STATISTICAL ANALYSIS PLAN

A PHASE IIA DOSE OPTIMISATION STUDY OF ASLAN003 IN ACUTE MYELOID LEUKEMIA

Date: 18 October 2019
Version: 2.0 (final)
Protocol Version: 3.0 dated 31 May 2018

SAP Approvals:

[redacted]

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Date

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Associate Director, Clinical Operations
ASLAN Pharmaceuticals

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LIST OF ABBREVIATIONS

AE	Adverse Event
AML	Acute Myeloid Leukemia
AUC_{tau}	Area Under the Plasma Concentration-Time Curve Over the Dosing Interval
$AUC_{tau\ ss}$	Area Under the Plasma Concentration-Time Curve Over the Dosing Interval at Steady State
BID	Twice a day
CBR	Clinical Benefit Rate
CI	confidence interval
CL/F	Apparent Total Clearance of the Drug from Plasma After Oral Administration
C_{max}	Maximum Observed Plasma Concentration
$C_{max\ ss}$	Maximum Observed Plasma Concentration at Steady State
CR	Complete Remission
CRF	Case Report Form
CRi	Complete Remission with Incomplete Hematologic Recovery
CSR	Clinical Study Report
C_{trough}	Trough plasma concentration
ECG	Electrocardiogram
EDC	Electronic Data Capture
EFR	Evaluable for Response
FAS	Full Analysis Set
GCP	Good Clinical Practice
IWG	International Working Group
LLN	Lower Limit of Normal
LLQ	Lower Limit of Quantification
MedDRA	Medical Dictionary for Regulatory Activities
MR	Metabolic Ratio
OCRR	Overall Complete Remission Rate
PID	Percentage of Intended Dose
PK	Pharmacokinetic
PR	Partial Remission
PT	Preferred Term
QD	Once Daily

Rac AUC	Accumulation Ratio for AUC
Rac C_{max}	Accumulation Ratio for C_{max}
RDI	Relative Dose Intensity
RFS	Relapse-Free Survival
SAE	Serious Adverse Event
SC	Steering Committee
SOC	System Organ Class
SOP	Standard Operating Procedure
std	Standard Deviation
$t_{1/2}$	Terminal Half-Life
$t_{1/2\ eff}$	Effective Elimination Half-Life at Steady State
TEAE	Treatment Emergent Adverse Event
t_{max}	Time Corresponding to Occurrence of Maximum Observed Plasma Concentration
$t_{max\ ss}$	Time Corresponding to Occurrence of Maximum Observed Plasma Concentration at Steady State
ULN	Upper Limit of Normal
V_{ss}/F	Apparent Volume of Distribution at Steady State after Oral Administration
WHO	World Health Organization

1. STUDY OBJECTIVES

1.1 Primary Objectives

The primary objectives of the study are:

Part 1:

- To determine the optimum dose of ASLAN003 monotherapy based on the efficacy, safety and tolerability profile in Acute Myeloid Leukemia (AML) patients who are ineligible for standard therapy.

Part 2:

- To provide a preliminary estimate of the efficacy of ASLAN003 at the optimum dose selected from Part 1.

1.2 Secondary Objectives

Part 1

- To evaluate the pharmacokinetics (PKs) of ASLAN003 and its metabolite LAS186558 in patients with AML.

Part 2

- To further assess the safety and tolerability data of ASLAN003 at the optimum dose selected from Part 1.

1.3 Exploratory Objectives

Part 1:

- To examine the myeloid differentiation effects of ASLAN003 using assays including but not limited to an *ex vivo* flow cytometry assay.

- To explore possible relationships between molecular abnormalities and measures of clinical response in patients with AML.

2. Study Design

2.1 Overall Study Design

This study is designed as a multicenter, single arm, non-randomized phase IIA study to evaluate ASLAN003 as a monotherapy in patients with AML.

AML patients who are ineligible for standard treatment including, but not limited to the following conditions, will be enrolled in the study:

- Newly diagnosed patients who are ineligible for standard therapy i.e., standard dose induction chemotherapy and reduced dose chemotherapy
- Patients with relapse from prior remission
- Patients with failed response to prior therapy including chemotherapy, hypomethylating agents, and bone marrow transplantation.

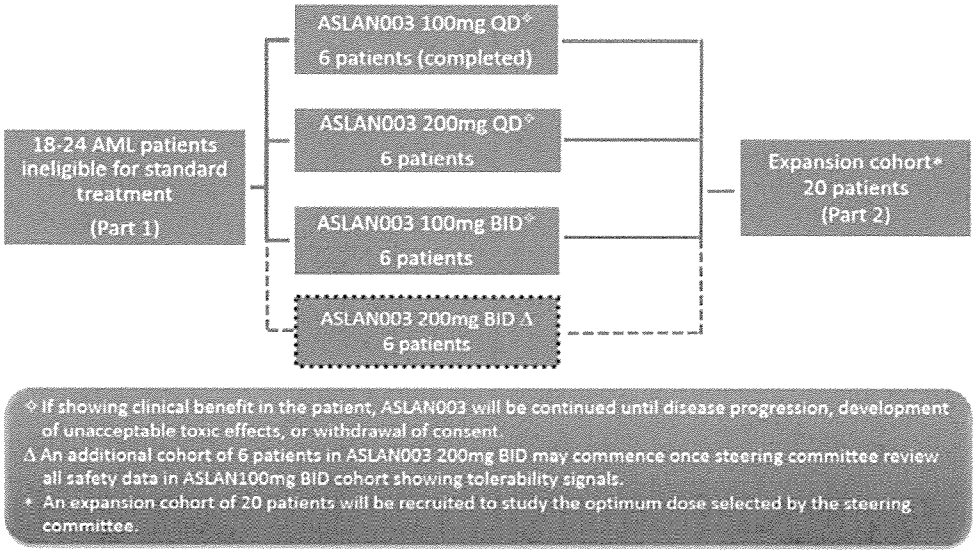
Part 1:

Up to a total of 24 patients will be enrolled into Part 1 of this study – 6 patients in each dose cohort (ASLAN003 100 mg once daily (QD), 200 mg QD, 100 mg twice daily (BID) and 200 mg BID, respectively). Once 6 patients have been enrolled into the cohort of 100 mg QD, recruitment will be started in the cohort of 200 mg QD. The same rule applies to the 100 mg BID and 200 mg BID cohorts. A steering committee (SC) meeting will be set up and meet to review all safety data. Details of the SC outcome will be specified in the SC charter.

Part 2:

An expansion cohort of 20 patients will be recruited to study the optimum dose selected by the SC. The optimum dose will be selected from at least one cohort showing tolerable safety profile and clinical benefit in disease presentation. Details will be specified in the SC charter.

Figure 1: Study Design



2.2 Methods of Assigning Patients to Treatment Groups

At Screening, each patient will receive a unique Screening number from electronic data capture system (EDC). The number will start with "S" and be followed by 4 digits starting with S0001 for Part 1 and S2001 for Part 2.

Part 1:

Following confirmation of eligibility, all patients will be sequentially assigned to the dose levels after being screened for eligibility and providing consent. At administration of the first dose of study drug, patients will be assigned with a 4-digit patient number in the order in which they are enrolled in the study starting from 0001. Enrolled patients who drop out of the study before receiving the study drug will retain their Screening number.

Part 2:

Following confirmation of eligibility and providing consent, all patients will be sequentially assigned to the dose level selected from Part 1. At administration of the first dose of study drug, patients will be assigned with a 4-digit patient number in the order in which they are enrolled in the study starting from 2001. Enrolled patients who drop out of the study before receiving the study drug will retain their Screening number.

2.2.1 Procedures for Randomization

Not applicable.

