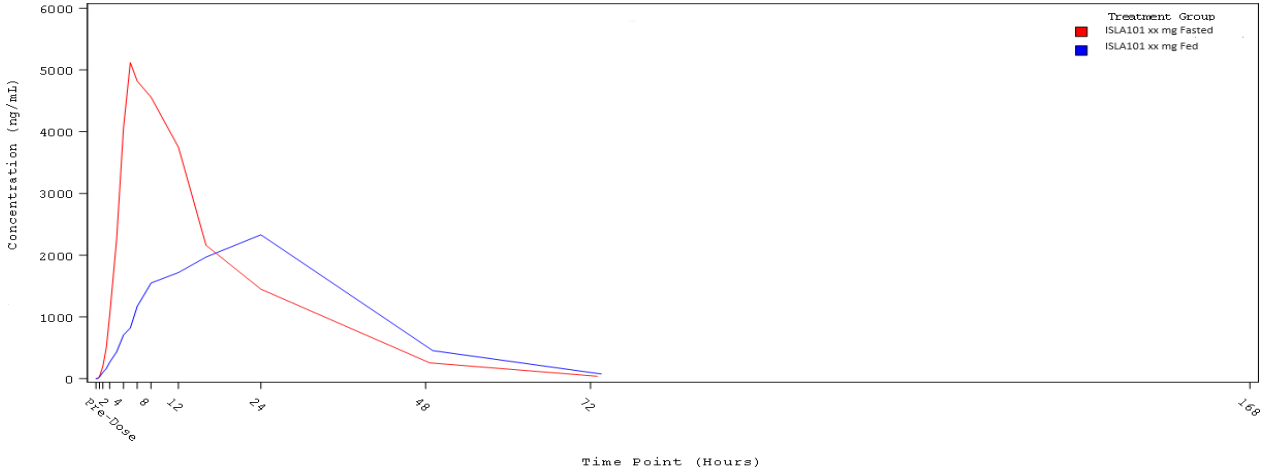
Programming Note:
The treatment group will be displayed as the following: ISLA101 XXX mg Fasted, and ISLA101 XXX mg Fed.

- x-axis will represent the actual study time in hours.
- Y-axis: Use the analyte name/unit as the axis label. Adjust tick marks based on the actual concentrations for the specific analyte across all the treatment groups to ensure that the y-axis range is the same across all plots. The y-axis should be presented on a linear scale.
- Legend: Subject Number.
- Present each subject with a different line type/color and present the Fasted and Fed Cohort in a separate plot.
- Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.1.1.3 Individual Plasma PK Concentrations over Time by Subject (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Subject Number: XXX-XXX



BLQ: Below the Lower Limit of Quantitation.
BLQ concentrations observed prior to the first quantificationse concentration were set to zero and other BLQ concentrations were treated as missing.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM Page 1 of x

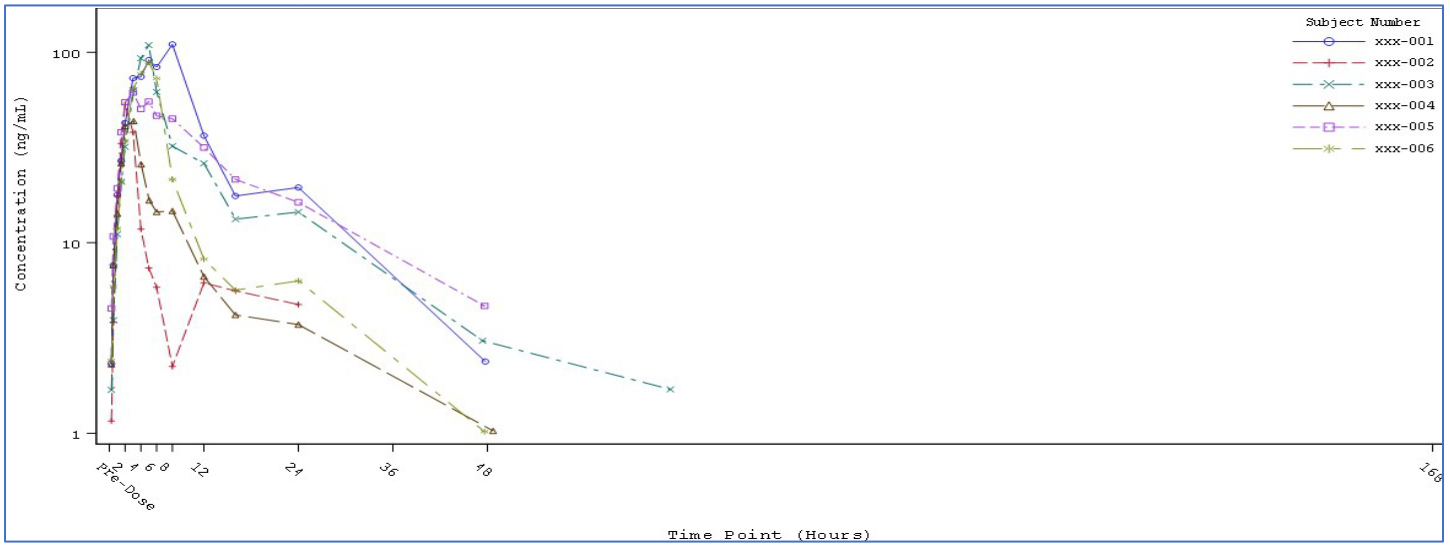
Programming Note:

