Statistical Analysis Plan

Title: Statistical Analysis Plan for Protocol SL03-OHD-105: An Open-Label, Phase 1b Study of SL-172154 (SIRPα-Fc-CD40L) Administered with Either Pegylated Liposomal Doxorubicin or Mirvetuximab Soravtansine in Subjects with Platinum-Resistant Ovarian Cancers

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LIST OF ABBREVIATIONS

ADA	Anti-drug antibodies
AE	Adverse event
AIBW	Adjusted ideal body weight
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AST	Aspartate aminotransferase
ATC	Anatomical Therapeutic Chemical
AUC	Area under the serum concentration time curve
C1D1	Cycle 1 Day 1
CBR	Clinical benefit rate
CL	Clearance
Cmax	Maximum observed concentration
Cmin	Minimum observed concentration
CI	Confidence interval
CR	Complete response
CTCAE	Common terminology criteria for adverse event
CV	Coefficient of variation
DAT	Direct antiglobulin test
DLT(s)	Dose-limiting toxicity(ies)
DOR	Duration of response
ECG	Electrocardiogram
ECHO	Echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
IBW	Ideal body weight
ICF	Informed consent form
ICH	International Conference of Harmonisation
IP	Investigational product
IV (i.v.)	Intravenous
MAD	Maximum administered dose
MedDRA	Medical Dictionary for Regulatory Activities
MIRV	Mirvetuximab soravtansine
MTD	Maximum tolerated dose
mTPI-2	Modified toxicity probability interval 2
NCI	National Cancer Institute
NCI-CTCAE	National Cancer Institute Common Terminology Criteria for Adverse Events
NE	Not evaluable
ORR	Objective response rate
OS	Overall survival
PD	Pharmacodynamic
PD	Progressive Disease
PFS	Progression-free survival
PK	Pharmacokinetic
PLD	pegylated liposomal doxorubicin
PR	Partial response
PT	Preferred term
RECIST	Response evaluation criteria in solid tumors
RP2D	Recommended phase 2 dose
SAE	Serious Adverse Event
SD	Stable disease
SIRPα	Signal regulatory protein alpha

SMC	Safety Monitoring Committee
SOC	System organ class
t½	Terminal elimination half-life
TEAE	Treatment-emergent adverse event
T_{max}	Time of maximum observed concentration
TTR	Time to response
ULN	Upper limit of normal
Vz	Volume of distribution
WHO	World Health Organization

1. INTRODUCTION

This statistical analysis plan outlines the planned analyses for Protocol SL03-OHD-105, An Open-Label, Phase 1b Study of SL-172154 (SIRPα-Fc-CD40L) Administered with Either Pegylated Liposomal Doxorubicin or Mirvetuximab Soravtansine in Subjects with Platinum-Resistant Ovarian Cancers:

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Original Version v0.0	13 May 2022
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The purpose of this analysis plan is to provide the specific guidelines for the analysis of data mainly obtained from the study electronic case report forms (eCRFs). All decisions regarding data analysis, as defined in this document, have been made prior to Database Lock of the study data. Any deviations from this plan will be documented in the clinical study report.

2. STUDY OBJECTIVES AND OUTCOME MEASURES

Study objectives and outcome measures are specified in Section 2 of the protocol.

Objective	**Outcome Measure**
Primary Objectives	
To evaluate the safety and tolerability of SL-172154 administered with pegylated liposomal doxorubicin (PLD) or mirvetuximab soravtansine (MIRV) in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• Incidence and severity of adverse events (AE) per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 5.0 • Change from baseline in laboratory values per NCI-CTCAE, version 5.0 • AEs leading to discontinuation • Maximum tolerated dose (MTD) of SL-172154 in each combination regimen based on the rate of dose limiting toxicities (DLTs) or the Maximum Administered Dose (MAD) of SL-172154
To select the recommended Phase 2 dose (RP2D) for SL-172154 administered with PLD or MIRV in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• Number and occurrence of DLTs as defined in the protocol • Available PK parameters • Available PD effects • Safety • Anti-tumor activity
Secondary Objectives	

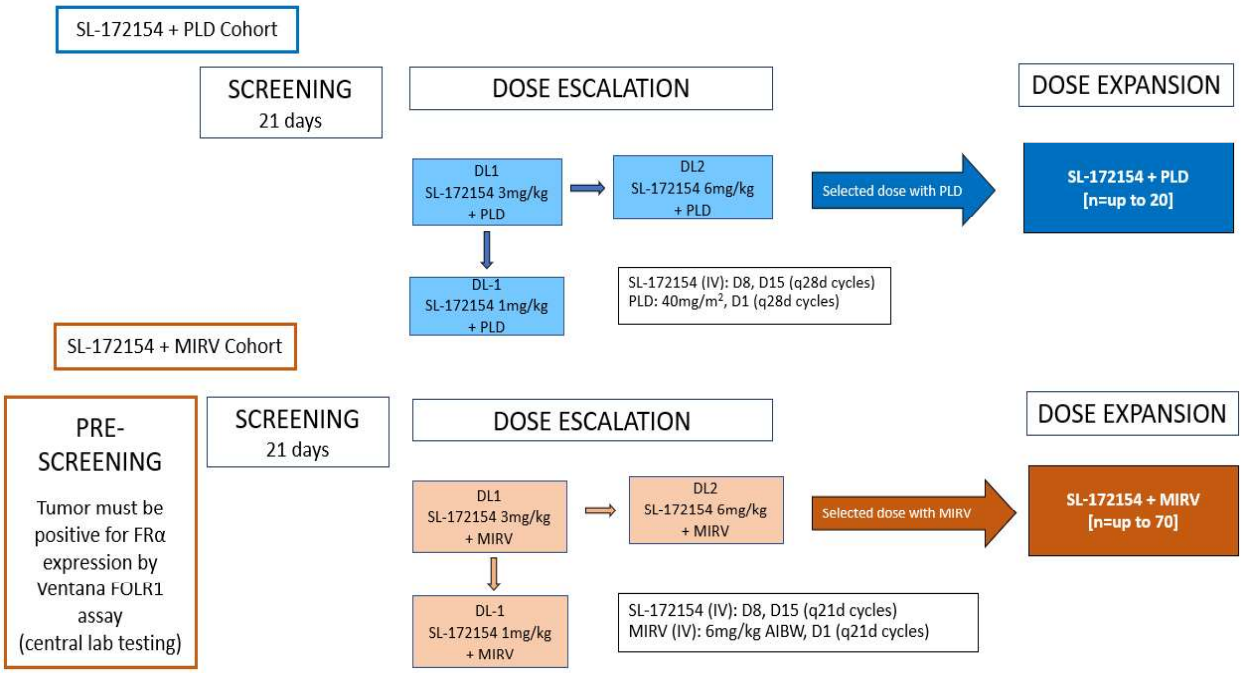
Objective	Outcome Measure
To assess preliminary evidence of anti-tumor efficacy of SL-172154 when administered with PLD or MIRV (overall as well as subgroups with high (PS2+ ≥75%), medium (PS2+ ≥50% and <75%), or low (PS2+ ≥25% and <50%) tumor FRα expression) in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• Objective response rate (ORR) based on Investigator-assessment by Response Evaluation Criteria in Solid Tumors (RECIST v1.1) • Clinical benefit rate (CBR) • Time to response (TTR) • Duration of response (DoR) • Progression free survival (PFS) based on Investigator assessment
To evaluate immunogenicity to SL-172154 or MIRV during and after treatment of SL-172154 administered with PLD or MIRV in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• Number/proportion of subjects with positive or negative anti-drug antibody (ADA) titer • Number/proportion of subjects with neutralizing anti-drug antibodies • ADA duration • Transient vs. persistent ADA
To assess the pharmacokinetic profile of SL-172154 when administered with PLD or MIRV in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• Maximum observed concentration (C_{max}), time at which the maximum concentration is observed (T_{max}), and minimum observed concentration (C_{min}) following single and multiple doses of SL-172154 • Area under the serum concentration-time curve (AUC) • Terminal elimination half-life ($t_{½}$), Clearance (CL) and Volume of Distribution (V_z), as data permit
To assess the pharmacokinetic profile of MIRV when administered with SL-172154 in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• PK exposure evaluation of MIRV, total antibody, and payload (DM4 and S-methyl DM4)
Exploratory Objectives	
To identify and assess pharmacodynamic biomarkers associated with ovarian cancer or the mechanism of action of SL-172154, PLD, or MIRV following treatment with SL-172154 administered with PLD or MIRV in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer	• Changes from baseline in select cytokines • Changes in immune cell subsets • CD47 and CD40 expression • Target-associated regulatory networks • Genomic alterations which may correlate with drug safety or efficacy
To explore the association of biological/clinical endpoints with PK parameters of SL-172154 administered with PLD or MIRV in subjects with platinum-	• To assess the relationship between SL-172154 PK exposure and the anti-tumor activity and safety of SL-172154, if feasible

Objective	Outcome Measure
resistant ovarian, primary peritoneal, or fallopian tube cancer	
Estimate overall survival (OS)	• OS: time from first dose to death

3. STUDY DESIGN

3.1 Study Design

This is an open-label, multicenter, Phase 1b trial designed to evaluate the safety, PK, PD effects, and preliminary anti-tumor activity of SL-172154 administered with either PLD or MIRV in subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancers. The study will consist of dose escalation followed by dose expansion for each of the combination regimens (see Study Schema below).



Abbreviations: AIBW=adjusted ideal body weight; D=day; DL=dose level; IV=intravenous

Doses explored in SL03-OHD-105 will not exceed the highest dose determined to be safe and tolerable in the ongoing monotherapy dose escalation study SL03-OHD-101.

This study will initially enroll subjects to dose escalation cohorts to receive 1 of 2 combination regimens (SL-172154 + PLD or SL-172154 + MIRV). In the initial cohort of each combination regimen, SL-172154 (3.0 mg/kg starting dose, IV) will be administered on Day 8 and Day 15 with either PLD (40 mg/m^2, IV, Day 1 of each 28-day cycle) or MIRV [6 mg/kg adjusted ideal body weight (AIBW), IV, Day 1 of each 21-day cycle]. Dose escalation of SL-172154 in each of

the combination regimens will continue until a safe dose of SL-172154 administered with either PLD or MIRV is identified.

In selecting the dose of SL-172154 to be evaluated in the expansion cohort of each combination regimen, the totality of the data from the dose escalation phase will be considered, including safety of the combination and PD activity. Upon identification of the selected SL-172154 dose administered with PLD, an expansion cohort will enroll approximately 20 subjects (including subjects from dose escalation at the same dose level) to further evaluate the safety and efficacy of the study treatment. Similarly, an expansion cohort will enroll approximately 70 subjects for the SL-172154 + MIRV regimen.

For all subjects in all cohorts, premedication as prophylaxis for infusion related reaction (IRR) with an antipyretic and antihistamines should be administered at least 30 minutes prior to each SL-172154 administration. For subjects enrolled to receive MIRV, premedication with an antipyretic, antihistamine, and dexamethasone will be administered approximately 30 minutes prior to each MIRV administration. Prophylactic use of eye drops with MIRV administration is also described in Section 5.3.2 of the protocol. Premedication (any agent except steroid) as prophylaxis for nausea and vomiting with PLD may be administered per institutional guidelines.

Further details of the study design and inclusion/exclusion criteria are described in Sections 3 and 4 of the protocol.

3.1.1 Dose Escalation

Subjects with platinum-resistant ovarian, primary peritoneal, or fallopian tube cancer will be enrolled in dose escalation cohorts to receive either SL-172154 with PLD or SL-172154 with MIRV. For Regimen (SL-172154 + MIRV), subjects must have a tumor that is positive for FRα expression (PS2+ ≥25%) as defined by the Ventana FOLR1 Assay. Subjects can be enrolled to only 1 of the combination regimens in this study.