3. ENDPOINTS

3.1 Efficacy Endpoints

Efficacy will be evaluated in accordance with the IWG Criteria[16] for AML (Cheson, 2003). Definitions of the primary and secondary efficacy variables are described in Sections 3.1.1 to 3.1.6. In addition, the following principles will be applied:

For the evaluation of OCRR, TTR and TTCR, if bone marrow and peripheral blood assessments are both performed, the assessment date used will be the date of the bone marrow assessment. If only blood assessments are performed, the assessment date will be the date of the blood assessment.

For RFS, the date of relapse will be the assessment date of the first component that fulfills the criteria for relapse (Section 3.1.2). For example, if both the peripheral blood and bone marrow were indicative of relapse, but the blood assessment was performed first, then the date of relapse would be the date of the peripheral blood assessment. Similarly, if relapse was first detected due to the development of cytologically proven extramedullary disease, the date of detection for the extramedullary disease would be the date of relapse, even if the bone marrow and peripheral blood assessments were not performed until a later date.

3.1.1 Overall Complete Remission Rate

Overall complete remission rate (OCRR) is a co-primary endpoint in Part 1 and the primary endpoint in Part 2. It will be derived programmatically from the BM aspiration and peripheral blood results based on the IWG Criteria[16] for AML (Cheson, 2003) as described below.

For patients without sufficient archival BM sample, BM aspiration will be performed during Screening. All patients will receive bone marrow aspiration for efficacy assessment on Day 1 of Cycle 2, 3, 4, 5 and will be repeated every 3 cycles after Cycle 5. Patients who've already achieved CR could omit the bone marrow aspiration at subsequent visits if there is a normal complete blood count with differential of the peripheral blood. Investigator may perform more frequent exam if required based on clinical judgment.

BM aspiration smears will be processed locally.

Following treatment discontinuation, patients who have achieved a CR or CRi, will continue to be followed up for every 12 weeks to assess the relapse free survival. For patients who have not achieved a CR or CRi during treatment, no further follow-up is required following treatment discontinuation.

These criteria categorize the visit response into the following response classifications:

- *CR with incomplete recovery of neutrophils and platelets (CRi):*

  Achievement of CRi requires patients to satisfy all of the following:

  - A disappearance of blasts in the peripheral blood.
  - A decrease in BM blasts to <5% total BM nucleated cells demonstrated in BM aspirate.
  - Absence of Auer rods
  - No persistent extramedullary leukaemia

- *Complete Remission:*

  Patient satisfies all of the criteria above and in addition has:

  - Recovery of Neutrophils to ≥1.0 x 10^9/L and Platelets to ≥ 100 x 10^9/L
  - Transfusion-independence

- *Partial Remission:*

  A PR is defined as recovery of neutrophils to to ≥1.0 x 10^9/L and Platelets to ≥ 100 x 10^9/L and either:

  - If the pre-treatment bone marrow blast percentage was 50% to 100%, the percentage of blast must decrease to a value between 5% and 25%
  - If the pre-treatment BM blast percentage was 20% to less than 49%, they must decrease by at least half to a value of more than 5%

- A reduction in BM blast cells to <5% but with persistence of Auer rods.

- *Treatment failure:*

  Failure to meet the criteria for CR, CRi or PR after 4 cycles of treatment will result in a best response of treatment failure.

For the evaluation of OCRR, a binary variable will be created to indicate complete response status of each patient (complete responder or non-responder) defined as follows:

A patient will be classified as a complete responder if either of the following are achieved during the study and prior to starting subsequent AML treatment:

- Achievement of CR
- Achievement of CRi

Patients who do not satisfy the OCCR criteria outlined above (including patients with PR, treatment failure and any patients without evaluable post-treatment assessments) will be classified as non-responders for the assessment of OCRR.

Best response status will also be assessed. A patient's best response is defined as the best AML visit response observed, ranked in the following order:

CR > CRi > PR > Treatment failure.

OCRR is defined as the number (%) of patients with a best response of complete remission (CR) or complete remission with incomplete hematologic recovery (CRi), defined in accordance with the International Working Group (IWG) Response Criteria in AML.

All efficacy data collected, whether based on scheduled or unscheduled visits, will be included in the assessment of OCRR, with the exception of data collected following the start of subsequent AML therapy, which will not be included in the assessment of OCRR.

In all study parts, the primary analysis of OCRR will be assessed based on the evaluable for response (EFR) set with a sensitivity analysis based on the full analysis set (FAS).

3.1.2 Relapse-Free Survival

Relapse-free survival (RFS) is a secondary endpoint in Parts 1 and 2 and is defined for the sub-group of patients classified as responders for OCRR.

RFS is defined as the time the criteria for remission (CR or CRi) are first met until there is evidence of patient relapse, regardless of whether the patient is still taking study drug or has started other anti-AML treatment prior to relapse. (Note, the onset of the CR/CRi must have been before the start of subsequent anti-AML treatment to be classified as a responder for OCRR). Relapse is defined as:

- The reappearance of leukemic blasts in the peripheral blood or >5% blasts in the bone marrow not attributable to any other cause
- The appearance of new dysplastic changes
- The reappearance of or development of cytologically proven extramedullary disease
- The reappearance of a cytogenetic or molecular abnormality
- Death by any cause

In the event that the blood and bone marrow response assessments for a visit are performed on different dates, RFS will be calculated using the earliest date at which a relapse was detected. For example, if both the peripheral blood and bone marrow were assessed and both found to be indicative of relapse, RFS will use the earlier of the two assessment dates. However, if both were assessed, but only the marrow was found to be indicative of relapse, the date of the marrow assessment would be used as the date of relapse.

As described above, patients who die without evidence of relapse will be considered to have relapsed at the date of death, provided that the death does not occur following two or more missed assessments (up to 56 days following previous assessment). If the death occurs more than 56 days following the previous response assessment, the patient will be censored for RFS at the date of the last efficacy assessment in which they were alive and relapse-free.

Similarly, patients who are determined to have met the criteria for relapse more than 56 days after the last efficacy assessment will also be censored for RFS at the date of the last efficacy assessment in which they relapse-free.

For the purpose of evaluating whether RFS should be censored due to missed visits, a patient will be considered to have missed two assessments if neither the peripheral blood or bone marrow have been assessed for >56 days.

In all study parts, the primary analysis of RFS will be assessed based on the EFR set with a sensitivity analysis based on the FAS.

3.1.3 Clinical Benefit Rate

Clinical benefit rate (CBR) is a secondary endpoint in Parts 1 and 2.

CBR is defined as the number (%) of patients with an AML IWG best response of CR, CRi or partial remission (PR). Data obtained up until progression, or last evaluable assessment in the absence of progression, will be included in the assessment of CBR. This will be irrespective of whether or not patients discontinued treatment or received a subsequent therapy prior to progression.

All efficacy data collected, whether based on scheduled or unscheduled visits, will be included in the assessment of CBR, with the exception of data collected following the start of subsequent AML therapy, which will not be included in the assessment of OCRR.

In all study parts, the primary analysis of CBR will be assessed based on the evaluable for response (EFR) set with a sensitivity analysis based on the full analysis set (FAS).

3.1.4 BM Blasts

The percentage change from baseline in BM blasts at Day 29 is a secondary endpoint in all study parts and will be evaluated for the EFR set (primary) and FAS (sensitivity).

3.1.5 Time to Response

Time to response (TTR) will be derived as the time from first dose to first response (CR, CRi or PR). As described in Section 3.1, if the peripheral blood and bone marrow assessments for a visit are performed on different dates, TTR will be calculated using the date of the bone marrow assessments.