- Present each subject in a separate plot and Repeat for the analyte = MPR and oxo-HPR.
- x-axis will represent the actual study time in hours.
- Y-axis: Use the analyte name/unit as the axis label. Adjust tick marks based on the actual concentrations for the specific analyte across all the treatment groups to ensure that the y-axis range is the same across all plots. The y-axis should be presented on a linear scale.
- Legend: show the two treatment groups for the Food Effect cohort 'ISLA101 XX mg Fasted', and 'ISLA101 XX Fed'.
- Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.1.2.1 Individual Plasma PK Concentrations over Time (Log-Linear) (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Cohort 1: ISLA101 300 mg Fasted



BLQ: Below the Lower Limit of Quantitation.
BLQ concentrations were treated as missing.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

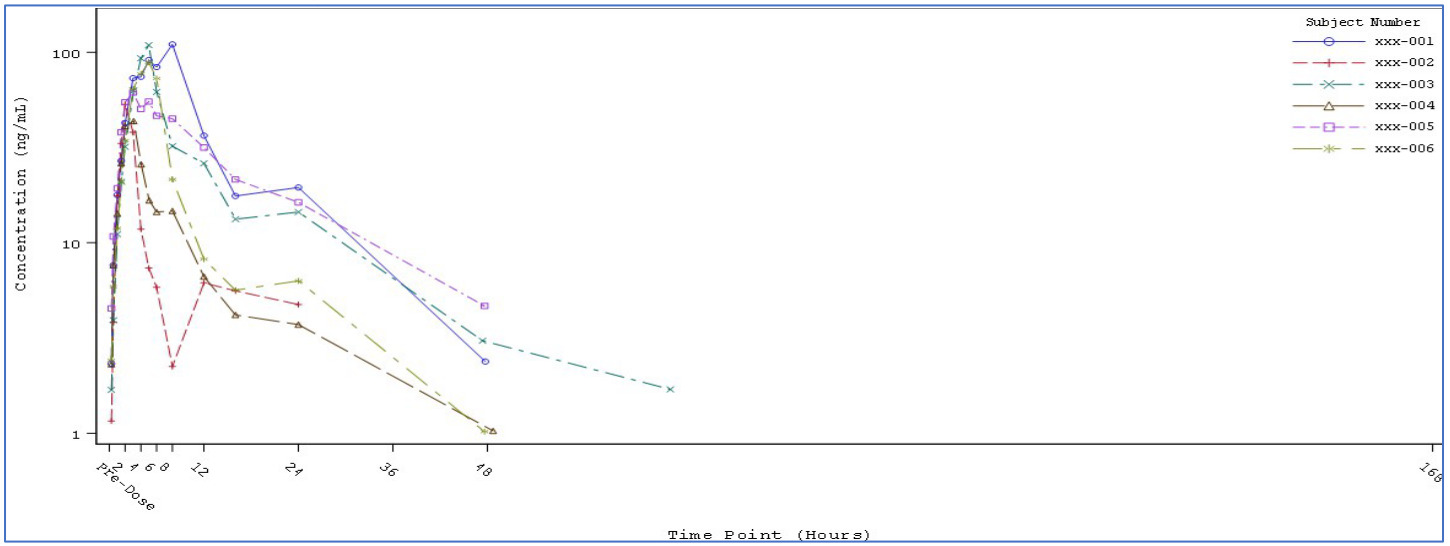
Programming Note:

- x-axis will represent the actual study time in hours.
- Y-axis: Use the analyte name/unit as the axis label. Adjust tick marks based on the actual concentrations for the specific analyte across all the treatment groups to ensure that the y-axis range is the same across all plots. The y-axis should be presented on a log-linear scale.
- Legend: Subject Number.
- Present each subject with a different line type/color and present each treatment group in a separate plot.
- Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.1.2.2 Individual Plasma PK Concentrations over Time (Log-Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Treatment: ISLA101 xxx mg Fasted (n=xx)



BLQ: Below the Lower Limit of Quantitation.
BLQ concentrations were treated as missing.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

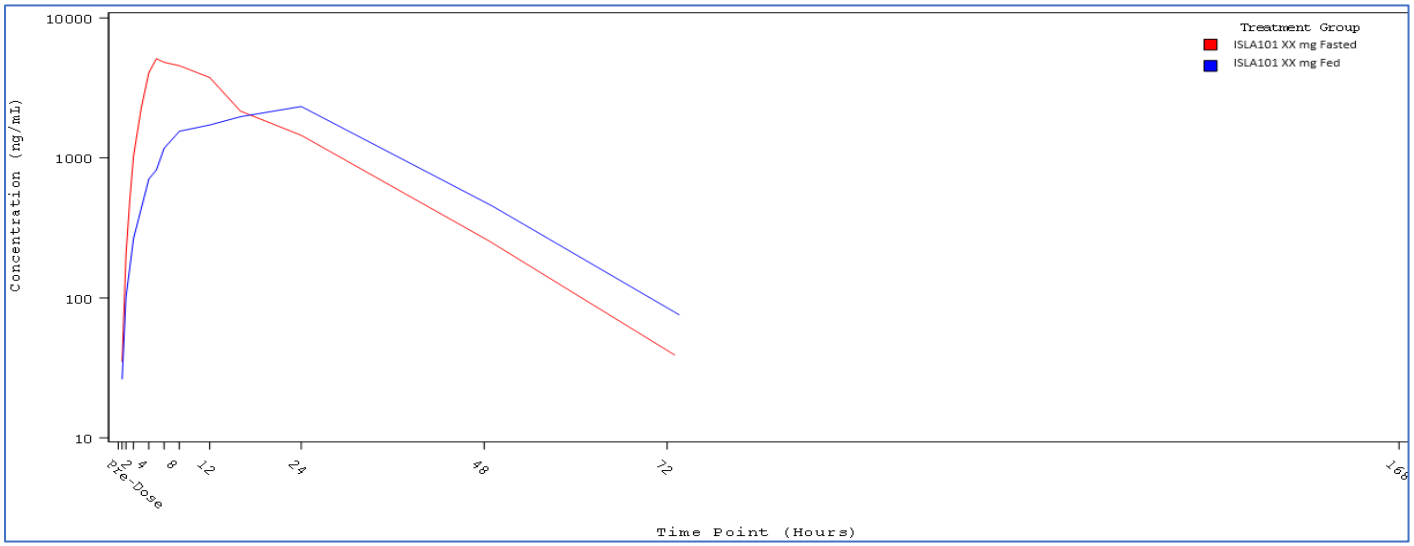
Programming Note:

- x-axis will represent the actual study time in hours.
- Y-axis: Use the analyte name/unit as the axis label. Adjust tick marks based on the actual concentrations for the specific analyte across all the treatment groups to ensure that the y-axis range is the same across all plots. The y-axis should be presented on a log-linear scale.
- Legend: Subject Number.
- Present each subject with a different line type/color and present the Food Effect Cohort in a separate plot.
- Repeat for the analyte = MPR and oxo-HPR
- The treatment group will be displayed as the following: ISLA101 XXX mg Fasted, and ISLA101 XXX mg Fed.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.1.2.3 Individual Plasma PK Concentrations over Time by Subject (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]
Subject Number: XXX-XXX



BLQ: Below the Lower Limit of Quantitation.
BLQ concentrations were treated as missing.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

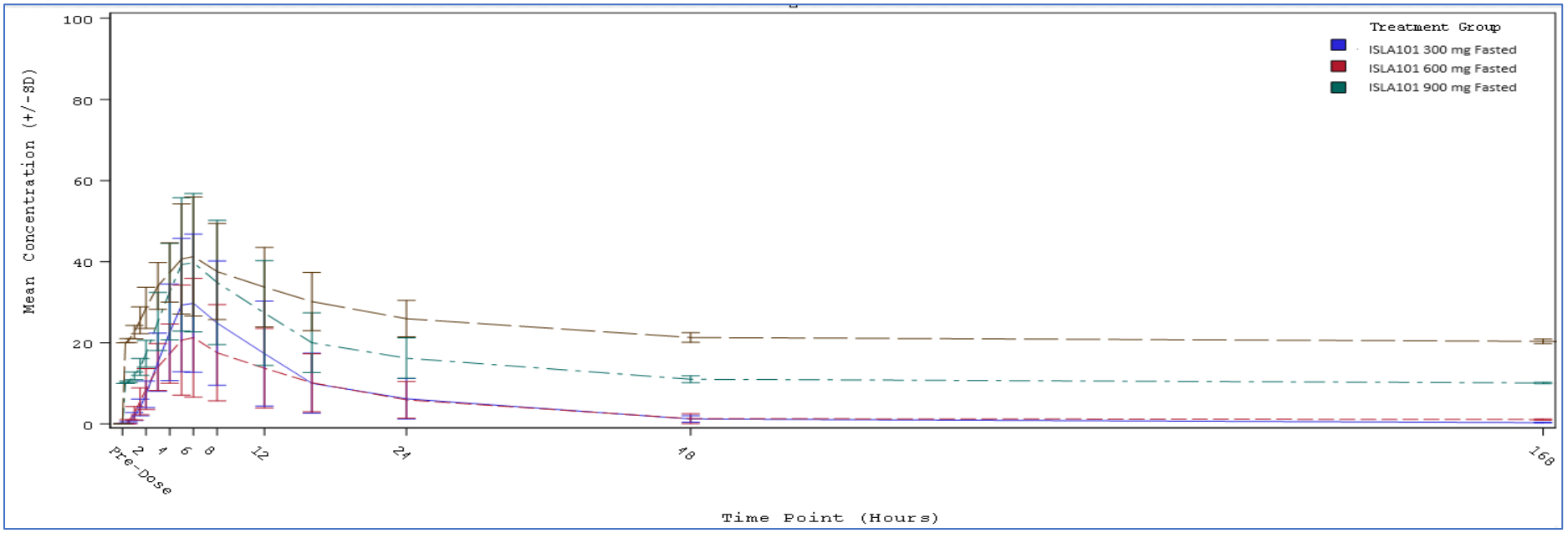
Programming Note:

- Present each subject in a separate plot and Repeat for the analyte = MPR and oxo-HPR.
- x-axis will represent the actual study time in hours.
- Y-axis: Use the analyte name/unit as the axis label. Adjust tick marks based on the actual concentrations for the specific analyte across all the treatment groups to ensure that the y-axis range is the same across all plots. The y-axis should be presented on a log-linear scale.
- Legend: show the two treatment groups for the Food Effect cohort 'ISLA101 XX mg Fasted', and 'ISLA101 XX Fed'.
- Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.2.1.1 Mean Plasma PK Concentrations over Time (Linear) (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]