SL-172154 Administered with PLD

SL-172154 (3.0 mg/kg starting dose) will be administered by intravenous (IV) infusion on Days 8 and 15 of each 28-day cycle. PLD (40 mg/m^2, IV) will be administered on Day 1 of each 28-day cycle.

The planned dose escalation of SL-172154 is outlined in Table 1; additional doses and/or schedules may be explored based on emerging safety, PK and PD data.

Subjects will be enrolled in cohorts of approximately 3 subjects into sequential dose levels of SL-172154 administered with PLD and evaluated for DLT during the 28-day DLT evaluation period. Treatment will be administered in 28-day cycles until at least one of the study treatment discontinuation criteria is met. The safety as well as available PK, PD, and efficacy data from these subjects will inform the dose of SL-172154 selected to be further evaluated in Dose Expansion.

Table 1 SL-172154 Dose Escalation Plan When Administered with PLD

Dose Level[a]	SL-172154 Dose[b] [D8 and 15 in each 28d cycle]	SL-172154 Infusion[c]	Pegylated liposomal doxorubicin (PLD)
-1[d]	1.0 mg/kg	60 min ± 10 min	PLD (40 mg/m^2) IV administered on Day 1 of each 28-day cycle Administer first dose on study (C1D1) as 1 mg/min IV infusion; after Cycle 1, if tolerated, PLD can be delivered as a 1-hour infusion
1 (Starting Dose)	3.0 mg/kg	120 min ± 15 min	
2	6 mg/kg	120 min ± 15 min	

a. Doses explored in SL03-OHD-105 will not exceed the highest dose determined to be safe and tolerable in the ongoing monotherapy dose escalation study SL03-OHD-101.
b. The actual body weight in kilograms (kg) will be used for SL-172154 dose calculation in all subjects whose body weight is ≤100 kg. For subjects with body weight >100 kg, the dose to be administered should be the same as that calculated for a subject weighing 100 kg.
c. Infusion time may change based on final drug volume needed for administration, safety and tolerability of the infusion for the subject and/or observed safety findings during the study. Please refer to the Study Pharmacy Manual (SPM) for details.
d. SL-172154 dose level -1 at 1.0 mg/kg will be evaluated if 3.0 mg/kg is not safe per mTPI-2.

SL-172154 Administered with MIRV

SL-172154 (3.0 mg/kg starting dose) will be administered by IV infusion on Day 8 and Day 15 of 21-day cycles. MIRV (6 mg/kg AIBW, IV) will be administered on Day 1 of each 21-day cycle.

The planned dose escalation of SL-172154 is outlined in Table 2; additional doses and/or schedules or intermediate doses may be explored based on emerging safety, PK, and PD data.

Subjects will be enrolled in cohorts of approximately 3 subjects into sequential dose levels of SL-172154 administered with MIRV and evaluated for DLT during the 21-day DLT evaluation period. Treatment will be administered in 21-day cycles until at least one of the study treatment discontinuation criteria is met.

The safety as well as available PK, PD, and efficacy data from these subjects will inform the dose of SL-172154 selected to be further evaluated in Dose Expansion.

Table 2 SL-172154 Dose Escalation Plan When Administered with MIRV

Dose Level[a]	SL-172154 Dose[b] [D8 and D15 in each 21d cycle]	SL-172154 Infusion[c]	Mirvetuximab soravtansine (MIRV)[e]
-1[d]	1.0 mg/kg	60 min ± 10 min	6 mg/kg AIBW, IV administered on Day 1 of each 21-day cycle Administer 1st dose on study (C1D1) at rate of 1 mg/min; after 30 min increase rate to 3 mg/min if well tolerated. If well-tolerated after 30 min at 3 mg/min, infusion rate may be increased to 5 mg/min. Subsequent infusions should be delivered at the tolerated rate.
1 (Starting dose)	3.0 mg/kg	120 min ± 15 min	
2	6 mg/kg	120 min ± 15 min	

AIBW = adjusted ideal body weight

a. Doses explored in SL03-OHD-105 will not exceed the highest dose determined to be safe and tolerable in the ongoing monotherapy dose escalation study SL03-OHD-101.
b. The actual body weight in kilograms (kg) will be used for SL-172154 dose calculation in all subjects whose body weight is ≤100 kg. For subjects with body weight >100 kg, the dose to be administered should be the same as that calculated for a subject weighing 100 kg.
c. Infusion time may change based on final drug volume needed for administration, safety, and tolerability of the infusion for the subject and/or observed safety findings during the study. Please refer to the Study Pharmacy Manual (SPM) for details.
d. SL-172154 dose level -1 at 1.0 mg/kg will be evaluated if 3.0 mg/kg is not safe per mTPI-2.
e. Administer premedication approximately 30 min prior to the start of MIRV infusion

3.1.2 Dose Expansion

The goal of the expansion cohort is to further evaluate the safety, PD effects, and efficacy of the regimen at a dose and schedule identified in the dose escalation part of the study. Enrolment to the dose expansion cohort for each combination regimen will not commence until the SL-172154 dose has been selected for the combination with PLD or MIRV.

SL-172154 Administered with PLD

Approximately 14 subjects will be enrolled in the dose expansion cohort. The goal is to enroll approximately 20 subjects at the potential RP2D for this combination regimen, including subjects in dose escalation and expansion that have received the same dose of SL-172154. Treatment will be administered in 28-day cycles until at least one of the study treatment discontinuation criteria is met. Alternate dose level(s) may be evaluated at the discretion of the Sponsor based on emerging clinical or nonclinical data in the SL-172154 program.

SL-172154 Administered with MIRV

Approximately 64 subjects will be enrolled in the dose expansion cohort. Approximately 70 subjects will be enrolled to have approximately 20 subjects at the potential SL-172154 RP2D in either dose escalation or dose expansion for each of the following three tumor FRα expression subgroups: high (PS2+ ≥75%), medium (PS2+ ≥50% and <75%), and low (PS2+ ≥25% and

<50%). This estimation is based on the anticipated frequency of subjects with high grade serous ovarian cancer who fall into each of these FRα expression subgroups. If this distribution is not achieved in any subgroup, approximately 10 additional subjects may be enrolled in this expansion cohort in order to achieve these subject numbers. Treatment will be administered in 21-day cycles until at least one of the study treatment discontinuation criteria is met. Alternate dose level(s) or treatment schedule(s) may be evaluated at the discretion of the Sponsor based on emerging clinical or nonclinical data in the SL-172154 program.

3.1.3 Selection of Recommended Phase 2 Dose

If an MTD is not observed, the MAD would then be the highest dose of SL-172154 administered as specified in the protocol. Selection of the recommended dose and schedule for SL-172154 for further study in combination with PLD and in combination with MIRV will be based upon the totality of the safety, tolerability, PK, PD, and efficacy data in subjects treated with each of the regimens in dose escalation and dose expansion cohorts. The RP2D is a dose of SL-172154 that can be safely administered with standard of care doses of PLD or with the recommended dose of MIRV. In addition, preliminary efficacy of each of the combination regimens will be assessed to determine whether either or both of the regimens warrant further evaluation in a Phase 2 study.

3.2 Statistical Design

3.2.1 Dose Escalation

The SL-172154 dose escalation will utilize a modified Toxicity Probability Interval-2 (mTPI-2) design [Guo, 2017] with target DLT rate of 30% for the MTD. The mTPI-2 design employs a simple Beta-Binomial Bayesian model with decision rules based on the unit probability mass from the posterior probability of DLT rate. With the target DLT rate of 30%, the posterior probability of DLT rate unit interval (0, 1) is divided into subintervals with equal length of 0.1 that correspond to different dose escalation decisions: subinterval of (0.25, 0.35) is to stay at the current dose, subintervals below 0.25 is to escalate to next higher dose, and subinterval above 0.35 is to de-escalate to the next lower dose. Subjects will be enrolled in cohorts of approximately 3 subjects during the dose escalation. After each cohort of approximately 3 subjects, the posterior unit probability for subintervals will be calculated based on a noninformative prior distribution for the DLT rate (Beta (1,1)) and the total number of subjects with DLTs and DLT evaluable subjects for the current dose. A dose escalation/stay/de-escalation decision that corresponds to the subinterval with the highest unit probability mass will be selected. A minimum of 3 DLT evaluable subjects will be enrolled to a dose level and evaluated for DLT before a dose escalation/stay/de-escalation decision can be made unless unacceptable toxicity is observed prior to the enrollment of 3 subjects e.g., two subjects experience DLT before the third subject enrolls. A dose level will be considered unsafe, with unacceptable toxicity and no additional subjects enrolled at that dose level and above, if it has an estimated 95% or more probability of exceeding the target DLT rate of 30%. The maximum number of subjects evaluated for DLT for each dose level will be 12 subjects (about 4 cohorts of 3 subjects) if the dose escalation decision is to stay at the current dose from the first 3 cohorts. Based on the above design, the dose escalation decision rules for each dose level are:

- Dose escalate if the observed DLT rate <25%;

- Stay at the current dose if the observed DLT rate between 25%-33%;
- Dose de-escalate if the observed DLT rate >33%;

See Table 3 for dose escalation decision rules based on the total number of subjects evaluable for DLT and the number of subjects with DLT observed.

Table 3 SL-172154 Dose Escalation Decision Rules for Each Dose Level Based on mTPI-2

Number of subjects with DLT	Number of DLT Evaluable Subjects									
	3	4	5	6	7	8	9	10	11	12
0	E	E	E	E	E	E	E	E	E	E
1	S	S	E	E	E	E	E	E	E	E
2	D	D	D	S	S	S	E	E	E	E
3	DU	DU	D	D	D	D	S	S	S	S
4	.	DU	DU	DU	D	D	D	D	D	S
5	.	.	DU	DU	DU	DU	DU	D	D	D
6	.	.	.	DU	DU	DU	DU	DU	DU	D
7	.	.	.	.	DU	DU	DU	DU	DU	DU
8	.	.	.	.	.	DU	DU	DU	DU	DU
E = escalate to the next higher dose level					**S = stay at the current dose level**					
D = de-escalate to the next lower dose level					**DU = de-escalate to the next lower dose level and current dose level will never be used again due to unacceptable toxicity**					

Note: For each dose level, a minimum of 3 evaluable subjects will be enrolled and evaluated before a dose escalation/stay/de-escalation decision can be made unless unacceptable toxicity is observed prior to the enrollment of 3 subjects e.g., two subjects experience DLT before the third subject enrolls.

3.2.2 Dose Expansion

For the SL-172154 + PLD expansion cohort, the goal is to enroll approximately 20 subjects treated at the potential RP2D in either dose expansion or dose escalation. The sample size of 20 is primarily chosen to obtain a preliminary assessment of the antitumor activity with a certain degree of precision. Table 4 provides the 90% confidence interval (CI) based on exact probability method for a range of possible responses out of 20 subjects. Approximately 14 of these subjects at the potential RP2D will be enrolled in the dose expansion cohort.

Table 4 Response Rate 90% CI out of 20 Subjects

#Responses/20 Subjects	Response Rate	90% CI
2	10%	1.8%, 28.3%
4	20%	7.1%, 40.1%
6	30%	14.0%, 50.8%
8	40%	21.7%, 60.6%
10	50%	30.2%, 69.8%
12	60%	39.4%, 78.3%
14	70%	49.2%, 86.0%
16	80%	59.9%, 92.9%
18	90%	71.7%, 98.2%

For the SL-172154 + MIRV expansion cohort, the goal is to enroll approximately 20 subjects treated at the potential RP2D for each of the following three tumor FRα expression subgroups in either dose expansion or dose escalation: high (PS2+ ≥75%), medium (PS2+ ≥50% and <75%), and low (PS2+ ≥25% and <50%). The sample size of 20 is primarily chosen to obtain a preliminary assessment of the antitumor activity with a certain degree of precision. Approximately 64 subjects treated at the potential RP2D will be enrolled in the dose expansion cohort.