3.1.6 Time to CR

Time to CR (TTCR) will be derived as the time from first dose to first CR or CRi. As described in Section 3.1, if the peripheral blood and bone marrow assessments for a visit are performed on different dates, TTCR will be calculated using the date of the bone marrow assessments.

3.2 Safety and Tolerability

3.2.1 Safety Endpoints

The assessment of safety and tolerability is a co-primary objective of Part 1, and a secondary endpoint of Part 2. In both study parts, the safety and tolerability of ASLAN003, in AML patients, will be assessed using the following endpoints:

- Adverse Events (AEs)
- Physical Examination
- Vital Signs (blood pressure [systolic and diastolic], heart rate, respiration rate, and body temperature)
- Laboratory assessments (clinical chemistry, hematology, coagulation and urinalysis)
- 12-lead Electrocardiogram (ECG) (P and QRS duration, RR, PQ, QT and QTc intervals using Bazett's and Fridericia's formulae)
- Treatment exposure and dose intensity

In addition, tolerability will be further explored by assessment of dose reductions, interruptions and modifications (see Section 3.2.2).

Adverse events will be coded by System Organ Class (SOC) and Preferred Term (PT) using the Medical Dictionary for Regulatory Activities (MedDRA) for concomitant diseases and AEs and World Health Organization (WHO) Drug for medications. All AEs will be evaluated for severity according to NCI-CTCAE version 4.03

Baseline will be defined as the last assessment prior to the start of study treatment. If multiple assessments are performed at the same pre-treatment timepoint, for example triplicate ECG assessments, the mean of the values will be used as the baseline reading.

Creatinine clearance will be derived as:

$$eC_{Cr} = \frac{(140 - Age) \times Mass\ (in\ kilograms) \times Constant}{Serum\ Creatinine\ (in\ \mu mol/L)}$$

where constant=1.23 for males and 1.04 for females, and will be categorized as 30-<60 ml/min, 60-<90 ml/min and =>90 ml/min. Creatinine clearance will be included in summaries of the clinical chemistry data.

QTcB will be derived as:

$$QTcB = \frac{QT}{\sqrt{RR}}$$

QTcF will be derived as:

$$QTcF = \frac{QT}{\sqrt[3]{RR}}$$

For derivation of post-baseline visit values, taking account of possible visit windows, see Section 3.2.1.1.

3.2.1.1 General Considerations for Safety Assessments

Missing safety data will not be imputed. However, safety assessment values of the form of "< x" (i.e., below the lower limit of quantification) or > x (i.e., above the upper limit of quantification) will be imputed as "x" in the calculation of summary statistics but displayed as "< x" or "> x" in the listings.

In order to produce data summaries by visit, visit time windows are required, and will be derived using the following conventions:

- The time windows will be exhaustive so that data recorded at any time point has the potential to be summarized. Inclusion within the time window should be based on the actual date and not the intended date of the visit.
- All unscheduled visit data should have the potential to be included in the summaries.
- The window for the visits following baseline will be constructed in such a way that the upper limit of the interval falls half way between the two visits (the lower limit of the first post-baseline visit will be Day 1). If an even number of days exists between two consecutive visits then the upper limit will be taken as the midpoint value minus 1 day.

Furthermore, the following principles will apply to the presentation of safety data:

- For summaries showing the maximum or minimum values, the maximum/minimum value recorded on treatment will be used (regardless of where it falls in an interval).

- For summaries of the ECG data, the mean value of the triplicate readings will be included in the summaries.

- Listings should display all values contributing to a time point for a patient.

- For visit based summaries:

  - If there is more than one value per patient within a time window then the closest value should be summarized, or the earlier in the event the values are equidistant from the nominal visit date. The listings should highlight the value for that patient that went into the summary table, wherever feasible.

  - To prevent very large tables or plots being produced that contain many cells with sparse data, for each treatment group, visit data should only be summarized if the number of observations is greater than 1/3 of patients dosed.

- For summaries at a patient level, all values should be included, regardless of whether they appear in a corresponding visit based summary, when deriving a patient level statistic such as a maximum.

- Baseline will be defined as the last non-missing measurement prior to dosing with study treatment. For laboratory data, any assessments made on day 1 will be considered pre-dose unless explicitly indicated otherwise. Where safety data are summarized over time, study day will be calculated in relation to date of first treatment (which will be termed day 1).

- Study Day will be calculated from the reference start date, and will be used to show start/ stop day of assessments and events.

  Reference start date is defined as the day of the first dose of study drug, (Day 1 is the day of the first dose of study drug), and will appear in every listing except medical history where an assessment date or event date appears.

  - If the date of the event is on or after the reference date then:

    - Study Day = (date of event – reference date) + 1

  - If the date of the event is prior to the reference date then:

    - Study Day = (date of event – reference date)

3.2.2 Treatment Exposure and Dose Intensity

To understand the general tolerability of ASLAN003, and the impact of interruptions and dose reductions, summaries of treatment exposure and dose intensity will be produced. For the purpose of this study, the term *exposure* relates to the number of days of treatment received (regardless of dose reductions), whereas *dose intensity*

relates to the proportion of intended dose received, taking account of interruptions and reductions.

For all patients, exposure to ASLAN003 will be calculated. To assess treatment exposure, the following will be calculated:

Intended Exposure to study treatment (days)

- Intended Exposure = last dose date – first dose date + 1

Actual Exposure to study treatment (days)

- Actual exposure = Intended exposure – total duration of dose interruptions

where the intended exposure is calculated as defined above, and dose interruptions include all days in which the patient receive no study medication, regardless of whether the interruption was intentional, or whether the patient forgot to take a dose.

Two measures of dose intensity will be calculated:

1. Percentage of Intended Dose (PID) – defined as the percentage of the actual dose delivered relative to the intended dose, *until treatment failure (for non-responders for OCRR) or relapse (for responders for OCRR)*.
2. Relative dose intensity (RDI) – defined as the percentage of the *actual* dose intensity delivered, relative to the *intended* dose intensity, *until the earlier of treatment discontinuation, treatment failure (for non-responders for OCRR) or relapse (for responders for OCRR)* (as defined by IWG and based on the site assessments).

The key difference between the two measures outlined above is that the former is based on the intended treatment plan of treatment until relapse (if responding) else for 4 cycles when treatment failure would be declared, and the latter takes account of treatment discontinuations prior to relapse/treatment failure (e.g. discontinuation due to toxicity), and calculates the dose intensity during the actual dosing period.

For the purpose of calculating both measures of dose intensity, the intended dose will be evaluated taking account of the patient's response status for OCRR. I.e. A responder will be a patient classified as having a best response of CR or CRi (Section 3.1.1) and a non-responder will be all other patients (including those with a best response of PR). Therefore:

- For patients with a best response of CR or CRi, in the event that the investigator does not discontinue study treatment relapse, any dosing information beyond treatment relapse will not be taken into account when calculating either measure of dose intensity.
- For patients with a best response of PR, any dosing data collected after the first 4 cycles will not be taken into account when assessing dose intensity
- For patients with a best response of treatment failure, in the event that the investigator does not discontinue study treatment after the protocol-defined window for treatment failure (4 cycles), any dosing information beyond treatment failure (the end of 4 cycles) will not be taken into account when calculating either measure of dose intensity.

Definitions of treatment failure and relapse can be found in Sections 3.1.1 and 3.1.2.

PID and RDI will be defined as follows:

PID = 100% * d/D, where d is the actual cumulative dose delivered up to treatment failure/relapse (or a censoring event) and D is the intended cumulative dose up to progression (or a censoring event). D is the total dose that would be delivered, if there were no modification to dose or schedule.