SD: Standard deviation

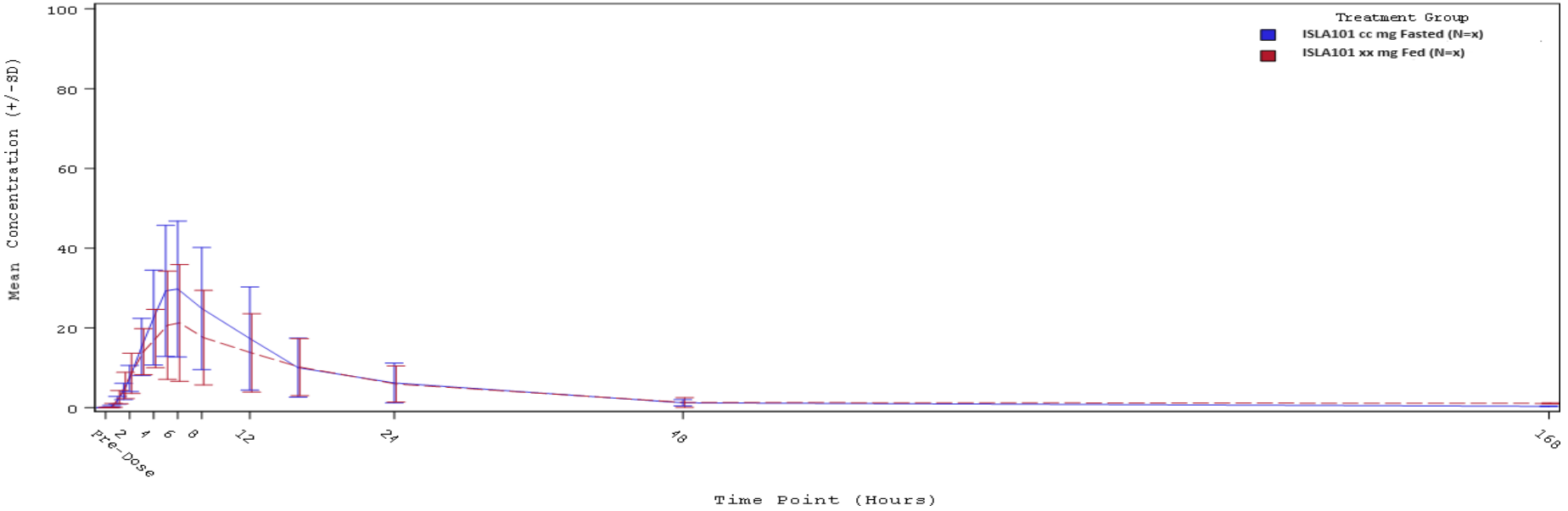
Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

Programming Note:
The x-axis will represent the scheduled study time in hours.
The y-axis will represent the mean Plasma Concentrations (ng/mL). The y-axis will be on the linear scale.
Legend: Show the treatment groups and the number of participants in each group. Present the legend in the top right corner of the plot unless the plots are overlapping with the legend (then move to best position on plot). Each treatment group will be presented as a distinct line type/color
Repeat for the analyte = MPR and oxo-HPR.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.2.1.2 Mean Plasma PK Concentrations over Time (Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]



SD: Standard deviation

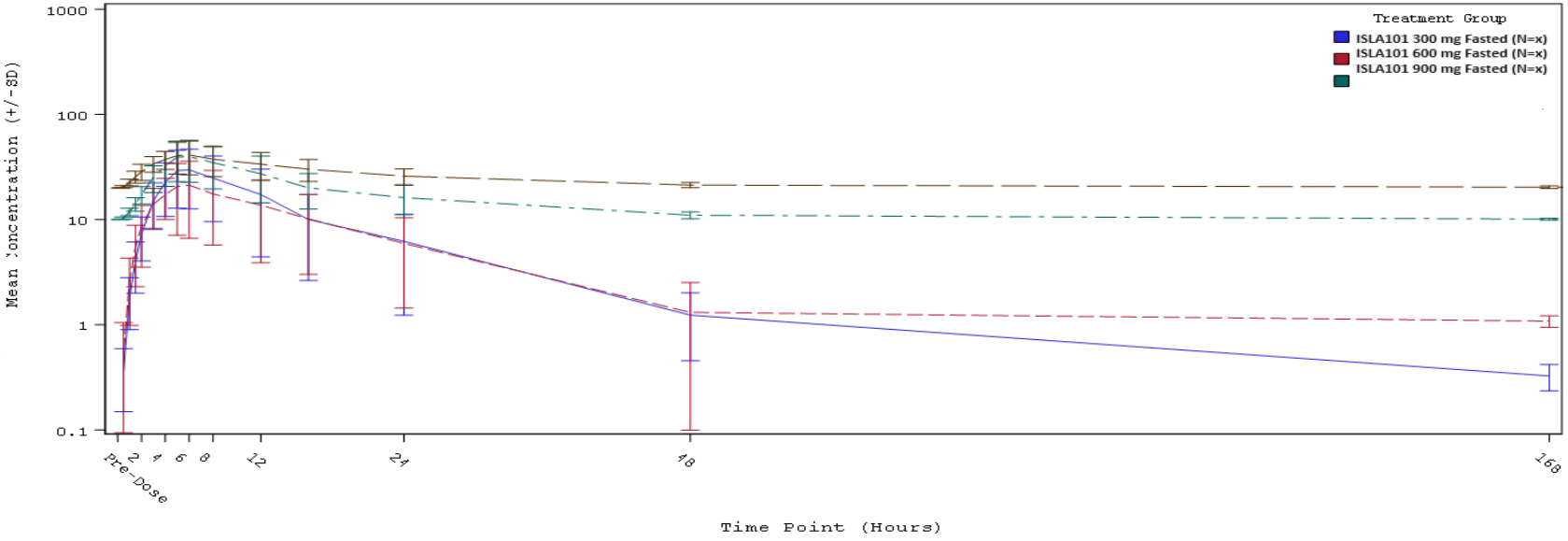
Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