Each expansion cohort will allow further characterization of the safety profile of SL-172154 in combination with either PLD or MIRV, with particular emphasis on toxicities leading to discontinuation of SL-172154 and the combination agents. Continuous toxicity monitoring based on a Pocock-type stopping boundary [Ivanova, 2005] will be used within each expansion cohort. Accrual will be temporarily stopped if an excessive number of subjects discontinue SL-172154 and a combination agent due to toxicities.

In the JAVELIN Ovarian 200 study, the discontinuation rate in the PLD monotherapy group due to AEs was 11% and treatment related AEs leading to treatment discontinuation was 7% [Pujade-Lauraine, 2021], thus a 20% rate of AE leading to treatment discontinuation regardless of causality is selected for the SL-172154 + PLD expansion cohort. Enrollment to the SL-172154 + PLD expansion cohort will be temporarily stopped if an excessive number of subjects experience AEs leading to treatment discontinuation; that is, if the number of subjects with AEs leading to treatment discontinuation is equal to or more than b_n out of n subjects as described in the table below. The sequential stopping boundaries are selected to have at least 70% probability to temporarily stop when the underlying true rate of subjects with AEs leading to treatment discontinuation is >30%.

Number of subjects, *n*	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Boundary, b_n	-	2	3	3	3	3	4	4	4	4	4	4	5	5	5	5	5	6	6	6

In the IMGN853-0401 study, 15% of the subjects at 6 mg/kg MIRV monotherapy discontinued treatment due to AEs (MIRV IB), thus a 20% rate of AE leading to treatment discontinuation regardless of causality is selected for the SL-172154 + MIRV expansion cohort. Enrollment to the SL-172154 + MIRV expansion cohort will be temporarily stopped if an excessive number of subjects experience AEs leading to treatment discontinuation; that is, if the number of subjects with AEs leading to treatment discontinuation is equal to or more than b_n out of n subjects as described in the table below. The sequential stopping boundaries are selected to have at least

82% probability to stop when the true underlying rate of subjects with AEs leading to treatment discontinuation is >30%.

Number of subjects, *n*	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Boundary, b_n	-	-	3	4	4	4	5	5	5	5	6	6	6	6	7	7	7
Number of subjects, *n*	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
Boundary, b_n	7	8	8	8	8	9	9	9	9	10	10	10	10	11	11	11	11
Number of subjects, *n*	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51
Boundary, b_n	11	12	12	12	12	12	13	13	13	13	14	14	14	14	14	15	15
Number of subjects, *n*	52	53	54	55	56	57	58	59	60	61	62	63	64	65			
Boundary, b_n	15	15	15	16	16	16	16	16	17	17	17	17	17	18			

3.3 Sample Size

The planned sample size is approximately 102 subjects, depending on the number of dose levels evaluated in dose escalation for each of the combinations. Approximately 24 subjects will be enrolled in dose escalation cohorts (12 subjects in PLD cohorts and 12 subjects in MIRV cohorts) and approximately 78 subjects will be enrolled in a dose expansion cohort (an additional 14 subjects at the selected dose in PLD cohort and an additional 64 subjects at the selected dose in MIRV cohort).

All subjects with tumors that are FRα positive (PS2+ ≥25%) enrolled in the MIRV combination cohort will be retrospectively binned in expression subgroups (high, medium, low) for study analysis. The goal is to enroll approximately 20 subjects at the potential RP2D in either dose expansion or dose escalation for each of the following three tumor FRα expression subgroups: high (PS2+ ≥75%), medium (PS2+ ≥50% and <75%), and low (PS2+ ≥25% and <50%). This estimation is based on the anticipated frequency of subjects with high grade serous ovarian cancer who fall into each of these FRα expression subgroups. If this distribution is not achieved in any subgroup, approximately 10 additional subjects may be enrolled in this expansion cohort in order to achieve it.

NOTE: The planned sample sizes may be revised if additional dose levels are evaluated or if more subjects (i.e., subjects available for dosing beyond the number required in a cohort) are enrolled than anticipated. The actual number of subjects to be enrolled for each combination dose escalation will depend upon the number of dose levels evaluated and the number of DLTs observed for each dose level and related dose escalation/stay/de-escalation decision. The Sponsor, in consultation with the Safety Monitoring Committee (SMC), may also elect to add subjects to the dose escalation cohorts if additional data is needed to select the dose level for the dose expansion cohort.

3.4 Study Treatment Discontinuation Criteria

A subject will receive the assigned study treatment (e.g., SL-172154 and PLD or SL-172154 and MIRV) until any of the following events occur during the study:

- Documented disease progression (radiological or clinical)
- A subject suffers an AE that, in the judgement of the investigator, Sponsor, or medical monitor, presents an unacceptable risk to the subject
- General or specific changes in the subject's condition (e.g., a significant intercurrent illness or complication) that, in the judgement of the investigator, are unacceptable for further administration of study treatment
- Subject decides to discontinue further study treatment
- Occurrence of pregnancy
- Significant non-compliance with protocol requirements
- Death
- Termination of the study by Sponsor

If one agent in the assigned regimen is permanently discontinued for any reason, at the investigator's discretion, the subject may continue to receive the other agent in the assigned regimen as monotherapy until meeting one of study treatment discontinuation criteria.

In the event of permanent discontinuation of all study treatment, subjects should be strongly encouraged to complete all scheduled assessments at the Post Treatment visit and the Survival Follow-up contacts.

3.5 Duration of Follow-up

Subjects who are withdrawn from study treatment for unacceptable AE(s) should be followed until the event(s) are resolved, the subject is lost to follow-up, the AE is otherwise explained, or further recovery is not deemed to be feasible. Data on these events should be collected on the AE eCRF.

Subjects who permanently discontinue study treatment for reasons other than progression will continue with disease assessments until progression or start of another anti-cancer therapy.

Subjects who discontinue study treatment for any reason other than withdrawal of consent will be followed for survival and will be contacted approximately every 3 months until death or the end of the study, whichever occurs first. During Survival Follow-up, the start date of the first anticancer therapy will be collected and entered in the Electronic Data Capture (EDC).

3.6 End of Study

The end of study is defined as the point of final data capture (e.g., the point at which all required data has been collected to answer the research questions in the protocol) or date the study is closed by the Sponsor, whichever occurs first.

After the end of study, subjects who are still in survival follow-up part of the study should receive standard of care treatment as determined by their health care provider after completion of the study.

3.7 Study Assessments and Procedures

The detailed study assessments and procedures are described in Section 6 of the protocol.

4. ANALYSIS POPULATIONS

The populations defined for analysis will include the following:

Population	Description
Screened	All subjects who have signed the main study Informed consent form (ICF).
Screen Failures	All subjects who have signed the main study ICF but have not received any study treatment.
All Treated	All subjects who receive at least one dose of study drug (SL-172154, PLD, or MIRV). Safety data will be evaluated based on this population.
DLT Evaluable	All subjects enrolled in the dose escalation cohorts who receive at least 50% of the scheduled doses of SL-172514 and 1 dose of PLD or MIRV and complete the safety follow-up through the DLT evaluation period or experience any DLT during the DLT evaluation period. DLT evaluable subjects will be used to guide dose escalation and to determine the MTD or MAD.
Response Evaluable	Subjects in the All Treated Population who have either had at least one post-baseline disease assessment or who have discontinued study treatment due to disease progression or death before any post-baseline disease assessment.
SL-172154 Pharmacokinetic	Subjects in All Treated Population who have at least one post SL-172154 dose PK sample obtained and analyzed.
SL-172154 Immunogenicity	Subjects in the All Treated Population who have at least one post SL-172154 dose immunogenicity measurement.
MIRV Pharmacokinetic	Subjects in All Treated Population who have at least one post MIRV dose PK sample obtained and analyzed.
MIRV Immunogenicity	Subjects in the All Treated Population who have at least one post MIRV dose immunogenicity measurement.
MIRV FRα Pre-screened	All subjects in MIRV regimen who have signed the pre-screen informed consent form for FRa test.

5. GENERAL ANALYSIS CONSIDERATIONS

5.1 Data Analysis During Dose Escalation

During the dose escalation, the number of subjects with DLTs will be determined after each cohort of approximately 3 subjects has been evaluated for DLT. The summary of DLTs will be based on the DLT Evaluable Population; the number of subjects with DLTs will be summarized

by dose level for each of the combination dose escalation cohorts. Select AE summary tables and listings may be provided during dose escalation to support dose escalation decisions.

5.2 Reporting Conventions

The statistical analyses will be reported using summary tables, figures, and data listings. The International Conference on Harmonisation (ICH) numbering convention will be used for tables, listings, and figures.

Data from all participating sites will be pooled prior to data summary or analysis. It is anticipated that subject accrual will be spread thinly across sites and summaries of data by site would be unlikely to be informative and will not, therefore, be provided.

Separate summary tables will be provided for each combination regimen (SL-172154 + PLD and SL-172154 + MIRV). Unless specified otherwise, the tables will be presented for each dose level of SL-172154 in dose escalation and dose expansion, subjects receiving the same dose level of SL-172154 from dose escalation and expansion cohorts combined, and all subjects receiving the same combination regimen. The study-level summary for the two regimens combined will be provided for demographic and baseline characteristics and other data if deemed necessary. Select safety summary tables may be provided for the dose escalation cohorts.

Separate listings will be provided for each regimen (SL-172154 + PLD and SL-172154 + MIRV). The study drug exposure listings will be presented by cohort (dose escalation/dose expansion), dose level and date of first dosing. All other individual listings will be presented by cohort (dose escalation/dose expansion), dose level and subject, unless specified otherwise. Data from all assessments, whether scheduled or unscheduled, will be included in the listings. Listings will present the data in their original format (without any imputation), unless specified otherwise.

Summaries by planned time point will include data from scheduled assessments and all data will be reported according to the nominal visit for which it will be recorded (i.e., no visit windows will be applied). Unscheduled data, when summarized, will be included only in calculation of the maximum or minimum value over time such as worst-case post-baseline. If multiple assessments are reported on the same date for the same scheduled planned time, then the worst-case result will be analyzed.

Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums. The precision of the original measurements will be maintained in summaries and listings, when possible. Generally, means and medians will be presented to one more decimal place than the raw data, and the standard deviations will be presented to two more decimal places than the raw data.

Categorical variables will be summarized by counts and by percentages of subjects in the corresponding categories. Percentages are routinely based on the total number of the specified population N if not specified otherwise. For frequency counts, categories whose counts are zero will be displayed for the sake of completeness. For example, if none of the subjects discontinue

due to "lost to follow-up", this reason will be included in the table with a count of 0. Categories with zero counts will not have zero percentages displayed.

All confidence intervals (CIs) will be constructed at the 95% confidence level, unless specified otherwise.

All analyses and tabulations will be performed using SAS® v9.4 or above.

5.3 Data Handling

The following sections provide a general description of the derived and transformed variables used to describe and analyze the data.

5.3.1 Premature Withdrawal and Missing Data

Subjects who prematurely withdraw from the study will be included in analyses up to the time of withdrawal, regardless of the duration of treatment and survival follow-up.

Missing data occurs when any requested data is not provided, leading to blank field on the collection instrument. Answers such as "Not applicable", "Not evaluable", etc. are not considered to be missing data and should be displayed as such.

For the time to event endpoints including DOR, PFS and OS, the missing data handling method will be censoring. Censoring mechanisms for these endpoints are described in Section 7.

All time to event endpoints will be analyzed using suitable statistical methods.

In the event that the study is prematurely discontinued, a review will be carried out by the study team to assess which statistical analyses are still considered appropriate.