RDI = 100% * d/D, where d is the actual cumulative dose delivered up to the earlier of progression (or a censoring event) or the actual last day of dosing and D is the intended cumulative dose up to the earlier of progression (or a censoring event) or the actual last day of dosing.

3.3 Pharmacokinetic Endpoints

Part 1

The PK of ASLAN003 and LAS186558 (active metabolite) will be determined at selected time points. The following PK parameters will be evaluated where possible for ASLAN003:

Cycle 1 Day 1 and Day 8:

- Maximum observed plasma concentration (C_{max})
- C_{max} at steady state ($C_{max\ ss}$)
- Trough plasma concentration (C_{trough})
- Time corresponding to occurrence of C_{max} (t_{max})
- Time corresponding to occurrence of $C_{max\ ss}$ ($t_{max\ ss}$)
- Area Under the Curve from 0 to the time of the last quantifiable concentration (AUC_{last})
- AUC_{last} at steady state ($AUC_{last\ ss}$)
- Area under the plasma concentration-time curve over the dosing interval (AUC_{tau})
- AUC_{tau} at steady state ($AUC_{tau\ ss}$)
- Terminal half-life ($t_{1/2}$)
- Effective elimination half-life at steady state ($t_{1/2\ eff}$)
- Area Under the Curve from 0 to infinity (AUC_{inf})
- Apparent total clearance of the drug from plasma after oral administration (CL/F)
- Apparent volume of distribution after oral administration (V_z/F)
- Accumulation ratio for AUC ($RacAUC_{tau}$ or $RacAUC_{last}$) (Day 8/Day 1)
- Accumulation ratio for C_{max} ($RacC_{max}$) (Day 8/Day 1)

The following PK parameters will be evaluated where possible for LAS186558 on Cycle 1 Day 1 and Day 8: C_{max}, $C_{max\ ss}$, C_{trough}, t_{max}, $t_{max\ ss}$, AUC_{last}, $AUC_{last\ ss}$, AUC_{tau}, $AUC_{tau\ ss}$, $t_{1/2}$, $t_{1/2\ eff}$, RacAUC, $RacC_{max}$, metabolic ratio (MR) for C_{max} (MRC_{max}) and AUC (MRAUC).

Dose-normalized C_{max}, $C_{max\ ss}$, AUC_{last}, $AUC_{last\ ss}$, and $AUC_{tau\ ss}$ parameters will be also calculated for ASLAN003 and its metabolite LAS186558.

3.4 Exploratory Endpoints

Exploratory endpoints are not covered in the scope of this analysis plan.

4. Analysis Populations

4.1 Safety Population

The safety population includes all patients who received at least 1 dose of study medication in the study and will be the primary analysis set for the assessment of safety and tolerability in the study.

For the purpose of data summaries, patients will be included in the Safety Population according to the dose level initially received, regardless of any subsequent dose adjustments.

4.2 Full Analysis Set

The FAS is based on the *intention-to-treat* principle and includes all treated patients analyzed in accordance with the intended dose group, regardless of the dose actually received. For Part 2 only, the FAS will be used to assess the sensitivity of the primary efficacy analyses to exclusions from the EFR set.

4.3 Evaluable for Response Set

The EFR set is defined as a subset of the FAS, excluding any patients with major protocol deviations. Deviations that would end to exclusion from the FAS are:

- Patient does not have AML as defined by the 2016 revision to the WHO classification of myeloid neoplasms and acute leukemia (failure of inclusion criteria 3)
- Patient is eligible for induction therapy (failure of inclusion criteria 5)
- Patients who are diagnosed with *de novo* myeloid sarcoma without bone marrow involvement (satisfying exclusion criteria 1)
- Patients who are diagnosed with acute promyelocytic leukemia with the *PML-RARA* (satisfying exclusion criteria 2)
- Patients who received any other standard or investigational treatment for their leukemia within the last 7 days before starting the first dose of study drug, with the exception of leukapheresis and hydroxyurea (satisfying exclusion criteria 3)

The EFR set will be the primary analysis set used for the evaluation of all efficacy objectives.

4.4 PK Analysis Set

The PK population contains all patients who have received one complete dose of ASLAN003 and have at least one measured concentration at a scheduled post-dose time point without any major protocol deviations or events that affect the PK concentrations. Patients in this population will be used for all PK analyses.

All PK data will be analyzed according to treatment received.

This population will comprise all data from patients who receive study treatment as per protocol (e.g. 100 mg QD, 200 mg QD, 100 mg BID or 200 mg BID) and did not violate or deviate from the protocol and planned dosing regimen in ways that would significantly affect the PK analyses (for example skipping doses, or taking reduced doses or taking concomitant medications with the potential to cause a drug-drug interaction) during the PK sampling period. Patients who did deviate from the planned dosing regimen may still provide some data for inclusion in the PK set, if they have at least one usable PK profile. The population, and decisions regarding which profiles are usable, will be defined by the Study Team Physician, Pharmacokineticist and Statistician prior to any analyses being performed.

4.5 Summary of Analysis Populations

A summary of the study outcome variables, and associated analysis sets is provided in Table 1.

Table 1 Summary of Outcome Variables and Analysis Populations

Outcome Variable	Analysis Population (Sensitivity Analysis Population)
Efficacy Data	
OCRR, RFS, CBR, TTR, TTCR, BM blasts	EFR (FAS for Part 2 only)
Demography	FAS
Pharmacokinetics	
PK	PK
Safety	
Exposure	Safety
Adverse Events	Safety
Laboratory measurements	Safety
Vital Signs	Safety
ECG	Safety
Physical Examination	Safety

5. Protocol Deviations

5.1 Major Deviations

Major protocol deviations are defined as those that would lead to exclusion from the EFR set (see Section 4).

The following will be classified as major deviations:

- Patient does not have AML as defined by the 2016 revision to the WHO classification of myeloid neoplasms and acute leukemia (failure of inclusion criteria 3)
- Patient is eligible for induction therapy (failure of inclusion criteria 5)
- Patients who are diagnosed with *de novo* myeloid sarcoma without bone marrow involvement (satisfying exclusion criteria 1)
- Patients who are diagnosed with acute promyelocytic leukemia with the *PML-RARA* (satisfying exclusion criteria 2)
- Patients who received any other standard or investigational treatment for their leukemia within the last 7 days prior to starting the first dose of study drug, with the exception of leukapheresis and hydroxyurea (satisfying exclusion criteria 3)
- Patients taking concurrent therapies for leukemia at any time during the study, with the exception of hydroxyurea during the first 14 days, which is permitted under the protocol.

For each part of the study, these protocol deviations will be listed and will be summarized by treatment group.

In addition to the programmatic determination of the major deviations, monitoring notes or summaries will be reviewed to determine any important post entry deviations that are not identifiable via programming, and to check that those identified via programming are correctly classified. The final classification will be made prior to database lock. For example, details of disallowed concomitant medication use will be reviewed by a physician and may be deemed major.

Note, failure of an inclusion/exclusion criteria will not automatically be classified as a major deviation.

5.2 Other Important Deviations

In addition to the programmatic determination of the major deviations as described in Section 5.1, the following *important deviations* will be programmatically derived and listed and summarized:

- Failure of any remaining inclusion/exclusion criteria

Errors in dispensing will be summarized and listed as *important deviations*. These include:

- Patients who receive no study treatment whatsoever for a period of more than one week due to errors in dispensing of medication. Note, this is not due to tolerability issues where patients may stop taking drug.
- Patients who at some point receive the incorrect dose of ASLAN003.