Programming Note:
The x-axis will represent the scheduled study time in hours.
The y-axis will represent the mean Plasma Concentrations (ng/mL). The y-axis will be on the linear scale.
Legend: Show the treatment groups: ISLA101 xx mg Fasted and ISLA101 xx mg Fed and the number of participants in each group. Present the legend in the top right corner of the plot unless the plots are overlapping with the legend (then move to best position on plot). Each treatment group will be presented as a distinct line type/color.
Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.2.2.1 Mean Plasma PK Concentrations over Time (Log-Linear) (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]



SD: Standard deviation

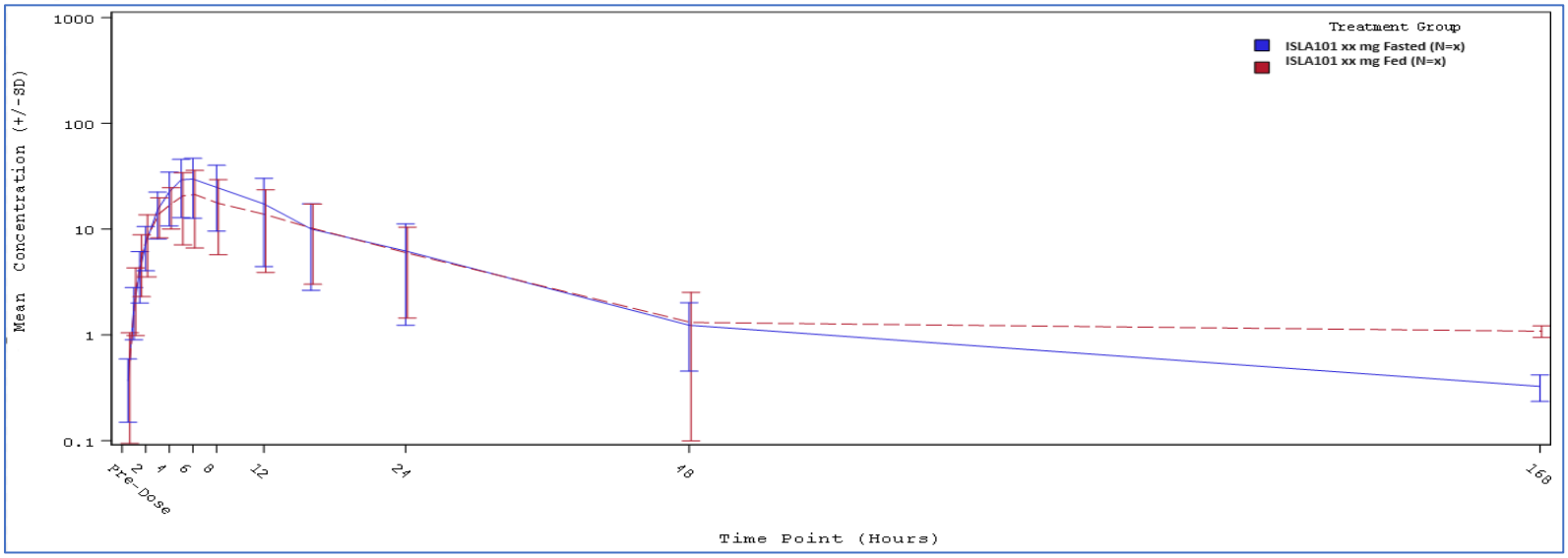
Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

Programming Note:
The x-axis will represent the scheduled study time in hours.
The y-axis will represent the mean Plasma Concentrations (ng/mL). The y-axis will be on the log-linear scale.
Legend: Show the treatment groups and the number of participants in each group. Present the legend in the top right corner of the plot unless the plots are overlapping with the legend (then move to best position on plot). Each treatment group will be presented as a distinct line type/color.
Repeat for the analyte = MPR and oxo-HPR.

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.2.2.2 Mean Plasma PK Concentrations over Time (Log-Linear) – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml) [LLOQ = x.xx ng/mL]



SD: Standard deviation

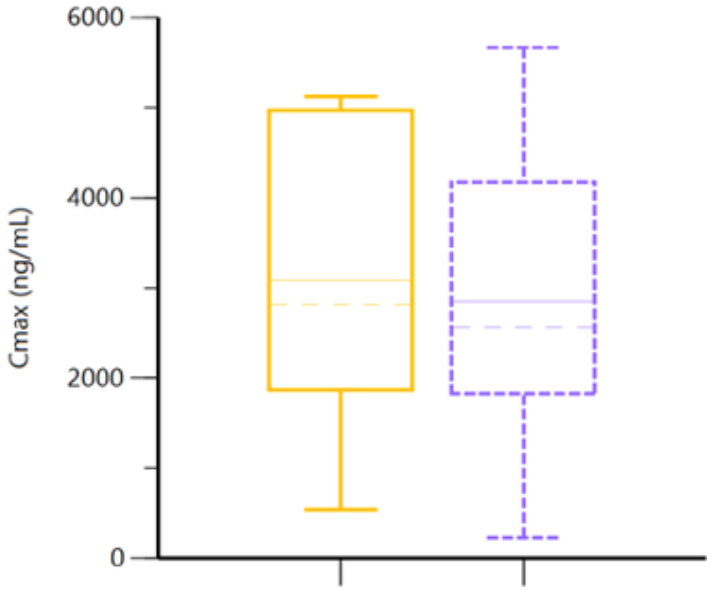
Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