5.3.2 Baseline and Change from Baseline

Unless otherwise specified, the baseline value is defined as the last value obtained on or before the date and time of the first dose of any study drug (SL-172154, PLD or MIRV). Post-baseline values are defined as value obtained after the first dose of study drug.

Change from baseline is calculated as:

- Post-baseline value - baseline value

Percent change from baseline is calculated as:

- (Post-baseline value - baseline value)*100/baseline value

If either baseline or post-baseline value is missing, the change from baseline and percent change from baseline will be missing.

5.3.3 Study Day, Duration, and Time from Event

The reference date for age calculation is the date of consent form signed as age is an eligibility requirement. The reference date for safety, efficacy and other data analyses is the date of the first dose of any study treatment with SL-172154, PLD or MIRV (first dose of study treatment).

- **Study Day –** Study Day 1 is defined as the date of the first dose of study treatment; the day before the first dose is defined as Study Day -1. There is no study day 0. For a given event date, Study Day is calculated relative to the date of first dose of study treatment.

  Study Day = [Event Date – First Dose of Study Treatment] (in days) + 1 day,
  where the event date is on or after the first dose of study treatment.

  Study Day = [Event Date – First Dose of Study Treatment] (in days),
  where the event date is before the first dose of study treatment.

- **Duration (days) –** A duration is calculated as the stop date minus the start date plus one.

  Duration (days) = [Stop Date – Start Date] (in days) + 1 day.

- **Time since an event -**Time since an event (e.g. time since initial diagnosis) is calculated as the reference date minus the event date. For time since initial diagnosis, the reference date is the first dose of study treatment.
- **Time to an event-** Time to an event (e.g. time to response, PFS, OS) is calculated as the event date minus the reference date+1. For time to response, PFS and OS, the first dose of study treatment is the reference date.

To convert days to months, divide the number of days by 30.4375 (365.25/12).

5.3.4 Imputation of Partial Date

Partial dates may be imputed for exploratory analysis. The imputed partial data will be flagged in the dataset to indicate the level of imputation. Raw dates, not imputed dates, will be displayed in the data listings.

6. STUDY POPULATION

Unless specified otherwise, all summary tables and data listings for this section will be based on the All Treated Population, and separate summary will be provided for each treatment regimen (SL-172154 + PLD and SL-172154 + MIRV).

6.1 Subject Disposition

Summaries of study population and subject disposition will include the number of subjects in each analysis population and the primary reason for end of study participation. Study population and subject disposition information will be presented in data listings. The prescreening data, including subjects prescreened and subjects with FRα of positive, negative or not evaluable, will also be summarized for the SL-172154 + MIRV regimen.

The primary reason for study treatment discontinuation of each study drug: SL-172154 and PLD or SL-172154 and MIRV will be summarized. Subject treatment discontinuation information will also be presented in data listings.

6.2 Protocol Deviations

Number of subjects for each protocol deviation type and subtype will be summarized for major deviations, minor deviations, and all deviations, respectively. Listings with deviation details will be provided for all protocol deviations and major deviations. A separate listing will be provided for subjects with inclusion and exclusion criteria not met. Other select categories of protocol deviations may be listed or summarized.

6.3 Demographic and Baseline Characteristics

Demographic variables include age, sex, ethnicity, race, weight, height, body surface area for subjects in the PLD regimen, and AIBW for the MIRV regimen.

Body surface area will be calculated as the following:

Body surface area (m^2) = SQRT[(height (cm) x weight (kg)/3600]

AIBW will be calculated as the following:

AIBW = IBW+0.4*(actual body weight in Kg -IBW),
where ideal body weight (IBW) = 0.9*height in cm-92

Descriptive statistics will be presented for age, weight, height, body surface area and AIBW. Frequency counts and percentages will be presented for age groups (18-<65 years, 65-<75 years and ≥75 years), sex, ethnicity, race, and baseline Eastern Cooperative Oncology Group (ECOG) score (0 or 1). FRα level subgroups [High (PS2+ >=75%), Medium (PS2+ >=50% - <75%), Low (PS2+ >=25% - <50%)] will also be summarized for the MIRV regimen. Other baseline characteristics may be summarized as appropriate. In addition to the summary for each combination regimen, a study-level summary of demographic and baseline characteristics will also be provided.

All demographic and baseline characteristics data will be presented in data listings for All Treated and Screen Failure population, respectively.

6.4 Study Cancer History

Study cancer history including the primary location at diagnosis, FIGO stage at initial diagnosis, histologic grade, histology, BRCA mutation status and homologous recombination deficiency status will be summarized in tables. Time since initial diagnosis will also be summarized. All study cancer history data will be presented in data listings.

6.5 General Medical and Surgical History

General medical and surgical history along with start/end date and ongoing status at study entry will be presented in data listings.

6.6 Prior Anti-Cancer Treatment

Prior study cancer systemic treatment drugs will be coded using the World Health Organization (WHO) Drug Dictionary. Prior study cancer systemic treatment including regimen number, drug name, start/end date, intent, regimen best response, type of progression, and date of progression will be presented in data listings. The following will be derived, undergo medical review as necessary, and included in the data listings as well.

- Time since progression on the most recent regimen
- Platinum free interval after the last platinum-based regimen, defined as the date of last dose of platinum in the last platinum-based regimen to the date of disease progression after the last dose of platinum
- Primary platinum-free interval, defined as the date of last dose of platinum in the first regimen to the date of disease progression after the last dose of platinum
- Platinum resistant and refractory status for the MIRV cohort: Primary platinum resistant is defined as progression >=3 to <=6 months after the last platinum dose date in the frontline regimen; Secondary platinum resistant is defined as progression <=6 months after the last platinum dose date in any non-frontline regimen; Secondary platinum refractory is defined as progression <=3 months after the last platinum dose date in any non-frontline regimen.

The following will be summarized for the PLD regimen and MIRV regimen, respectively:

- Number of prior systemic regimens, regardless of intent
- Number of prior platinum-based regimens, regardless of intent
- Number of prior regimens for platinum-resistant disease
- Platinum-free interval after the last platinum-based regimen
- Primary platinum-free interval
- Subjects with primary platinum resistant, secondary platinum resistant, or secondary platinum refractory for the MIRV cohort
- Prior exposure to Taxanes, Liposomal doxorubicin, PARP inhibitors, Bevacizumab, or Topotecan
- Time since progression on the most recent regimen
- Prior radiotherapy (Yes/No)
- Prior surgical treatment (Yes/No)

Prior anti-cancer surgical treatment including the date and intent of procedure will be presented in data listings.

Prior anti-cancer radiotherapy including site of treatment, start/end date and intent of radiotherapy will be presented in data listings.

6.7 Premedications

Premedications will be recorded on "Premedications" CRF page. Premedications will be coded to Anatomical Therapeutic Chemical (ATC) class and Generic Drug Names using the WHO Drug Dictionary and will be listed.

6.8 Prior and Concomitant Medications

Prior and concomitant medications will be recorded during the screening period and throughout the study. These medications will be coded to ATC class and Generic Drug Names using the WHO Drug Dictionary.

Prior medications are defined as medications that end prior to the date of the first dose of study treatment. Concomitant medications are defined as medications taken at any time on or after the date of the first dose of study treatment. Medications that start prior to the date of the first dose but continue beyond the date of first dose will be categorized as concomitant medications. Prior and concomitant medications along with dose, route, start/end date, frequency, and indication for each medication will be presented in data listings.

If both the start and end dates are completely missing, the medication will be considered concomitant. For cases where start or end dates are partially recorded, the following imputation algorithms will be used for the purpose of determining prior or concomitant medications:

- Missing start day, but month and year present:

If year and month are same as first dosing year and month, assign the day of first dosing date to the partial date. Otherwise, assign 1st of the month to the partial date.

- Missing start day and month, but year present:

If year is same as first dosing year, assign the month and day of first dosing date to the partial date. Otherwise, assign January 1st to the partial date.

- Missing end day, but month and year present:

If year and month are same as end of study participation year and month, assign the day of end of study participation to the partial date. Otherwise, assign the last day of the month to the partial date.

- Missing end day and month, but year present:

If year is same as end of study participation year, assign the month and day of end of study participation date to the partial date. Otherwise, assign December 31st to the partial date.

If the study is ongoing (e.g. interim analysis) and the study end date is not available, the cut-off date will be used instead.

6.9 Concomitant Procedure

Concomitant procedures will be recorded during the study. Concomitant procedures along with start/end date, and indication for the procedure will be presented in data listings.

6.10 Post Treatment Anti-Cancer Treatment

The first post treatment systemic anti-cancer therapy will be collected during survival follow-up and will be coded to ATC class and Generic Drug Names using the WHO Drug Dictionary. The drug name, start and end date, and best response will be listed.

7. EFFICACY ANALYSES

The efficacy endpoints include ORR, CBR, TTR, DOR, PFS, and OS. The efficacy endpoints ORR, CBR, TTR, DOR, and PFS will be based on the investigator disease assessment per RECIST 1.1.

The efficacy analyses will be based on the All Treated population and/or Response Evaluable population, as appropriate. For the summaries using all treated population, subjects who do not have any post-baseline disease assessment will be considered as non-responders in the calculation of response rate. Efficacy data analyses will be performed separately for each treatment regimen (SL-172154 + PLD and SL-172154 + MIRV).

For Regimen (SL-172154 + MIRV), all efficacy tables will be summarized or analyzed for each of these three tumor FRα expression level subgroups: high (PS2+ ≥75%), medium (PS2+ ≥50% and <75%), and low (PS2+ ≥25% and <50%), as appropriate. In the case of limited data, medium and low subgroups may be combined for summary and analyses.

Disease assessment will be performed at baseline (screening visit) and at post baseline visits per the schedule of assessments in protocol. Confirmatory scans should be performed at least 4 weeks (>28 days) after initial documentation of an objective response. If study treatment is withdrawn for reasons other than disease progression, radiographic disease assessments should continue as per the schedule of assessments until documented disease progression, the start of new anti-cancer therapy, withdrawal of consent or death.

7.1 Objective Response Rate

The ORR is defined as the proportion of subjects whose best overall response is a confirmed complete response (CR) or confirmed partial response (PR) based on investigator assessment according to RECIST 1.1 [Eisenhauer, 2009]. The ORR will be estimated with a 95% CI using the exact probability method. The number and percent of subjects with the best overall response of CR, PR, stable disease (SD), progressive disease (PD) and not evaluable (NE) will be summarized. Summary of objective response will be provided for the All Treated population and Response Evaluable population, respectively.

The best overall response based on RECIST 1.1 is defined as the best overall response among all post-baseline time point assessments until the first PD per RECIST 1.1 or start of new anti-cancer therapy, whichever is earlier. For subjects who have not met the criteria for PD per RECIST1.1 or have not started a new anti-cancer therapy, the best overall response is defined as the best overall response among all post-baseline timepoint assessments.

Based on the investigator assessment of overall response per RECIST 1.1 at post-baseline assessments, the best overall response will be determined programmatically as the following and in Table 5:

- CR > PR > SD > PD > NE
- CR = at least two determinations of CR with at least 4 weeks apart before progression.
- PR = at least two determinations of PR or better with at least 4 weeks apart before progression (and not qualifying for CR).
- SD
    - For SL-172154 + PLD regimen, SD = at least one SD or better ≥ 49 days after the first dose and before progression (and not qualifying for a CR or PR). The minimum interval from the first dose date for the best response of SD is 8 weeks minus 7 days to allow for visit windows of ± 7 days (49 days).
    - For SL172154 + MIRV regimen, SD = at least one SD or better ≥ 35 days after the first dose and before progression (and not qualifying for a CR or PR). The minimum interval from the first dose date for the best response of SD is 6 weeks minus 7 days to allow for visit windows of ± 7 days (35 days).
- If the minimum interval for SD is not met, the best response will depend on the subsequent assessments. For example, a subject who has SD at first assessment, PD at second and does not meet minimum duration for SD, will have a best response of PD. The same subject lost to follow-up after the first SD assessment will be considered NE.
- PD is considered the best overall response when PD is documented and a best overall response of CR, PR, or SD could not be established before documentation of PD. Clinical deterioration will not be considered as documented disease progression in the determination of the best overall response.
- NE is considered the best overall response when PD has not been documented and a best response of CR, PR or SD could not be established.