In addition, other non-programmable important deviations will be collected on the case report form (CRF), listed and summarized including, but not limited to:

- Patients of child-bearing potential not practicing acceptable methods of birth control from the time they enter the screening period until 3 months after the last cycle of treatment.
- Patients breast feeding at any point between the time they enter the screening period until 3 months after the last cycle of treatment.

Compliance will be assessed by Study Team review of protocol procedures with specific attention paid to missed dosing due to reasons other than AEs. (E,g, patients receiving <75% of intended doses) and will not be assessed programmatically. Any compliance issues considered likely to impact on the interpretation of safety or efficacy will be added to the deviation CRF page.

Finally, monitoring notes or summaries will be reviewed to determine any important post entry deviations that are not identifiable via programming, and to check that those identified via programming are correctly classified. The final classification will be made prior to database lock. For example, details of disallowed concomitant medication use will be reviewed by a physician and if deemed important, may also be included in the listing of important deviations.

All patients who failed any inclusion/exclusion criteria will be listed along with details of the failed criteria. This information will also be summarized in terms of the number (%) of patient failing any of the inclusion/exclusion criteria and will be based on the FAS. Note, failure of an inclusion/exclusion criteria will not automatically be classified as a major deviation.

Other deviations may occur during the trial, which are considered minor and not believed to have any significant impact on the interpretation of the study results. All of these deviations will be recorded by the study monitors but will not be listed or summarized as part of the clinical study report (CSR).

Examples of minor deviations include:

- Visits outside of protocol visit windows
- Incomplete assessments
- Use of concomitant medication related to safety

This list is not exhaustive and other minor deviations may occur.

6. General Statistical Considerations

All statistical analyses will be performed by or under the direct auspices of ASLAN Pharmaceuticals, using SAS® version 9.3 or higher.

Unless specified otherwise, data from Part 1 and Part 2 will be presented separately in the Tables, Figures and Listings.

The following descriptive statistics will be presented in summary tables:

- Continuous variables: number (non-missing cases), mean, median, standard deviation (SD), minimum, and maximum
- Categorical variables: will be summarised by treatment group using frequency tables (frequencies and percentages). Percentages are routinely based on the total category count excluding the missing category if not otherwise mentioned. Missing category with zero count will not be presented
- Time to event endpoints: Will be summarised based on Kaplan Meier estimates

In general, the number of decimal places displayed for each statistic will be determined as follows with a maximum of three decimal places with the exception of the summary of PK results described separately below:

- Mean and median: one more than the number of decimal places allotted in the raw data received from data management
- SD: two more than the number of decimal places allotted in the raw data
- Minimum and maximum: equal to the number of decimal places allotted in the raw data
- Confidence Intervals (CIs) will be presented using the number of decimal places plus one as the parameters (e.g. mean) as appropriate
- P-values greater than or equal to 0.0001, in general, will be presented to four decimal places. P-values less than 0.0001 will be presented as "<0.0001 and p-value greater than >0.9999 will be presented as 1.0000
- Percentages will be reported to one decimal place

Specific rules for pharmacokinetics:

Plasma concentrations of ASLAN003 and LAS186558 will be presented descriptively by study day and nominal time point for the PK analysis set including number of subjects (N), number of observations (n), mean, SD, coefficient of variation (CV%) median, minimum, and maximum. The below limit of quantification (BLQ) PK concentration values will be set to zero prior to computing descriptive statistics of PK concentrations. Missing concentrations will be omitted from the calculation of descriptive statistics.

Individual plasma and mean concentration-time plots will be provided using a linear and semi-logarithmic scale.

Descriptive statistics for PK parameters (see Section 7.11 for calculations) will be summarized by study day (N, n, arithmetic mean, SD of the arithmetic mean, CV%, median, minimum, maximum geometric mean [GeoMean], and geometric coefficient of variation [GeoCV%]). For t_{max}, only n, minimum, median, and maximum will be reported. For calculation and presentation of PK parameter descriptive statistics, values as presented in the data listings will be used as the source data. Minimum, maximum, mean, GeoMean, and median will be presented to the same significant figure precision as listed data. Standard deviation will be presented to 1 significant figure more than the precision of the data listed. The CV% and GeoCV% will always be reported to 1 decimal place. Derived parameters will be reported to 3 significant

figures, except for parameters that are taken directly from concentration data which will be reported using similar precision to those from which they were derived or elapsed sampling times which will be reported as 2 decimal places.

Scatter plots of individual subject and geometric mean dose-normalized AUC_{tau} (or AUC_{last}), $AUC_{tau\ ss}$ (or $AUC_{last\ ss}$), C_{max} and $C_{max\ ss}$ values versus dose will be presented.

6.1 Sample Size Estimation

This Phase IIA study is not formally powered.

6.1.1 Part 1

For Part 1, the proposed design of up to 6 patients per dose level has been selected to provide an assessment of the safety, tolerability and efficacy of up to 3 dose levels of ASLAN003, in order to select the most appropriate dose for further exploration in Part 2.

6.1.2 Part 2

The sample size of 20 patients for Part 2 has been selected to provide further efficacy and tolerability data at the selected dose level from Part 1, prior to conducting larger randomized trials in AML.

6.1.3 Sample Size Re-estimation

There are no planned sample size re-estimations.

6.2 Adjustments for Covariates

There are no planned adjustments for covariates.

6.3 Handling of Dropouts or Missing Data

In general, missing data will remain missing and will not be included in analyses. Exceptions are described below.

- Missing Baseline Data

If a baseline (Day 1) value is not available and a screening value is available for the same parameter, then the last screening value will be used as baseline. This value will also be used for calculations of changes from baseline.

6.4 Monitoring and Interim Analyses

6.4.1 Monitoring

The study will be monitored to ensure that the study is conducted and documented properly according to the protocol, good clinical practice (GCP), and all applicable regulatory requirements.

6.4.2 Interim Analysis

There are no interim analyses planned during Part 1 or Part 2.

6.5 Multiple Testing Strategy

There are no formal statistical analyses thus no corrections are planned for multiple testing.

6.6 Examination of Subgroups

Due to the small sample size, no subgroup analyses will be performed.

6.7 Stratification Factors

There are no stratification factors in this study.

7. Methods of Analysis

7.1 Overall Complete Remission Rate

A binary variable will be created to indicate complete response status for each patient (complete responder [CR or CRi] or non-responder [partial remission {PR} or treatment failure]).

For Part 1, AML response data will be listed, and summarized showing frequency and proportion of the best response (CR, CRi, PR or treatment failure) and OCRR (complete responder or non-responder) dose level and overall.

For Part 2, AML response data will be listed, and summarized showing frequency and proportion of the best response and OCRR, along with corresponding two-sided 80% confidence intervals (CIs) based on the Clopper-Pearson exact method.

7.2 Relapse-Free Survival

RFS will be listed for both study parts. For Part 2 only, if there are sufficient events, RFS will be summarized by using the Kaplan-Meier estimates to present 25th, 50th (median), and 75th percentiles, as well as the number and percentage of events and censored observations.

7.3 Clinical Benefit Rate

For Part 1, AML response data will be listed, and summarized showing frequency and proportion of CBR by dose level and overall.

For Part 2, AML response data will be listed, and summarized showing frequency and proportion of CBR, along with corresponding two-sided 80% CIs based on the Clopper-Pearson exact method.

7.4 BM blasts

Waterfall plots of the % change from baseline in BM blasts at Day 29, and the best % change from baseline in BM blasts will be presented. These plots will present each patient's value as a separate bar, with the bars ordered from the largest increase to the largest decrease.

For Part 1, all dose levels will be included on the same plot, but different bar types will be used to distinguish the different dose levels.

7.5 Time to Response

TTR data will be listed only.

7.6 Time to CR

TTCR data will be listed only.