Programming Note:
The x-axis will represent the scheduled study time in hours.
The y-axis will represent the mean Plasma Concentrations (ng/mL). The y-axis will be on the log-linear scale.
Legend: Show the treatment groups: ISLA101 xx mg Fasted and ISLA101 xx mg Fed and the number of participants in each group. Present the legend in the top right corner of the plot unless the plots are overlapping with the legend (then move to best position on plot). Each treatment group will be presented as a distinct line type/color.
Repeat for the analyte = MPR and oxo-HPR

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.3.1.1 Box Plots of Plasma PK Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml)
Parameter: C_{max} (ng/ml)



AUC: Area under the curve.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

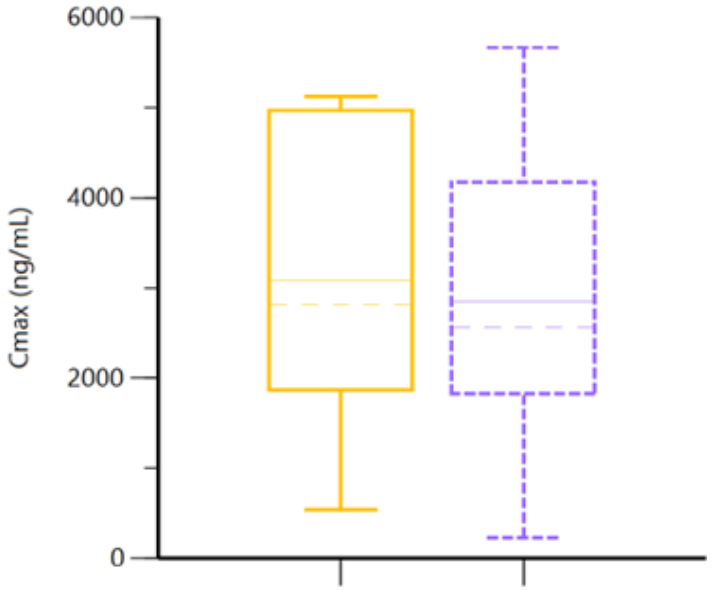
Programming Note:

- Present the treatment groups: ISLA101 XXX mg Fasted, and ISLA101 XXX mg Fed in the plot.
- Y-axis: Use the parameter name/unit as the axis label.
- X-axis: Add tick marks between the treatments (equally spaced) and use the treatment label and the number of subjects in the treatment arm as the label (i.e., 'ISLA101 XXX mg Fasted (N=xx)', 'ISLA101 xxx mg Fed (N=xx)').
- Repeat for AUC_{inf} and AUC_{last}
- for the analyte = Fenretinide (ng/ml) only

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.4.1.1 Box-Whisker Plots of Dose-Normalized Plasma PK Parameters (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml)
Parameter: DN_C_{max} (ng/ml)



AUC: Area under the curve.DN: Dose-Normalized

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

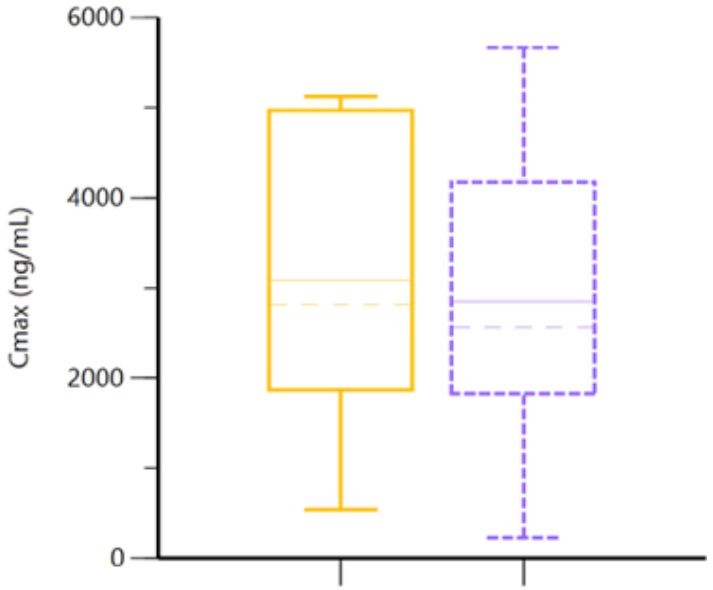
Programming Note:

- Present the treatment groups: ISLA101 300 mg Fasted, 600 mg Fasted and 900 mg Fasted in the plot showing the results for each treatment by increasing dose level.
- Y-axis: Use the parameter name/unit as the axis label.
- X-axis: Add tick marks between the treatments (equally spaced) and use the treatment label and the number of subjects in the treatment arm as the label (i.e., 'ISLA101 300 mg Fasted (N=xx)', 'ISLA101 600 mg Fasted (N=xx)' etc.).
- for the analyte = Fenretinide (ng/ml) only
- Repeat for AUC_{inf} and AUC_{last}

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.4.1.2 Box-Whisker Plots of Dose-Normalized Plasma PK Parameters – Fasted and Fed Cohorts (Pharmacokinetic Population)

Analyte (Unit): Fenretinide (ng/ml)
Parameter: DN_C_{max} (ng/ml)



AUC: Area under the curve.