Table 5 Best overall response with confirmation of CR and PR required

Overall response First time point	Overall response Subsequent time point	BEST overall response
CR	CR	CR
CR	PR	SD, PD or PR[a]
CR	SD	SD provided minimum criteria for SD duration met, otherwise, PD

Overall response First time point	Overall response Subsequent time point	BEST overall response
CR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
PR	CR	PR
PR	PR	PR
PR	SD	SD, provided minimum criteria for SD duration met, otherwise, PD
PR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
PR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
NE	NE	NE

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease,
NE = not evaluable.
[a] If a CR is truly met at the first time point, then any disease seen at a subsequent time point, even disease meeting PR criteria relative to baseline, makes the disease PD at that point (since disease must have reappeared after CR). Best response would depend on whether minimum duration for SD was met. However, sometimes "CR" may be claimed when subsequent scans suggest small lesions were likely still present and in fact the subject had PR, not CR at the first time point. Under these circumstances, the original CR should be changed to PR and the best response is PR.

Disease assessment at baseline including sum of target lesion diameters and the number of subjects with target lesions and non-target lesions will be summarized. The percent change from baseline in target lesion sum of diameters for all post-baseline disease assessments will be plotted by subject. The percent change from baseline will only be calculated when all target lesions at baseline are accounted at a post baseline visit. The best percent change from baseline in target lesion sum of diameters is defined as the largest reduction or smallest increase (in the case where a reduction does not occur) from baseline observed over post-baseline disease assessments with all target lesions identified at baseline measured up to the first PD and will be presented using a waterfall plot. Target lesion, non-target lesion, new lesion and response assessments will be presented in data listings. The percent change from baseline/nadir in target lesion sum of diameters will be displayed with 2 decimal places (xx.xx%) without rounding in the data listing. Nadir in target lesion sum of diameters at a visit is the smallest sum of diameters reported at prior study visits. The response of PD will be assessed based on the percent increase of the sum of diameters of target lesions relative to the nadir.

7.2 Clinical Benefit Rate

For SL-172154 + PLD regimen, the CBR based on RECIST 1.1 is defined as the proportion of subjects whose best overall response is a confirmed CR, confirmed PR or SD ≥ 16 weeks, where SD ≥ 16 weeks is defined as at least one SD or better for ≥ 15 weeks (16 weeks with 1 week visit window) and not qualifying for a confirmed CR or PR as in Table 6.

Table 6 Best overall response of SD ≥ 16 weeks in SL-172154 + PLD regimen

Response at Week 8 assessment	Response at Week 16 assessment	Response at Week 24 assessment	SD ≥ 16 weeks

SD	SD/PR/CR	Any	Yes
SD	PD	Any	No
SD	NE/missing	SD/PR/CR	Yes
SD	NE/missing	PD/NE/missing	No
CR/PR	PD	Any	No
PR	SD	Any	Yes
NE	SD	Any	Yes

For SL-172154+MIRV regimen, the CBR based on RECIST 1.1 is defined as the proportion of subjects whose best overall response is a confirmed CR, confirmed PR or SD ≥ 12 weeks, where SD ≥ 12 weeks is defined as at least one SD or better for ≥ 11 weeks (12 weeks with 1 week visit window) and not qualifying for a confirmed CR or PR as in Table 7.

Table 7 Best overall response of SD ≥ 12 weeks in SL-172154 + PLD regimen

Response at Week 6 assessment	**Response at Week 12 assessment**	**Response at Week 18 assessment**	**SD ≥ 12 weeks**
SD	SD/PR/CR	Any	Yes
SD	PD	Any	No
SD	NE/missing	SD/PR/CR	Yes
SD	NE/missing	PD/NE/missing	No
CR/PR	PD	Any	No
PR	SD	Any	Yes
NE	SD	Any	Yes

The CBR will be estimated with a 95% CI using the exact probability method. Summary of CBR will be provided for the All Treated population and Response Evaluable population.

7.3 Time to Response

The TTR based on RECIST 1.1 is defined as the time from the first dose until the first documentation of a subsequently confirmed objective response (confirmed CR or confirmed PR). Only subjects who have achieved confirmed objective response will be evaluated for TTR, and individual TTR will be presented in data listings. If data warrants, TTR will be summarized descriptively and graphically using Kaplan-Meier methods. The Kaplan-Meier estimate for the median TTR along with 95% confidence intervals and the first and third quartiles will be determined. Brookmeyer-Crowley method will be used for the confidence interval calculation. For SL-172154 + PLD regimen, Kaplan-Meier estimate of TTR rate at 2 months, 4 months, and other timepoints of interest will be included in the summary table. For SL-172154 + MIRV

regimen, Kaplan-Meier estimate of TTR rate at 2 months, 4 months, and other timepoints of interest will be included in the summary table.

7.4 Duration of Response

The DOR based on RECIST 1.1 is defined as the time from the date of the first CR or PR (confirmed at least 28 days later) to the date of first documented disease progression per RECIST 1.1 or death, whichever occurs first. Only subjects who have achieved a confirmed CR or confirmed PR will be evaluated for DOR, and individual DOR will be presented in data listings.

If a disease progression does not occur, DOR will be censored as of the date of the last evaluable disease assessment. The evaluable disease assessment is defined as an assessment for which the overall response can be determined. The censoring guidance and the date of PD/death or censoring are same as those for PFS in Section 7.5. If data warrants, DOR will be summarized descriptively and graphically using Kaplan-Meier methods. The Kaplan-Meier estimate for the median DOR along with 95% confidence intervals and the first and third quartiles will be determined. Brookmeyer-Crowley method will be used for the confidence interval calculation. For SL-172154 + PLD regimen, Kaplan-Meier estimate of DOR rate at 2 months, 4 months, and other timepoints of interest will be included in the summary table. For SL-172154 + MIRV regimen, Kaplan-Meier estimate of DOR rate at 2 months, 4 months, and other timepoints of interest will be included in the summary table.

7.5 Progression Free Survival

The PFS based on RECIST 1.1 is defined as time from the first day of treatment to the first documented disease progression per RECIST 1.1 or death from any cause, whichever occurs first. Subjects who have not progressed at the time of analysis will be censored at the date of their last evaluable disease assessment. Subjects who start new anticancer therapy prior to the documented PD will be censored at the last evaluable disease assessment prior to the start of new anticancer therapy. The censoring guidance and the date of PD/death or censoring are given in the Table 8 below.

Table 8 Summary of Censoring Guidelines for PFS based on RECIST1.1

Situation	Date of PD/Death or Censoring	PFS Outcome
Documented PD or death from any cause	Date of the PD or death, whichever comes first	Event (unless the censoring rule specified below is met)
Start new anticancer therapy before documented PD	Date of last evaluable disease assessment prior to the start of new anticancer therapy	Censored
Death or PD immediately after ≥ 2 consecutive missed or non-evaluable disease assessments[1] as per the protocol specified assessment schedule	Date of last evaluable disease assessment prior to missed or non-evaluable assessments, or the first dose of investigational product, whichever occurred last	Censored
No PD or death at time of analysis or lost to follow-up	Date of last evaluable post-baseline disease assessment	Censored
(No baseline disease assessment OR no post-baseline disease assessment) AND no death	Date of first dose with a duration of 1 day	Censored

[1] Two or more consecutive disease assessments derivation is based on the disease assessment schedule in Section 6 of the protocol for each treatment regimen (SL-172154 + PLD and SL-172154 + MIRV), with a one-week visit window considered. If a subject has two or more consecutive missed or non-evaluable assessments followed by an assessment showing no radiologic disease progression, then the assumption will be that the subject did not progress during the missed or non-evaluable assessments.

If data warrants, PFS will be summarized descriptively and graphically using Kaplan-Meier methods. The Kaplan-Meier estimate for the median PFS along with approximate 95% confidence intervals and the first and third quartiles will be determined. Brookmeyer-Crowley method will also be used for the confidence interval calculation. For SL-172154+PLD regimen, Kaplan-Meier estimate of PFS rate at 2 months, 4 months, and other timepoints of interest will be included in the summary table. For SL-172154+MIRV regimen, Kaplan-Meier estimate of PFS rate at 2 months, 4 months, and other timepoints of interest will be included in the summary table. PFS will be summarized and listed for the All Treated population.

7.6 Overall Survival

The OS is defined as time from the first day of treatment to the date of death. A subject alive at the end of study or lost to follow-up will be censored for OS at the last date when the subject was known to be alive, i.e., the last date on study.

If data warrants, the median and quartiles of OS and their 95% CIs will be assessed using the Kaplan-Meier method. Brookmeyer-Crowley method will also be used for the confidence interval calculation. The proportion of subjects alive at 3 months, 6 months and other timepoints of interest will be estimated using the Kaplan-Meier method. OS will be summarized and listed for the All-Treated population.

7.7 CA-125

The CA-125 at baseline and post-baseline assessments, and maximum changes in CA-125 from baseline among all post baseline assessments will be summarized. Number of subjects with >=50%, >=75% and 100% decreases or increase from baseline will be summarized. The percent change from baseline in CA-125 for all post-baseline assessments over time will be plotted by subject. The CA-125 test results along with change from baseline and percent change from baseline will be presented in data listings.

8. SAFETY ANALYSES

Unless specified otherwise, all safety data summaries will be presented by dose levels for all subjects in the All Treated population for each treatment regimen. Select safety summaries will be provided for DLT evaluable populations.

8.1 Study Drug Exposure

8.1.1 Study Drug Treatment Duration

For SL-172154 + PLD regimen, the study drug treatment duration will be calculated as minimum of (date of death + 1 day, data cutoff date + 1 day, and date of last dose + 7 days if last dose is on D1 (or D8) of a cycle or + 14 days if last dose is on D15 of a cycle) - date of first dose of study treatment.

For SL-172154 + MIRV regimen, the study drug treatment duration will be calculated as minimum of (date of death + 1 day, data cutoff date + 1 day, and date of last dose + 7 days) - date of first dose of study treatment.

Study drug treatment duration will be listed and summarized. Study drug treatment duration will be plotted by subject using a horizontal bar graph with information regarding the time of first PR/CR and the first PD, dose level, best response (RECIST 1.1) and treatment discontinuation information for each subject.

8.1.2 SL-172154

The actual body weight (kg) will be used for SL-172154 dose calculation in all subjects whose body weight is <=100 kg. For subjects with body weight >100 kg, weight of 100 kg will be used for dose calculation. The subject should be dosed according to their C1D1 weight throughout the study (mg/kg) unless there is >=10% change (increase or decrease) in their weight from the weight recorded at the C1D1 visit, in which case the expected dose will be re-calculated.

The actual dose received (mg) in each dosing day will be calculated as the following:

- Total dose in mg to be administered *(actual total volume received /total volume to be administered)

Total number of doses received, cumulative dose received (mg), average dose received (mg), relative dose intensity, overdose, and infusion outcome (number of infusions completed and interrupted, and number of infusions not completed) will be summarized. Average dose received is calculated as the cumulative dose (mg) that a subject received divided by the total number of doses received.

Relative dose intensity is defined as the total mg of SL-172154 actually infused divided by the total mg of SL-172154 assigned, expressed as a percentage.

SL-172154 administration for individual subjects will be provided in a data listing by cohort (escalation and expansion), dose level, and date of first dose. In addition to the data captured on the CRF page, the actual dose received and the infusion rate for each infusion period and if there is any interruption, will also be calculated and listed.