7.7 Assessment of Safety and Tolerability

7.7.1 Assessment of Safety

All safety data will be assessed for the safety population.

All AE data will be listed along with information regarding initial study dose, dose at onset, onset time, duration, severity, and relationship to study treatment.

Treatment emergent AEs (TEAEs) are defined as AEs with an onset date on or after the start of treatment. The following summaries will be produced for both study parts, by dose group and overall for Part 1, for all TEAEs:

- An overview table of the incidence of TEAEs, grade 3+ TEAEs, SAEs, TEAEs leading to treatment discontinuation and TEAEs leading to death. For each summary category, the results will be shown overall (regardless of causality), and for the incidence of causally related TEAEs. For example, the overall incidence of TEAEs will be presented, as well as the incidence of TEAEs classified as at least possibly related to ASLAN003 by the Investigator.
- Summary of TEAEs by SOC and PT: Both the number and percentage of patients in each category (patient-level summary) and the number of episodes (episode-level summary). This summary table will be repeated for TEAEs attributed as causally related to study treatment.
- Summary of TEAEs, sorted in descending order of frequency (i.e. most frequent event shown first) presented by dose group (Part 1 only) and overall. The order of frequency will be determined by the most frequent preferred term overall. For each event, the results will be presented for all CTC grades, and also split by grade 1-2, and grade 3+.
- Summary of TEAEs attributed as causally related to study treatment, sorted in descending order of frequency (i.e. most frequent event shown first) presented by dose group (Part 1 only) and overall. The order of frequency will be determined by the most frequent preferred term overall. For each event, the results will be presented for all CTC grades, and also split by grade 1-2, and grade 3+.

- Summary of CTC grade 3 and above TEAEs sorted in descending order of frequency (i.e. most frequent event shown first). The order of frequency will be determined by the most frequent preferred term overall. Results will be presented by dose group (Part 1) and overall.
- A summary of CTC grade 3 and above TEAEs attributed as causally related to study treatment sorted in descending order of frequency (i.e. most frequent event shown first). The order of frequency will be determined by the most frequent preferred term overall. Results will be presented by dose group (Part 1) and overall.
- Summary of serious adverse events (SAEs) by PT.
- Summary of SAEs attributed as causally related to study treatment, sorted by PT.

Additionally, the following will be listed:

- AEs with outcome of death along with the date of onset, study day, initial study dose, dose at onset, treatment status at onset (pre-treatment, ongoing or post-treatment) and investigator's assessment of severity and relationship to study drug.
- All SAEs along with the date of onset, study day, initial study dose, dose at onset, treatment status at onset (pre-treatment, ongoing or post-treatment), date of resolution (if AE is resolved), investigator's assessment of severity and relationship to study drug.
- AEs leading to discontinuation of study drug, listed along with the date of onset, study day, initial study dose, dose at onset, treatment status at onset (pre-treatment, ongoing or post-treatment) and investigator's assessment of severity and relationship to study drug.

An AE will be considered to be causality related if a causality assessment of possibly, probably or definitely related is assigned by the Investigator.

If an AE is reported more than once during the study period the greatest severity and the worst-case attribution will be presented in summary tables. Any AEs commencing >28 days after discontinuation of study drug will not be included in the tabulations of AE data.

All clinical laboratory data (clinical chemistry, hematology and urinalysis data), vital signs and ECG data will be listed. In addition, all data measured on a continuous scale (except respiration rate and pulse) will be displayed graphically as described below:

- Patient profile plots over time including reference lines at the lower limit of normal (LLN) and upper limit of normal (ULN) where applicable for laboratory, vital signs and ECG data. For Part 1, separate plots will be produced for each cohort.
- For all continuous data except the haematological parameters, patient profile plots of the percentage change from baseline will be produced, including a reference line at zero. For Part 1, separate plots will be produced for each cohort.
- For all continuous data except the haematological parameters, box plots of the change from baseline over time, by dose group (Part 1), including a horizontal reference line at zero
- For haematological parameters, box plots of the absolute values over time, by dose group (Part 1), including a horizontal reference line at zero

To enable assessment of the potential for drug-induced liver injury, for all study parts the following outputs will be produced:

- A scatter plot of maximum on-treatment alanine aminotransferase (ALT) versus maximum on-treatment total bilirubin (x-axis), both expressed as multiples of the ULN, including reference lines at 3×ULN for ALT, and 2×ULN for total bilirubin. For each patient, the maximum ALT and maximum total bilirubin may occur at different visits
- A scatter plot of maximum on-treatment aspartate aminotransferase (AST) versus maximum on-treatment total bilirubin (x-axis), both expressed as multiples of the ULN, including reference lines at 3×ULN for AST, and 2×ULN for total bilirubin. For each patient, the maximum AST and maximum total bilirubin may occur at different visits.

In the event that the scatter plots of ALT or AST against bilirubin identify any potential Hy's law cases (patients with either both ALT > 3 x ULN and total bilirubin > 2 x ULN, or both AST > 3 x ULN and total bilirubin > 2 x ULN), profile plots over time will be produced for these patient's liver function tests (ALT, AST, ALP and total bilirubin), expressed in multiples of the ULN, showing all four FLT parameters on the same plot.

Physical examination data will be listed.

To further assess the tolerability of ASLAN003, dose intensity and treatment exposure, as defined in Section 3.2.2, will be listed and summarized by treatment arm. Dose intensity and exposure summaries will be presented by cycle for the first 3 cycles, and overall.

Swimmer plots of the time on treatment will be presented for all patients in the EFR set. The bars on these plots will be ordered as follows:

CR patients at the top, CRi patients next, PR next, non-responders next and NE patients at the bottom. Within each category they will be sorted from longest treatment duration to shortest treatment duration. Patients whose time on treatment is censored will be indicated. For responding patients, the start and end (actual or censored) time for response will also be indicated.

This plot will be repeated to account for dose modifications and interruptions.

7.8 Disposition of Patients

Patient disposition, including but not limited to, the date of informed consent, date of first dose and reasons for discontinuation from study treatment, will be listed and summarized by treatment group.

7.9 Demographics and Baseline Characteristics

Demographic and baseline characteristic data will be presented based on the FAS.

Baseline demographic data, including, but not limited to:

- age (as derived on the CRF)
- gender

- weight
- height
- race
- ethnicity

will be listed and summarized using appropriate descriptive statistics.

7.10 Medical History and Prior and Concomitant Medications

Relevant medical history and prior treatment for AML will be listed. Prior therapies will also be summarized by dose group (Part 1 only), type of therapy (induction, consolidation, salvage, maintenance or conditioning prior to transplant) and for the most recent therapy only, the response classification.

All medications received following the start of treatment (including those that were ongoing prior to first dose) will be listed.

Medications will be presented for the Safety population and coded using WHO Drug dictionary.

Frequency and percentage of concomitant medications use will be presented by Anatomical Therapeutic Chemical (ATC) level 2 and preferred name. Tables will also show the Total number and percentage of subjects receiving at least one treatment of a particular preferred name. Subjects receiving multiple medications within the same preferred names will be counted only once under that preferred name. Classification of Prior and concomitant medications will be based on medications start date and stop date as entered in prior and concomitant medications page of eCRF.

- 'Prior' medications are medications which started and stopped prior to the first capsule of study drug
- 'Concomitant' medications are medications which:
    - started prior to, on or after the first capsule of study drug and started before the end of study drug, and ended on or after the date of first dose of study drug or were ongoing at the end of the study drug
- 'Post treatment' medications are medications which are started after the last capsule of study drug and at or before the follow up visit

Concomitant medications will be summarised by ATC level 2 and preferred term based on Safety population.