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

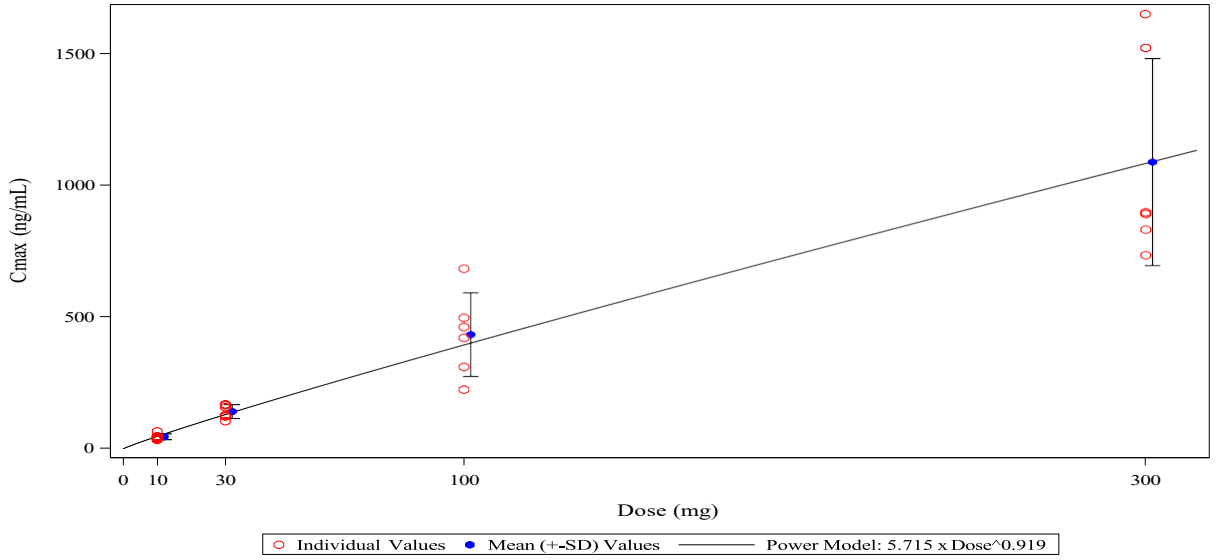
Programming Note:

- Present the treatment groups: ISLA101 XXX mg Fasted, and ISLA101 XXX mg Fed in the plot.
- Y-axis: Use the parameter name/unit as the axis label.
- X-axis: Add tick marks between the treatments (equally spaced) and use the treatment label and the number of subjects in the treatment arm as the label (i.e., 'ISLA101 XXX mg Fasted (N=xx)', 'ISLA101 xxx mg Fed (N=xx)').
- Repeat for DN_AUC_{inf} and DN_AUC_{last}
- for the analyte = Fenretinide (ng/ml) only

Sponsor: Island Pharmaceuticals Ltd
Protocol: ISLA101-P01-CT001

Figure 14.2.5.1 Scatterplots of Natural Log-Transformed Plasma PK Parameters (Pharmacokinetic Analysis Set)

Analyte (Unit): Fenretinide (ng/ml)
Parameter: C_{max} (ng/ml)



SD: Standard deviation.
A power model was used to assess dose proportionality: Natural log-transformed(PK Parameter Result) = α + β * Natural Log-transformed(Dose).

Program Name: xxx.sas, Creation Date/Time: YYYY-MM-DD HH:MM

Programming Note:

- Present scatter plots of the natural log-transformed AUC_{inf}, AUC_{last} and C_{max} values on the y-axis vs the natural log-transformed dose values on the x-axis. Use the actual numerical values for the x-axis and label the tick marks as described below.
- Y-axis: Use the parameter name/unit as the axis label.
- X-axis: The x-axis label should be 'Dose ISLA101 (mg)' and the tick marks should be:
  - '300', '600', '900'.

Include the power model regression line and 90% confidence limits.
For the Analyte (Unit) = Fenretinide (ng/ml)only.

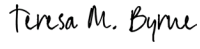
DocuSign

Certificate Of Completion

Envelope Id: 64A712DB30C24F8C8FED7E6FB171863A
Status: Completed
Subject: Complete with DocuSign: Island_ISLA101-P01-CT001_SAP with mock shells_Final_Version_1.0_2023-12...
Source Envelope:
Document Pages: 137
Signatures: 2
Envelope Originator:
Certificate Pages: 5
Initials: 0
Ella Liu
AutoNav: Enabled
ella.liu@rgcro.com
EnvelopeId Stamping: Enabled
IP Address: 27.131.74.15
Time Zone: (UTC+10:00) Canberra, Melbourne, Sydney

Record Tracking

Status: Original
12/7/2023 1:57:35 PM
Holder: Ella Liu
ella.liu@rgcro.com
Location: DocuSign

Signer Events	Signature	Timestamp
Ella Liu ella.liu@rgcro.com Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 0C83B3ED-F8A2-4B68-B0BE-A6F9B10AE82A Using IP Address: 27.131.74.15 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I am the author of this document	Sent: 12/7/2023 2:02:43 PM Viewed: 12/7/2023 2:03:03 PM Signed: 12/7/2023 2:03:35 PM
Electronic Record and Signature Disclosure: Not Offered via DocuSign		
Teresa M. Byrne tbyrne@islandpharmaceuticals.com Security Level: Email, Account Authentication (Required)	 Signature Adoption: Pre-selected Style Signature ID: 992ABD57-5D8B-4DF7-A369-F4B7AAFE9F75 Using IP Address: 108.36.201.28 With Signing Authentication via DocuSign password With Signing Reasons (on each tab): I approve this document	Sent: 12/7/2023 2:03:37 PM Viewed: 12/9/2023 6:42:59 AM Signed: 12/9/2023 6:43:19 AM
Electronic Record and Signature Disclosure: Accepted: 12/9/2023 6:42:59 AM ID: 68d425e8-124a-465b-baa5-b4834093f621 Company Name: Resolutum Global		