8.1.3 PLD

PLD (40 mg/m^2) will be administered IV on Day 1 of each 28-day cycle for the combination regimen (SL-172154 + PLD). The dose of PLD administered will be based on the subject's body surface area (m^2). All subjects should be weighed within 3 days prior to dosing for every cycle. If a subject experiences either a weight loss or gain >10% compared to the weight used for the last dose calculation, the dose of PLD will be recalculated.

Total number of doses received and infusion outcome (number of infusions completed and interrupted, and number of infusions not completed) will be summarized. The cumulative dose (mg/m^2), calculated as the cumulative dose (mg) divided by baseline body surface area (m^2), will also be summarized as a continuous variable. The number of subjects with cumulative dose >450mg/m^2 will be provided as well. PLD administration for individual subjects will be provided in a data listing by cohort (escalation and expansion), dose level, and date of first dose.

8.1.4 MIRV

MIRV (6 mg/kg AIBW) will be administered IV on Day 1 of each 21-day cycle for the combination regimen (SL-172154 + MIRV). The dose of MIRV administered will be based on the subject's AIBW. The weight used for calculation will be obtained before MIRV administration on C1D1 (-14 days). Dosing may be modified per institutional standard of care for changes in body weight on subsequent cycles. Dosing will be modified for significant (≥10%) changes in body weight (not influenced by weight gain or loss attributed to fluid retention).

Total number of doses received and infusion outcome (number of infusions completed and interrupted, and number of infusions not completed) will be summarized. MIRV administration for individual subjects will be provided in a data listing by cohort (escalation and expansion), dose level, and date of first dose.

8.2 Maximum Tolerated Dose Evaluation

The MTD evaluation will be based on the DLT Evaluable Population. The number and percentage of subjects with DLT will be presented by dose level for the dose escalation cohorts. The MTD level will be indicated in the summary.

The MTD will be estimated using isotonic regression (based on the DLTs observed in the DLT evaluable subjects). A MAD will be reported if the DLT rate never reaches ≥25%. Otherwise, an MTD will be reported. Isotonic regression is a way to estimate the MTD under the assumption that toxicity increases with dose. When using isotonic regression, the first step is to identify the doses where the dose-toxicity monotonicity assumption is violated. The DLT estimate is then adjusted for the violators such that the final estimate of the DLT rate increase with the dose. The target DLT rate is then used to select the MTD. For example, suppose that when the trial is completed, the observed DLT rates [# subjects who experienced DLT]/[# evaluable subjects] at four dose levels are (0/3, 1/3, 0/3, 4/15). In this example the observed DLT rate at Dose Level 2 (i.e., 1/3=33%) is higher than the observed DLT rate at Dose Level 3 (i.e., 0/3=0%). To adjust for this violation, the DLT estimates are replaced with their average, i.e., (1/3+0/3)/2=1/6, resulting in the isotonic regression DLT estimates (0/3, 1/6, 1/6, 4/15) = (0%, 16.7%, 16.7%, 26.7%), which monotonically increases with the dose level. Based on this isotonic estimate, assuming that the trial goal is to find the dose with the DLT rate of 30%, Dose Level 4 will be selected as the MTD. If there are no violators of the dose-toxicity monotonicity assumption, isotonic regression directly uses the observed DLT rates as the final estimates for MTD selection.

In the case of dose levels with estimated toxicity of equal distance (tied dose levels) from the target toxicity of 30%, the following approach will be used: among all tied dose levels the highest dose level with target toxicity ≤ 30% will be selected, unless all tied dose levels have estimated toxicity > 30%, in which case the lowest dose level will be selected.

8.3 Adverse Events

Safety reporting of AEs commences when a subject has signed the ICF, throughout the course of treatment, and up to 30 days after the last dose of study drug. If another anti-cancer agent is started within 30 days after the last dose of study drug, only serious adverse events (SAEs) and AEs that occur prior to starting the new anti-cancer therapy should be recorded. After signing of informed consent, but prior to initiation of study drug, only AEs caused by a protocol-mandated procedure will be collected (e.g., AEs related to invasive procedures such as biopsies).

The AE terms on the eCRFs will be mapped to the preferred terms (PT) and system organ classes (SOC) using the Medical Dictionary for Regulatory Activities (MedDRA) in the most current version available at time of analysis. Drug-related AEs are defined as AEs with relationship to study treatment being related or possible related. A worst-case scenario approach will be taken to handle missing data, i.e. AEs with missing relationship to a study drug will be treated as drug-related AEs.

All AEs with onset dates on or after the first dose of study treatment are defined as treatment-emergent adverse events (TEAEs). Only TEAEs will be included in AE tables. All AEs will be

listed, and pretreatment AE, defined as AEs that start prior to the first date of the study treatment, will be flagged in relevant listings.

If both the start and end dates are completely missing, the AE will be considered treatment-emergent. Partial start and end dates may be imputed similarly as described for prior and concomitant medications in Section 6.8 for the purpose of determining treatment-emergent and AE duration.

An overview summary of TEAEs will be produced, including the counts and percentages of subjects with any TEAE, drug-related TEAEs (separate rows for SL-172154, PLD, and MIRV), serious TEAEs, drug-related serious TEAEs (separate rows for SL-172154, PLD, and MIRV), infusion related reaction AEs, Grade 3 or 4 AEs, drug-related Grade 3 or 4 AEs (separate rows for SL-172154, PLD, and MIRV), fatal TEAEs, and TEAEs leading to infusion interrupted, dose reduced, dose not given/delayed, and drug withdrawn.

The TEAE by maximum toxicity grade summary tables will use the following algorithms for counting subjects:

- **PT rows:** each subject is counted once within each unique PT at the maximum grade. For example, if a subject has two headaches, the subject is counted only once under the PT "Headache". Subjects experiencing the same PT several times with different grades will only be counted once at the maximum grade.
- **SOC rows:** each subject is counted only once at the maximum grade at each SOC level although they may have several different PT events within the same SOC.
- **Any event row**: each subject with at least one TEAE will be counted only once at the maximum grade no matter how many events they have.

All TEAEs and drug-related TEAEs will be summarized by MedDRA SOC, PT and maximum toxicity grade. The SOC and PT will be ordered by descending order of the subject incidence of SOC and PT within each SOC based on all subjects in the analysis population.

The following summary tables will be presented by MedDRA PT, in which the PT will be order by descending order of subject incidence of PT based on all subjects in the analysis population:

- Summary of all TEAEs
- Summary of DLTs
- Summary of serious TEAEs
- Summary of drug-related TEAEs (separate tables for SL-172154, PLD, and MIRV)
- Summary of drug-related serious TEAEs (separate tables for SL-172154, PLD, and MIRV)
- Summary of fatal TEAEs
- Summary of Grade 3 or 4 TEAEs

- Summary of drug-related Grade 3 or 4 TEAEs (separate tables for SL-172154, PLD, and MIRV)
- Summary of TEAEs leading to infusion interrupted, dose reduced, dose not given/delayed, and drug withdrawn (separate tables for SL-172154, PLD, and MIRV)

Additional summaries for SL-172154-related IRR (toxicity grade, seriousness, number of events, action taken) at event-level, at subject-level, and number of subjects with IRR at each dosing visit among the first two cycles and during all subsequent cycles combined will be provided. For the MIRV cohort, MIRV-related Grade 3 or 4 ocular toxicity TEAEs, with SOC='Eye disorders', will be listed and summarized.

Listings of all AEs, drug-related AEs, DLTs, Grade 3 or 4 AEs, fatal AEs, and SAEs will be provided. Separate listings will be provided for AEs leading to infusion interruption, dose reduction, dose not given/delayed, and drug withdrawal with SL-172154, PLD, and MIRV, respectively. SL-172154-related IRR along with signs/symptoms, premedication and concomitant medication for IRR will also be listed. All AEs for the Screen Failures population will be presented in a listing as well.

8.4 Clinical Laboratory Evaluation

The clinical laboratory evaluation includes the following:

- Hematology: hemoglobin, hematocrit, platelet count, red blood cell count, white blood cell count, neutrophils, lymphocytes, monocytes, eosinophils, basophils, and mean corpuscular volume
- Clinical chemistry: blood urea nitrogen, creatinine, glucose, sodium, potassium, calcium, magnesium, phosphorus, total protein, albumin, lactate dehydrogenase, bicarbonate (or CO_2), haptoglobin, ferritin and liver panel [alanine aminotransferase (ALT), aspartate aminotransferase (AST), total and direct bilirubin, and alkaline phosphatase].
- Coagulation: prothrombin time, international normalized ratio, activated partial thromboplastin time, fibrinogen, and D-dimer.
- Thyroid: thyroid stimulating hormone and free thyroxine 4.

The clinical laboratory grades will be reported using the CTCAE v5.0. Separate listings will be provided for hematology, clinical chemistry, coagulation and thyroid tests. For each listing, baseline value will be specified for each subject.

Clinical laboratory results (hematology, clinical chemistry, coagulation) will be summarized for worst case shift from baseline toxicity grade. Frequencies of maximum observed Grade 0-4 toxicity, as defined by the NCI CTCAE v5.0, will be presented for each laboratory parameter. The determination of the maximum grade post-baseline takes into account both planned and unscheduled assessments. Separate summaries indicating hyper- and hypo- directionality of change will be produced, where appropriate.

All laboratory values will be categorized as “low”, “normal”, or “high” relative to the normal ranges, or “unknown” if no valid result is available. For those laboratory parameters that do not have NCI CTCAE v5.0 grading criteria, worst case shift from baseline to post-baseline will be summarized. Shift to low includes normal to low, high to low, and unknown to low. Shift to high includes normal to high, low to high, and unknown to high. If a subject has worst case shifts to both “low” and “high”, the subject will be counted in both categories.

Subjects with elevated worst post-baseline ALT, AST, Total Bilirubin, or alkaline phosphatase (ALP) values that fall into the following categories or other categories as needed will be identified and summarized:

- ALT in the categories of <=1x upper limit of normal range (ULN), >1x ULN, >3x ULN, >5x ULN, >10x ULN;
- AST in the categories of <=1x ULN, >1x ULN, >3x ULN, >5x ULN, >10x ULN;
- total bilirubin in the categories of <=1x ULN, >1x ULN, >2x ULN
- ALP in the categories of <=1x ULN, >1x ULN, >1.5x ULN, >2x ULN
- Potential Hy’s law, defined as at least one case of post-dose total bilirubin > 2 x ULN occurred at the same day or after the first incidence date of ALT or AST > 3 x ULN post treatment.

For subjects who meet potential Hy’s law criterion, their liver enzyme (ALT, AST, ALP, and total bilirubin) value over time will be plotted.

All laboratory results will be presented by subject in data listings.

8.5 Death

All death records will be presented in data listings. Subject incidence of deaths within and outside of 30 days of last dose of study treatment and the cause of death will be summarized.

8.6 Vital Signs and Pulse Oximetry

Vital signs (blood pressure, heart rate, respiration rate, temperature), pulse oximetry, and weight (with percent change from baseline) will be presented in data listings.

8.7 ECOG Performance Status

ECOG performance status scores will be summarized for baseline, and worst-case shift from baseline in a table and presented in data listings.

8.8 Cardiac Assessments

Cardiac assessments including electrocardiogram (ECG) and echocardiogram (ECHO) assessment date and results along with clinical significance will be presented in data listings. For SL-172154 + PLD regimen, ECHO percent change from baseline and a flag “Low” will be displayed if a value is lower than the lower limit of normal.

8.9 Blood Phenotype and Direct Antiglobulin Test

Blood phenotype and direct antiglobulin test (DAT) assessment date and results will be presented in data listings.

8.10 Transfusion

Transfusions data will be presented in data listings.