7.11 Pharmacokinetic Analysis

The determination of the plasma concentration data will be performed at CPR Pharma Services using validated methods. The analytical methods will be conducted according to CPR Standard Operating Procedures (SOPs) for PK analyses unless otherwise specified.

Computation of pharmacokinetic parameters will be the responsibility of the pharmacokineticist at IQVIA, Overland Park, Kansas. The PK summaries, data listings,

and figures as well as the statistical analysis of the PK parameters will be the responsibility of the study biostatistician at IQVIA.

Standard non-compartmental methods with Phoenix® WinNonlin® 8.0 or higher (Certara, L.P., Princeton, New Jersey, US) or SAS® Version 9.2 or higher (SAS Institute, Inc., Cary, North Carolina, US). Actual elapsed time from dosing will be used for final plasma PK parameter calculations.

The pharmacokinetic analysis will be performed on the PK population after database lock following Part 1 of the study.
Where possible the following PK parameters will be determined for ASLAN003 and LAS186558 following single dose on Day 1.

- C_{max} Maximum plasma concentration (ng/mL) obtained directly from the observed concentration versus time data
- AUC_{last} Area under the plasma concentration-time curve from 0 to the time of the last quantifiable concentration (ng*h/mL), calculated by linear up/log down trapezoidal summation
- AUC_{tau} Area under the plasma concentration-time curve during the dosing interval, tau, (ng*h/mL), calculated by linear up/log down trapezoidal summation
- AUC_{inf} Area under the plasma concentration-time curve from time zero (pre-dose) extrapolated to infinity (ng*h/mL) calculated by linear up/log down trapezoidal summation and extrapolated to infinity by the addition of the last quantifiable concentration divided by the terminal rate constant: $AUC_{0\text{-}t}+C_{last}/\lambda_z$
- t_{max} Time to maximum plasma concentration (h) obtained directly from the observed concentration versus time data
- CL/F Apparent plasma clearance for ASLAN003 only (L/h), estimated as dose divided by AUC_{inf}
- V_z/F Apparent volume of distribution for ASLAN003 only (L), estimated by dividing the apparent clearance by λ_z
- λ_z Terminal rate constant (1/h) estimated by log-linear least-squares regression of the terminal part of the concentration-time curve
- $t_{1/2}$ Terminal elimination half-life (h). Visual assessment will be used to identify the terminal linear phase of the concentration-time profile

- MR — Metabolite to parent ratio (LAS186558 to ASLAN003) for AUC_{tau} and C_{max} ($MRAUC_{tau}$ and MRC_{max})
- C_{max}/D — Dose-normalized C_{max} (ng/mL/mg).
- AUC_{last}/D — Dose-normalized AUC_{last} (ng.h/mL/mg).
- AUC_{tau}/D — Dose-normalized AUC_{tau} (ng.h/mL/mg).

The following PK parameters will be calculated for ASLAN003 and LAS186558 for diagnostic purposes and listed but not summarized:

- λ_z, Interval — The time interval (h) of the log-linear regression to determine $t_{1/2}$
- λ_z, N — Number of data points included in the log-linear regression analysis
- Rsq(adj) — Coefficient of determination for calculation of λ_z. A value of >0.800 is indicative of good correlation and will be used as the criteria for reliable estimations of λ_z, $t_{1/2}$, and related parameters will not be reported if Rsq(adj) is ≤0.8
- %AUC — Percentage of AUC obtained by extrapolation, calculated as $[(C_{last}/\lambda_z)/AUC_{inf}*100]$. If value is >20%, AUC_{inf}, CL/F, and V_z/F will be listed but not included in any summaries or inferential analyses.

Where possible the following PK parameters will be determined for ASLAN003 and LAS186558 following multiple dosing on Day 8.

- $AUC_{tau\ ss}$ — Area under the plasma concentration-time curve during the dosing interval, tau, (ng*h/mL), calculated by linear up/log down trapezoidal summation
- $C_{max\ ss}$ — Maximum plasma concentration (ng/mL) obtained directly from the observed concentration versus time data
- $t_{max\ ss}$ — Time to maximum plasma concentration (h) obtained directly from the observed concentration versus time data
- $AUC_{last\ ss}$ — Area under the plasma concentration-time curve from 0 to the time of the last quantifiable concentration (ng*h/mL), calculated by linear up/log down trapezoidal summation

- C_{trough} Plasma concentration obtained prior to dosing on Day 8
- $t_{½\ eff}$ Effective elimination half-life at steady state calculated as
  ln2/ Lambda_z (eff)=
  [-ln2*tau/ln{1-[AUC_{tau}, Day 1 / AUC_{tau}, Day 8]}] with
  tau= 24 hours for QD dosing and 12 hours for BID dosing
- CL_{ss}/F Apparent plasma clearance for ASLAN003 only (L/h), estimated as dose divided by $AUC_{tau\ ss}$
- MR Metabolite to parent ratio (LAS186558 to ASLAN003) for $AUC_{tau\ ss}$ and $C_{max\ ss}$, ($MRAUC_{tau\ ss}$ and $MRC_{max\ ss}$)
- RacAUC Accumulation ratio for AUC calculated as $AUC_{tau\ ss}/AUC_{tau}$ or $AUC_{last\ ss}/AUC_{last}$
- RacCmax Accumulation ratio for C_{max} calculated as $C_{max\ ss}/C_{max}$
- $C_{max\ ss}/D$ Dose-normalized $C_{max\ ss}$ (ng/mL/mg).
- $AUC_{last\ ss}/D$ Dose-normalized $AUC_{last\ ss}$ (ng.h/mL/mg).
- $AUC_{tau\ ss}/D$ Dose-normalized $AUC_{tau\ ss}$ (ng.h/mL/mg).

7.11.1 Concentration Values

All concentration values below the lower limit of quantification (LLQ) and samples with no reportable value occurring prior to dosing will be replaced by "0". For tabulation, graphical representation and calculation of summary statistics, all samples <LLQ or with no reportable value observed after the drug administration will be treated as missing.

7.11.2 Calculation of the Actual Sampling Times

For all sampling times, the actual sampling times will be calculated as the difference between the sample collection actual clock time and the actual clock time of oral administration.

Therefore:
Actual clock time of sample collection = actual clock time of dosing + difference

The actual sampling times expressed in hours will be used to calculate the PK parameters, except for pre-dose samples, which will always be reported as zero (0.00), regardless of the time difference.

7.11.3 Pharmacokinetic Analysis

Not applicable

8. REFERENCES

Not applicable

9. LIST OF TABLES, FIGURES AND LISTINGS

9.1 Tables

Unless otherwise stated, tables will be all repeated for part 1 and part 2.