In Person Signer Events	Signature	Timestamp

Editor Delivery Events	Status	Timestamp

Agent Delivery Events	Status	Timestamp

Intermediary Delivery Events	Status	Timestamp

Certified Delivery Events	Status	Timestamp

Carbon Copy Events	Status	Timestamp

Witness Events	Signature	Timestamp

Notary Events	Signature	Timestamp

Envelope Summary Events	Status	Timestamps
Envelope Sent	Hashed/Encrypted	12/7/2023 2:02:43 PM
Certified Delivered	Security Checked	12/9/2023 6:42:59 AM
Signing Complete	Security Checked	12/9/2023 6:43:19 AM
Completed	Security Checked	12/9/2023 6:43:19 AM

Payment Events	Status	Timestamps

Electronic Record and Signature Disclosure

ELECTRONIC RECORD AND SIGNATURE DISCLOSURE

From time to time, Resolutum Global (we, us or Company) may be required by law to provide to you certain written notices or disclosures. Described below are the terms and conditions for providing to you such notices and disclosures electronically through the DocuSign system. Please read the information below carefully and thoroughly, and if you can access this information electronically to your satisfaction and agree to this Electronic Record and Signature Disclosure (ERSD), please confirm your agreement by selecting the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

Getting paper copies

At any time, you may request from us a paper copy of any record provided or made available electronically to you by us. You will have the ability to download and print documents we send to you through the DocuSign system during and immediately after the signing session and, if you elect to create a DocuSign account, you may access the documents for a limited period of time (usually 30 days) after such documents are first sent to you. After such time, if you wish for us to send you paper copies of any such documents from our office to you, you will be charged a $0.00 per-page fee. You may request delivery of such paper copies from us by following the procedure described below.

Withdrawing your consent

If you decide to receive notices and disclosures from us electronically, you may at any time change your mind and tell us that thereafter you want to receive required notices and disclosures only in paper format. How you must inform us of your decision to receive future notices and disclosure in paper format and withdraw your consent to receive notices and disclosures electronically is described below.

Consequences of changing your mind

If you elect to receive required notices and disclosures only in paper format, it will slow the speed at which we can complete certain steps in transactions with you and delivering services to you because we will need first to send the required notices or disclosures to you in paper format, and then wait until we receive back from you your acknowledgment of your receipt of such paper notices or disclosures. Further, you will no longer be able to use the DocuSign system to receive required notices and consents electronically from us or to sign electronically documents from us.

All notices and disclosures will be sent to you electronically

Unless you tell us otherwise in accordance with the procedures described herein, we will provide electronically to you through the DocuSign system all required notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you during the course of our relationship with you. To reduce the chance of you inadvertently not receiving any notice or disclosure, we prefer to provide all of the required notices and disclosures to you by the same method and to the same address that you have given us. Thus, you can receive all the disclosures and notices electronically or in paper format through the paper mail delivery system. If you do not agree with this process, please let us know as described below. Please also see the paragraph immediately above that describes the consequences of your electing not to receive delivery of the notices and disclosures electronically from us.

How to contact Resolutum Global:

You may contact us to let us know of your changes as to how we may contact you electronically, to request paper copies of certain information from us, and to withdraw your prior consent to receive notices and disclosures electronically as follows:
To contact us by email send messages to: admin@rgcro.com

To advise Resolutum Global of your new email address

To let us know of a change in your email address where we should send notices and disclosures electronically to you, you must send an email message to us at admin@rgcro.com and in the body of such request you must state: your previous email address, your new email address. We do not require any other information from you to change your email address.

If you created a DocuSign account, you may update it with your new email address through your account preferences.

To request paper copies from Resolutum Global

To request delivery from us of paper copies of the notices and disclosures previously provided by us to you electronically, you must send us an email to admin@rgcro.com and in the body of such request you must state your email address, full name, mailing address, and telephone number. We will bill you for any fees at that time, if any.

To withdraw your consent with Resolutum Global

To inform us that you no longer wish to receive future notices and disclosures in electronic format you may:

i. decline to sign a document from within your signing session, and on the subsequent page, select the check-box indicating you wish to withdraw your consent, or you may;

ii. send us an email to admin@rgcro.com and in the body of such request you must state your email, full name, mailing address, and telephone number. We do not need any other information from you to withdraw consent.. The consequences of your withdrawing consent for online documents will be that transactions may take a longer time to process..

Required hardware and software

The minimum system requirements for using the DocuSign system may change over time. The current system requirements are found here: https://support.docusign.com/guides/signer-guide-signing-system-requirements.

Acknowledging your access and consent to receive and sign documents electronically

To confirm to us that you can access this information electronically, which will be similar to other electronic notices and disclosures that we will provide to you, please confirm that you have read this ERSD, and (i) that you are able to print on paper or electronically save this ERSD for your future reference and access; or (ii) that you are able to email this ERSD to an email address where you will be able to print on paper or save it for your future reference and access. Further, if you consent to receiving notices and disclosures exclusively in electronic format as described herein, then select the check-box next to 'I agree to use electronic records and signatures' before clicking 'CONTINUE' within the DocuSign system.

By selecting the check-box next to 'I agree to use electronic records and signatures', you confirm that:

- You can access and read this Electronic Record and Signature Disclosure; and
- You can print on paper this Electronic Record and Signature Disclosure, or save or send this Electronic Record and Disclosure to a location where you can print it, for future reference and access; and
- Until or unless you notify Resolutum Global as described above, you consent to receive exclusively through electronic means all notices, disclosures, authorizations, acknowledgements, and other documents that are required to be provided or made available to you by Resolutum Global during the course of your relationship with Resolutum Global.