8.11 Ocular Symptom Assessment and Ophthalmic Examination [MIRV Regimen Only]

For subjects enrolled in Regimen (SL172154 + MIRV), ocular symptom assessment and ophthalmic examination will be performed per the schedule of assessments in protocol. Relevant findings will be reported as AE data. In addition to AE tables and listings, the ocular symptom assessment results will be presented in a data listing as well.

9. PHARMACOKINETIC ANALYSES

9.1 SL-172154 PK Analyses

The merge of SL-172154 serum concentration with CRF data will be performed after database lock by Shattuck Labs to generate a dataset with actual PK sampling times, actual time relative to the start of infusion, and SL-172154 concentrations. Derivation of PK parameters will be performed by Certara using Phoenix WinNonlin (Version 8.4 or higher).

Unless otherwise specified, all PK data analyses will be based on the SL-172154 PK population and summarized for each treatment regimen.

9.1.1 Data Handling

The nominal time relative to the start of infusion will be calculated as the planned time relative to the end of infusion plus the planned infusion duration. The actual time relative to the start of infusion will be calculated as the actual sampling time relative to the start of infusion (SOI) or the SOI of the first infusion period if there is (are)with infusion interruption(s). Missing PK sampling time will be handled as the following when calculating the actual time relative to SOI:

- If a sampling time is missing and no infusion interruption, the actual time relative to SOI will be calculated as time from SOI to end of infusion (EOI) plus planned time relative EOI.
- If a sampling time is missing and there is interruption(s) during the infusion, the actual time relative to SOI will be calculated as time from the SOI of first infusion period to the EOI of the last infusion period plus planned infusion time relative to EOI.

Concentration values that are below the limit of quantification (BLQ) will be handled as the following:

- If a BLQ value occurs at the predose, the BLQ value will be assigned as zero concentration. If one or more BLQ values occur in a profile after infusion but before the first measurable concentration, the BLQ values will be assigned a value of zero

concentration. For linear plots, zero concentration value(s) will be included in the plot. For log-linear plots, zero concentration value(s) will be assigned a missing value.

- If a BLQ value occurs after a measurable concentration in a profile and is followed by a measurable concentration, then the BLQ will be set as missing.
- If a BLQ value occurs after the last measurable concentration in a profile, then the BLQ values will be set as missing.
- If two or more BLQ values occur in succession after a measurable concentration, the profile will be deemed to have terminated at the first BLQ value (BLQ values will be set to missing) and any subsequent concentration will be set as missing.
- BLQ values that are set to be missing will be omitted from PK parameter generation, concentration summary, and the individual PK profile plots.
- For the time point that all concentrations are BLQ and all BLQ results are imputed to be zero, then the mean/median concentration will be reported as zero.
- For the time point that only some concentrations are BLQ and BLQ values are imputed to be zero, the mean/median will be reported unless the mean/median value is below the LLQ (10 ng/ml), in which case the value will be assigned as BLQ.

9.1.2 SL-172154 Concentration Measures

SL-172154 concentration values will be sorted by sample collection day, and nominal time points in the listing. All SL-172154 concentration values including BLQ will be listed in the same precision as the source data.

SL-172154 concentration will be summarized for each nominal time point relative to the EOI. Standard summary statistics will be calculated (i.e., mean, standard deviation, median, minimum, maximum, coefficient of variation (CV%), geometric mean, geometric CV%).

9.1.3 SL-172154 PK Parameters

The PK parameters will be derived from the concentration-time data using the actual collection time from SOI. The PK parameters will be calculated by standard non-compartmental analysis (NCA) as data permits. At least one post-dose concentration at planned time of end of infusion or 0.5 hour post end of infusion is required for C_{max} calculation, and at least three consecutive post-dose concentrations are required for AUC parameter calculation.

Table 9 SL-172154 PK Parameters

C_{max}	Maximum observed concentration over a dosing interval
C_{trough}	Observed concentration at the end of a dosing interval.
T_{max}	Time of maximum observed concentration
$AUC_{0\text{-last}}$	The area under the serum concentration time curve, from time 0 to the last quantifiable concentration, calculated by a combination of linear and logarithmic trapezoidal methods (Linear up/log down method).

$AUC_{0\text{-}inf}$	Area under the serum concentration time curve from time 0 extrapolated to infinity, calculated as AUC_{last} + C_{last}/terminal elimination rate constant (λ_z). Reliability of $AUC_{0\text{-}inf}$ values is contingent on the percent of the total area obtained by extrapolation: $AUC_{0\text{-}inf}$ values with <20% of the total area coming from C_{last}/λ_z are considered acceptable. Any exceptions to the above procedures will be clearly documented/justified in the PK report.
AUC_{tau}	The area under the serum concentration time curve over the dosing interval, calculated by a combination of linear and logarithmic trapezoidal methods (Linear up/log down method).
$\%AUC_{ext}$	Percentage of $AUC_{0\text{-}inf}$ due to extrapolation from T_{last} to infinity
$t_{½}$	Terminal elimination half-life, estimated using the equation [ln(2)/λ_z]
CL	Clearance; calculated as Dose/$AUC_{0\text{-}inf}$ for C1D1 and Dose/AUC_{tau} for later time unless specified otherwise
Vz	Volume of distribution, calculated as Dose/(λ_z * $AUC_{0\text{-}inf}$) for C1D1 and Dose/(λ_z * AUC_{tau}) for later time unless specified otherwise
AR_{AUCtau}	Accumulation ratio of AUC_{tau} or $AUC_{0\text{-}xx}$ (over the dosing interval), C1D15/C1D8 and C2D8/C1D8.
AR_{Cmax}	Accumulation ratio of C_{max} (C1D15/C1D8 and C2D8/ C1D8).

The elimination rate constant (λ_z) will be determined if the log-linear terminal elimination phase is apparent and excludes C_{max}. The λ_z will only be considered reliable if the adjusted coefficient of determination (adj-R^2) is greater than or equal to 0.8. Parameters dependent on λ_z (i.e., $t_{1/2}$, $AUC_{0\text{-}inf}$, $AUC_{\%ext}$, CL, Vz) will not be presented if λ_z cannot be estimated.

The following PK parameters will be calculated for diagnostic purposes and listed but not be summarized:

- λ_z lower: Lower limit of time (h) included in the calculation of λ_z
- λ_z N: Number of data points used in the calculation of λ_z
- λ_z upper: Upper limit of time (h) included in the calculation of λ_z
- Adjusted-R^2: Regression coefficient for calculation of λ_z

All PK parameters will be listed and summarized for each PK sample collection day. For each of the PK parameters, except T_{max}, the following summary statistics will be calculated: median, minimum, maximum, arithmetic mean, standard deviation, CV%, geometric mean, and geometric CV%. For T_{max}, median, minimum, and maximum will be calculated. All PK parameters will be reported with the same precision as the source concentration data except that T_{max} and $t_{1/2}$ will be reported with 2 decimal places and λ_z will be reported with at least 3 significant figures.

9.2 MIRV PK Analyses

All MIRV PK data analyses will be based on the MIRV PK population. Blood samples for MIRV PK will be collected at predose and EOI of Day 1 for each cycle and at PTV. MIRV concentration data will be summarized for each nominal time point relative to the EOI. Standard summary statistics will be calculated (i.e., mean, standard deviation, median, minimum,

maximum, CV%, geometric mean, geometric CV%). All MIRV concentration data will also be listed.

10. IMMUNOGENICITY

10.1 SL-172154 ADA Data Analyses

All SL-172154 ADA data summaries and analyses will be performed for subjects included in the SL-172154 immunogenicity population.

SL-172154 treatment induced ADA is defined as positive sample after first SL-172154 dose for subjects with negative or missing ADA at first SL-172154 predose. Sustained ADA response is defined as treatment induced ADA in ≥2 consecutive samples without a subsequent negative sample or in the last sample. Persistent ADA response is defined as treatment induced ADA in ≥2 samples, with the first and last samples (irrespective of any negative in between) separated by ≥16 weeks, or only in 1 sample but the last sample, or only in 1 sample but less than 16 weeks before a negative last sample.

A summary of SL-172154 ADA at first SL-172154 predose and during the study will be provided. The summary of onset and duration of treatment induced ADA during the study will also be provided in a table. All SL-172154 ADA data along with any available Nab data will be listed for all subjects in Immunogenicity population.

10.2 MIRV ADA Data Analyses

All MIRV ADA data summaries and analyses will be performed for subjects included in the MIRV immunogenicity population.

MIRV treatment induced ADA is defined as positive sample after C1D1 first dose for subjects with negative or missing ADA at C1D1 predose. The summary of MIRV ADA at C1D1 predose and treatment induced ADA during the study will be provided. All MIRV ADA data along with available Nab data will be listed for all subjects in Immunogenicity population.

11.CHANGE FROM PROTOCOL-SPECIFIED ANALYSES

There are no changes from the protocol-specified analyses.

12. LITERATURE REFERENCES

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Guo W, Wang SJ, Yang S, Lynn H, Ji Y. A Bayesian interval dose-finding design addressing Ockham's razor: mTPI-2. Contemp Clin Trials 2017;58:23-33.

Ivanova A, Qaqish BF, Schell MJ. Continuous toxicity monitoring in phase II trials in oncology. Biometrics 2005;61:540-5.

National Cancer Institute Common Terminology Criteria for Adverse Events v5.0, NCI, NIH, DHHS, November 27, 2017.

Pujade-Lauraine E, Fujiwara K, Ledermann JA, et al. Avelumab alone or in combination with chemotherapy versus chemotherapy alone in platinum-resistant or platinum-refractory ovarian cancer (JAVELIN Ovarian 200): an open-label, three-arm, randomised, phase 3 study. Lancet Oncol 2021;22:1034-46.

13. APPENDIX: LIST OF TABLES, FIGURES AND LISTINGS

The table, figure and listing titles proposed in this section apply to both Regimen (SL-172154 + PLD) and Regimen (SL-172154 + MIRV), unless specified otherwise. The regimen will be indicated in the numbering and output titles. Regimen (SL-172154 + PLD) output numbering will end with “a”, and Regimen (SL-172154 + MIRV) output numbering will end with “b”. In titles where there is “PLD” wording for Regimen (SL-172154 + PLD), “PLD” will be replaced with “MIRV” for Regimen (SL-172154 + MIRV) outputs. Additional details for Regimen (SL-172154 + MIRV) outputs will be specified in the table, figure, and listing shells as necessary. If the study is prematurely terminated, select tables, figures, and listings as agreed upon by the study team will be produced for the abbreviated clinical study report (aCSR).