Table Number	Table Title
14.1.1	Patient Disposition and Withdrawals – All Patients
14.1.2	Analysis Populations – All Patients
14.1.3.1	Major Protocol Deviations – Full Analysis Set
14.1.3.2	Other Important Protocol Deviations – Full Analysis Set
14.1.4	Demographic Characteristics – Full Analysis Set
14.1.5	Prior Therapies for AML – Full Analysis Set
14.2.1.1	Summary of Overall Complete Remission Rate – EFR Population
14.2.1.2	Summary of Overall Complete Remission Rate – Full Analysis Set
14.2.2.1	Summary Statistics for Relapse-Free Survival – EFR Population
14.2.2.2	Summary Statistics for Relapse-Free Survival – Full Analysis Set
14.2.3.1	Summary of Clinical Benefit Rate – EFR Population
14.2.3.2	Summary of Clinical Benefit Rate – Full Analysis Set
14.2.5.1	Summary of Plasma Concentrations – ASLAN003 – PK Population
14.2.5.2	Summary of Plasma Concentrations – LAS186558 – PK Population
14.2.5.3	Summary of Plasma Pharmacokinetic Parameters – ASLAN003 - PK Population
14.2.5.4	Summary of Plasma Pharmacokinetic Parameters – LAS186558 - PK Population
14.3.1.1	Summary Statistics for Exposure – Safety Population
14.3.1.2	Summary Statistics for Dose Intensity – Safety Population
14.3.2.1	Overview of TEAEs – Safety Population

Table Number	Table Title
14.3.2.2	Incidence of TEAEs by System Organ Class and Preferred Term – Patient and Episode Level – Safety Population
14.3.2.3	Incidence of Causally Related TEAEs by System Organ Class and Preferred Term – Patient and Episode Level – Safety Population
14.3.2.4	Incidence of most frequent (>10%) TEAEs by Preferred Term – Safety Population
14.3.2.5	Incidence of most frequent (>10%) Causally Related TEAEs by Preferred Term – Safety Population
14.3.2.6	Incidence of TEAEs CTCAE Grade 3 or Higher by System Organ Class and Preferred Term – Safety Population
14.3.2.7	Incidence of Causally Related TEAEs CTCAE Grade 3 or Higher by System Organ Class and Preferred Term – Safety Population
14.3.2.8	Incidence of Serious TEAEs by System Organ Class and Preferred Term – Safety Population
14.3.2.9	Incidence of Serious Causally Related TEAEs by System Organ Class and Preferred Term – Safety Population
14.3.3	Summary of Deaths – Safety Population

9.2 Listings

Unless otherwise stated, listings will be all repeated for part 1 and part 2.

Listing Number	Listing Title
16.2.1	Discontinuation Information – Safety Population
16.2.2.1	Inclusion/Exclusion Criteria Eligibility – All Patients
16.2.2.3	Screening Failure Data – All Patients
16.2.3.1	Major Protocol Deviations – Safety Population
16.2.3.2	Other Important Deviations – Safety Population
16.2.3.3	Analysis Populations - All Patients
16.2.4.1	Demographic Characteristics – Safety Population

Listing Number	Listing Title
16.2.4.2	Medical History – Safety Population
16.2.4.3	Prior and Concomitant Medications – Safety Population
16.2.4.4	Primary Leukemia Diagnosis – Safety Population
16.2.4.5	Prior AML Therapy – Safety Population
16.2.4.7	Surgical History – Safety Population
16.2.4.8	Prior Transplant History – Safety Population
16.2.4.9	Concomitant Therapies – Safety Population
16.2.4.10	Subsequent Antileukemic Treatment – Safety Population
16.2.5.1	Study Drug Administration – Safety Population
16.2.5.2	Study Drug Exposure and Dose Intensity – Safety Population
16.2.5.3	Study Drug Dispensing – Safety Population
16.2.5.4	Study Drug Compliance – Safety Population
16.2.6.1.1	Plasma Concentrations – Safety Population
16.2.6.1.2	Plasma Pharmacokinetic Parameters – PK Population
16.2.6.2.1	IWG Response – FAS Population
16.2.6.2.2	Response Status – FAS Population
16.2.6.3.1	Investigator's Assessment of IWG Response – FAS Population
16.2.6.3.2	Flowcytometry – FAS Population
16.2.6.3.3	Extramedullary Leukemia - FAS Population
16.2.6.3.4	Bone Marrow Aspiration - FAS Population
16.2.6.4.1	Survival Status – FAS Population
16.2.6.4.2	Relapse-Free Survival – Safety Population
16.2.6.4.3	Time to Response – Safety Population
16.2.7.1	Adverse Events – Safety Population

Listing Number	Listing Title
16.2.7.2	Adverse Events Leading to Discontinuation of Study Medication – Safety Population
16.2.7.3	Serious Adverse Events – Safety Population
16.2.7.4	Adverse Events Leading to Death – Safety Population
16.2.7.5	Deaths – Safety Population
16.2.8.1	Haematology Parameters – Safety Population
16.2.8.2	Clinical Chemistry Parameters – Safety Population
16.2.8.3	Urinalysis Parameters – Safety Population
16.2.8.4	Coagulation Parameters – Safety Population
16.2.8.5	Serology Parameters – Safety Population
16.2.8.6	Pregnancy Test Results – Safety Population
16.2.9.1	ECG Assessment– Safety Population
16.2.9.2	Vital Signs – Safety Population
16.2.9.3	Physical Examination – Safety Population
16.2.9.4	ECOG Assessment – Safety Population

9.3 Figures

Unless otherwise stated, figures will be all repeated for safety run-in, part 1 and part 2.

Figure Number	Figure Title
14.2.4.1	Waterfall Plot of Percentage Change from Baseline in BM Blasts at day 29 – EFR Population
14.2.4.2	Waterfall Plot of Percentage Change from Baseline in BM Blasts at day 29 – Full Analysis Set
14.2.5.5	Profile Plots of Plasma Concentrations on a Linear Scale – ASLAN003 - PK Population

Figure Number	Figure Title
14.2.5.6	Profile Plots of Plasma Concentrations on a Log Scale – ASLAN003 - PK Population
14.2.5.7	Mean Profile Plots of Plasma Concentrations on a Linear Scale - LAS186558 – PK Population
14.2.5.8	Mean Profile Plots of Plasma Concentrations on a Log Scale - LAS186558 – PK Population
14.2.5.9	Dose-Normalised Plasma Pharmacokinetic Parameters – ASLAN003 – PK Population
14.2.5.10	Dose-Normalised Plasma Pharmacokinetic Parameters – LAS186558 – PK Population
14.2.5.11	Geometric Mean Dose-Normalised Plasma Pharmacokinetic Parameters – ASLAN003 – PK Population
14.2.5.12	Geometric Mean Dose-Normalised Plasma Pharmacokinetic Parameters – LAS186558 – PK Population
14.3.1.3	Swimmer Plot of Time on Treatment by Response Category – FAS Population
14.3.1.4	Swimmer Plot of Time on Treatment by Response Category, Accounting for Dose Modifications and Interruptions – FAS Population
14.3.4.1	Profile Plots of Haematology Parameters – Safety Population
14.3.4.2	Profile Plots of Clinical Chemistry Parameters – Safety Population
14.3.4.3	Profile Plots of Urinalysis Parameters – Safety Population
14.3.4.4	Profile Plots of Percentage Change from Baseline in Clinical Chemistry Parameters – Safety Population
14.3.4.5	Profile Plots of Percentage Change from Baseline in Urinalysis Parameters – Safety Population
14.3.4.6	Box Plots of Haematology Parameters – Safety Population
14.3.4.7	Box Plots of Change from Baseline in Clinical Chemistry Parameters – Safety Population
14.3.4.8	Box Plots of Change from Baseline in Urinalysis Parameters – Safety Population

Figure Number	Figure Title
14.3.4.9	Scatter Plots of Maximum ALT vs Maximum Total Bilirubin – Safety Population
14.3.4.10	Scatter Plots of Maximum AST vs Maximum Total Bilirubin – Safety Population
14.2.4.11.x	Hys Law Plot for Patient XXXXX – Safety Population
14.3.5.1	Profile Plots of Vital Signs Parameters – Safety Population
14.3.5.2	Profile Plots of Change from Baseline in Vital Signs Parameters – Safety Population
14.3.5.3	Box Plots of Change from Baseline in Vital Signs Parameters – Safety Population
14.3.6.1	Profile Plots of ECG Parameters – Safety Population
14.3.6.2	Profile Plots of Change from Baseline in ECG Parameters – Safety Population
14.3.6.3	Box Plots of Change From Baseline in ECG Parameters – Safety Population