13.1 List of Tables

ICH Heading	Table Number	Table Description	Analysis Population	aCSR
12.1		**Demographics**		
	14.1.1	Study Populations and Subject Disposition	All Enrolled	Yes
	14.1.2	SL-172154 Treatment Status	All Treated	Yes
	14.1.3	PLD Treatment Status	All Treated	Yes
	14.1.4	Protocol Deviations	All Treated	Yes
	14.1.5	Demographic and Baseline Characteristics	All Treated	Yes
	14.1.6	Study Cancer History	All Treated	Yes
	14.1.7	Prior Anti-Cancer Treatment	All Treated	Yes
14.2		**Efficacy**		
	14.2.1	Objective Response with Confirmation Based on RECIST 1.1	All Treated	Yes
	14.2.2	Objective Response with Confirmation Based on RECIST 1.1	Response Evaluable	Yes
	14.2.3	Time to Response and Duration of Response Based on RECIST 1.1	Response Evaluable	Yes

ICH Heading	Table Number	Table Description	Analysis Population	aCSR
	14.2.4	Progression-Free Survival Based on RECIST 1.1	All Treated	Yes
	14.2.5	Overall Survival	All Treated	Yes
	14.2.6	Tumor Assessment at Baseline	All Treated	No
	14.2.7	Summary of CA-125	All Treated	No
14.3		**Safety**		
14.3.1		**Study drug exposure/adverse event**		
	14.3.1.1	SL-172154 Exposure and Study Drug Treatment Duration	All Treated	Yes
	14.3.1.2	PLD Exposure	All Treated	Yes
	14.3.1.3	Overall Summary of Adverse Events	All Treated	Yes
	14.3.1.4	Dose Limiting Toxicities by Preferred Term	DLT Evaluable	Yes
	14.3.1.5	All Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade	All Treated	Yes
	14.3.1.5.2	All Adverse Events by System Organ Class and Preferred Term	All Treated	Yes
	14.3.1.5.3	Non-Serious Adverse Events (>=5%) by System Organ Class and Preferred Term	All Treated	Yes
	14.3.1.6	SL-172154-Related Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade	All Treated	Yes
	14.3.1.7	PLD-Related Adverse Events by System Organ Class, Preferred Term and Maximum Toxicity Grade	All Treated	Yes
	14.3.1.8	All Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.9	Serious Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.10	SL-172154-Related Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.11	PLD-Related Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.12	SL-172154-Related Serious Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.13	PLD-Related Serious Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.14	Maximum Toxicity Grade 3 or 4 Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.14.2	Toxicity Grade 3 and Above Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.15.1	SL-172154-Related Grade 3 or 4 Adverse Events by Preferred Term	All Treated	Yes
	14.3.1.15.2	PLD-Related Serious Grade 3 or 4 Events by Preferred Term	All Treated	Yes
	14.3.1.16.1	Adverse Events Leading to SL-172154 Infusion Interrupted by Preferred Term	All Treated	Yes

ICH Heading	Table Number	Table Description	Analysis Population	aCSR
	14.3.1.16.2	Adverse Events Leading to PLD Infusion Interrupted by Preferred Term	All Treated	Yes
	14.3.1.17.1	Adverse Events Leading to SL-172154 Dose Reduced by Preferred Term	All Treated	Yes
	14.3.1.17.2	Adverse Events Leading to PLD Dose Reduced by Preferred Term	All Treated	Yes
	14.3.1.18.1	Adverse Events Leading to SL-172154 Dose Not Given or Delayed by Preferred Term	All Treated	Yes
	14.3.1.18.2	Adverse Events Leading to PLD Dose Not Given or Delayed by Preferred Term	All Treated	Yes
	14.3.1.19.1	Adverse Events leading to SL-172154 Drug Withdrawn by Preferred Term	All Treated	Yes
	14.3.1.19.2	Adverse Events leading to PLD Drug Withdrawn by Preferred Term	All Treated	Yes
	14.3.1.20.1	Summary of SL-172154-Related Infusion Related Reaction at Subject Level	All Treated	No
	14.3.1.20.2	Summary of Symptoms of SL-172154-Related Infusion Related Reaction at Subject Level	All Treated	Yes
	14.3.1.20.3	Summary of Symptoms of SL-172154-Related Infusion Related Reaction at Event Level	All Treated	Yes
	14.3.1.21.1	Summary of SL-172154-Related Infusion Related Reaction at Event Level	All Treated	Yes
	14.3.1.22.1	Summary of SL-172154-Related Infusion Related Reaction by Dosing Visit	All Treated	No
	14.3.1.23	Deaths	All Treated	Yes
	14.3.1.24b	MIRV-Related Grade 3 or 4 Ocular Toxicity Treatment-Emergent Adverse Events by Preferred Term	All Treated	Yes
14.3.5		**Laboratory**		
	14.3.5.1	Hematology – Maximum CTCAE Grade Shift from Baseline	All Treated	No
	14.3.5.2	Chemistry – Maximum CTCAE Grade Shift from Baseline	All Treated	No
	14.3.5.2.2	Liver Function Tests – Maximum CTCAE Grade Shift from Baseline	All Treated	Yes
	14.3.5.3	Coagulation – Maximum CTCAE Grade Shift from Baseline	All Treated	No
	14.3.5.4	Laboratory Tests without CTCAE - Maximum Shift from Baseline with Respect to Normal Range	All Treated	No
	14.3.5.5	Post-Baseline Potential Serious Hepatoxicity	All Treated	Yes
14.3.6		**Other Safety Data**		
	14.3.6.1	ECOG Performance Status – Maximum Shift from Baseline	All Treated	Yes
14.3.7		**PK Data**		
	14.3.7.1	SL-172154 Serum Concentration	SL-172154 PK	Yes

ICH Heading	Table Number	Table Description	Analysis Population	aCSR
	14.3.7.2	SL-172154 PK Parameters	SL-172154 PK	Yes
	14.3.7.3b	MIRV Serum Concentration	MIRV PK	Yes
14.3.8		**ADA Data**		
	14.3.8.1	Treatment Induced SL-172154 Anti-Drug Antibodies	SL-172154 Immunogenicity	Yes
	14.3.8.2	SL-172154 Onset and Duration of Treatment Induced SL-172154 Anti-Drug Antibodies	SL-172154 Immunogenicity	Yes
	14.3.8.3b	Treatment Induced MIRV Anti-Drug Antibodies	MIRV Immunogenicity	Yes

13.2 List of Figures

ICH Heading	Figure Number	Figure Description	Analysis Population	aCSR
14.2	14.2.1	Horizontal Bar Plot of Study Drug Treatment Duration by Response	All Treated	Yes
	14.2.2	Waterfall Plot of Target Lesions Maximum Reduction in Sum of Lesion Diameters	All Treated	Yes
	14.2.3	Plot of Target Lesions Percent Change from Baseline Sum of Lesion Diameters Over Time	All Treated	Yes
	14.2.4	Kaplan-Meier Plot of Time to Response Based on RECIST 1.1	Response Evaluable	No
	14.2.5	Kaplan-Meier Plot of Duration of Response Based on RECIST 1.1	Response Evaluable	No
	14.2.6	Kaplan-Meier Plot of Progression-Free Survival Based on RECIS T1.1	All Treated	Yes
	14.2.7	Kaplan-Meier Plot of Overall Survival	All Treated	Yes
	14.2.8	Plot of Percent Change from Baseline for CA-125 Over Time	All Treated	No
14.3	14.3.5.1	Plot of Liver Enzyme Value Over Time for Subjects Who Meet Potential Hy's Law Criterion	All Treated	No

13.3 List of Data Listings (all listings will be delivered for aCSR)

ICH Heading	Listing Number	Listing Description	Analysis Population
16.2		**SUBJECT DATA LISTINGS**	

ICH Heading	Listing Number	Listing Description	Analysis Population
16.2.1		**Discontinued subjects**	
	16.2.1.1	Study Population and Subject Disposition	All Enrolled
	16.2.1.2	Study Treatment Discontinuation	All Treated
	16.2.1.3	Informed Consent and Protocol Amendment Re-Consent	All Treated
16.2.2		**Protocol deviations**	
	16.2.2.1	Protocol Deviations	All Treated
	16.2.2.2	Major Protocol Deviations	All Treated
	16.2.2.3	Inclusion and Exclusion Criteria Deviations	All Treated
16.2.4		**Demographics**	
	16.2.4.1	Demographic and Baseline Characteristics	All Treated
	16.2.4.2	Medical and Surgical History	All Treated
	16.2.4.3	Study Cancer History	All Treated
	16.2.4.4	Prior Anti-Cancer Systemic Treatment	All Treated
	16.2.4.5	Prior Radiotherapy	All Treated
	16.2.4.6	Prior Surgery Treatment	All Treated
	16.2.4.7	Premedications	All Treated
	16.2.4.8	Prior and Concomitant Medications	All Treated
	16.2.4.9	Concomitant Procedures	All Treated
	16.2.4.10	Post-Treatment Anti-Cancer Treatment	All Treated
	16.2.4.11	Demographic and Baseline Characteristics for Screen Failure Subjects	Screen Failure
16.2.5		**Study Drug Exposure, PK, and ADA**	
	16.2.5.1.1	SL-172154 Administration (I)	All Treated
	16.2.5.1.2	SL-172154 Administration (II)	All Treated
	16.2.5.1.3	SL-172154 Administration Overdose	All Treated
	16.2.5.2	PLD Administration	All Treated
	16.2.5.3	SL-172154 Serum Concentration-Time Data	SL-172154 PK Population
	16.2.5.4	SL-172154 PK Parameters	SL-172154 PK Population
	16.2.5.5b	MIRV Serum Concentration-Time Data	MIRV PK Population
	16.2.5.6	SL-172154 Anti-Drug Antibodies	SL-172154 Immunogenicity Population
	16.2.5.7b	MIRV Anti-Drug Antibodies	MIRV Immunogenicity Population

ICH Heading	Listing Number	Listing Description	Analysis Population
16.2.6		**Individual efficacy response data**	
	16.2.6.1	Tumor Assessment: Target Lesions	All Treated
	16.2.6.2	Tumor Assessment: Non-Target Lesions	All Treated
	16.2.6.3	Tumor Assessment: New Lesions	All Treated
	16.2.6.4	Tumor Responses Based on RECIST 1.1	All Treated
	16.2.6.5	Time to Response and Duration of Response Based on RECIST 1.1	All Treated
	16.2.6.6	Progression-Free Survival Based on RECIST 1.1	All Treated
	16.2.6.7	Overall Survival	All Treated
	16.2.6.8	CA-125 Values	All Treated
16.2.7		**Adverse Event Listings**	
	16.2.7.1	All Adverse Events	All Treated
	16.2.7.2	Dose Limiting Toxicities	DLT evaluable
	16.2.7.3	SL-172154-Related Adverse Events	All Treated
	16.2.7.4	PLD-Related Adverse Events	All Treated
	16.2.7.5	Adverse Events with Toxicity Grade 3 or 4	All Treated
	16.2.7.6	Fatal Adverse Event	All Treated
	16.2.7.7	Serious Adverse Events	All Treated
	16.2.7.8	SL-172154 Infusion Related Reaction Adverse Events	All Treated
	16.2.7.9.1	Adverse Events Leading to SL-172154 Infusion Interrupted	All Treated
	16.2.7.9.2	Adverse Events Leading to PLD Infusion Interrupted	All Treated
	16.2.7.10.1	Adverse Events Leading to SL-172154 Dose Reduced	All Treated
	16.2.7.10.2	Adverse Events Leading to PLD Dose Reduced	All Treated
	16.2.7.11.1	Adverse Events Leading to SL-172154 Dose Not Given or Delayed	All Treated
	16.2.7.11.2	Adverse Events Leading to PLD Dose Not Given or Delayed	All Treated
	16.2.7.12.1	Adverse Events Leading to SL-172154 Drug Withdrawn	All Treated
	16.2.7.12.2	Adverse Events Leading to PLD Drug Withdrawn	All Treated
	16.2.7.13	SL-172154 Infusion Related Reaction Signs and Symptoms	All Treated
	16.2.7.14	Death	All Treated
	16.2.7.15b	All MIRV-Related Grade 3 or 4 Ocular Toxicity Adverse Events	All Treated

ICH Heading	Listing Number	Listing Description	Analysis Population
	16.2.7.16	All Adverse Events for Screen Failure Population	Screen Failure
16.2.8		**Individual Laboratory Measurements**	
	16.2.8.1	Hematology	All Treated
	16.2.8.2	Clinical Chemistry (including ferritin and haptoglobin)	All Treated
	16.2.8.3	Coagulation and Thyroid Function	All Treated
16.2.9		**Listing of other safety data**	
	16.2.9.1	Vital Signs and Pulse Oximetry	All Treated
	16.2.9.2	ECOG Performance Status	All Treated
	16.2.9.3	Cardiac Assessments: ECG	All Treated
	16.2.9.4	Cardiac Assessments: ECHO	All Treated
	16.2.9.5	Blood Phenotyping and Direct Antiglobulin Test	All Treated
	16.2.9.6	Transfusions	All Treated
	16.2.9.7b	Ocular Symptom Assessment [Regimen (SL-172154 + MIRV) only]	All Treated