Statistical Analysis Plan

Plexxikon Inc.

PLX121-01

A Phase 1b and 2a Study to Assess Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of PLX9486 as a Single Agent and in Combination with PLX3397 or Sunitinib (Sutent®) in Patients with Advanced Solid Tumors and Patients with Locally Advanced, Unresectable, or Metastatic Gastrointestinal Stromal Tumor (GIST) Who Have Been Previously Treated with Imatinib Mesylate/KIT-Directed Tyrosine Kinase Inhibitor (TKI) Therapy

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS

AE	Adverse event
BID	Twice daily
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
CI	Confidence interval
CR	Complete response
CRF	Case report form
CSR	Clinical study report
CTCAE	Common Terminology Criteria for Adverse Events
C*x*D*y*	Cycle *x* Day *y*
DLT	Dose limiting toxicity
DOR	Duration of response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
GIST	Gastrointestinal stromal tumor
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum tolerated dose
NE	Not evaluable
ORR	Overall Response Rate
PD	Progressive disease
PFS	Progression-free survival
PK	Pharmacokinetic
PR	Partial Response
QD	Once a day
QTcF	Heart-rate-corrected QT interval (Fridericia's formula)
RECIST	Response Evaluation Criteria In Solid Tumors
RP2D	Recommended phase 2 dose
SAE	Serious adverse event
SD	Stable disease
TEAE	Treatment-emergent adverse event
TKI	Tyrosine Kinase Inhibitor
WHO	World Health Organization

DEFINITIONS

Adverse Event (AE)	An adverse event (AE) is any untoward medical occurrence in a patient administered a pharmaceutical product, which does not necessarily have a causal relationship with the treatment. An AE can be any unfavorable and unintended sign (e.g., including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the study drug, whether or not it is considered to be study drug related. This includes any newly occurring event or previous condition that has increased in severity or frequency since the administration of study drug.
Dose Limiting Toxicity (DLT)	Dose Limiting Toxicities (DLTs) are defined as AEs occurring during the first 28 days of study drug administration that are classified as possibly or probably related to the study drug, and meet one of the Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria listed in Section 3.1 of the SAP.
Safety Population	The Safety Population will include all patients treated with at least one dose of study drug.
Efficacy Evaluable Population	The Efficacy Evaluable Population will include all patients who have taken at least 1 dose of study drug and have had at least 1 post-baseline tumor assessment or discontinue study medication due to disease progression or death.
Pharmacokinetic (PK) Population	All patients who have adequate pharmacokinetic (PK) data.
Serious AE (SAE)	A serious AE (SAE) is an AE occurring at any dose that: results in death; is a life-threatening experience; requires inpatient hospitalization longer than 24 hours or prolongation of an existing hospitalization; results in a persistent or significant disability/incapacity; is a congenital anomaly or birth defect, or is an important medical event.
Treatment-emergent AE (TEAE)	A treatment-emergent AE (TEAE) is an AE that started or worsened in severity on or after the date of the initial dose of study drug.

1. INTRODUCTION

This document outlines the statistical methods to be implemented during the analyses of data collected within the scope of Plexxikon Protocol Number PLX121-01 "A Phase 1b and 2a Study to Assess Safety, Pharmacokinetics, Pharmacodynamics, and Preliminary Efficacy of PLX9486 as a Single Agent and in Combination with PLX3397 or Sunitinib (Sutent®) in Patients with Advanced Solid Tumors and Patients with Locally Advanced, Unresectable, or Metastatic Gastrointestinal Stromal Tumor (GIST) Who Have Been Previously Treated with Imatinib Mesylate/KIT-Directed Tyrosine Kinase Inhibitor (TKI) Therapy" Amendment 7 dated 23 July, 2019.

This study is designed in 7 parts. Part 1 will establish the maximum tolerated dose/recommended Phase 2 dose of PLX9486 in patients with advanced solid tumors (including GIST) as well as evaluate the efficacy of PLX9486 in solid tumors. Parts 2[redacted] will assess safety, tolerability, and efficacy of PLX9486 as a single agent or in combination with PLX3397 or sunitinib in patients advanced solid tumors (including GIST) or patients with advanced solid tumors/advanced solid tumor with KIT mutations.

The purpose of this analysis plan is to provide specific guidelines from which the analysis of Part 1, Part 2b and Part 2e will proceed [redacted]. Any deviations from these guidelines will be documented in the clinical study report (CSR).

Details of the pharmacokinetic (PK) statistical analysis plan will be outlined in a separate document and a formal PK report will be written for inclusion in the final study report.

2. STUDY OBJECTIVES

2.1 Part 1 (Dose-Evaluation Cohort) Objectives

2.1.1 Primary Objectives

The primary objectives of Part 1 of this study are:

- To evaluate safety and pharmacokinetics (PK) of orally administered PLX9486 as single and as multiple doses
- To establish the maximum tolerated dose/recommended Phase 2 dose (MTD/RP2D) in patients with advanced solid tumors (including GIST).

2.1.2 Secondary Objectives

The secondary objective of Part 1 of this study is to evaluate the efficacy of PLX9486 in solid tumors as measured by Overall Response Rate (ORR) using Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 criteria, Duration of Response (DOR), and Progression-Free Survival (PFS).

2.1.3 Exploratory Objectives

The exploratory objective of Part 1 of this study is to assess biomarkers in peripheral blood, archival tumor tissue, and available tumor biopsies.

2.2 Part 2 (Extension Cohorts: Parts 2b and 2e) Objectives

2.2.1 Primary Objectives

The primary objectives of Part 2b and Part 2e of this study are:

- Part 2b: To assess the safety and tolerability of the combination of PLX9486 and PLX3397 and to establish an RP2D of PLX9486 in combination with PLX3397 in patients with advanced solid tumors (including GIST).
- Part 2e: To assess the safety and tolerability of the combination of PLX9486 and sunitinib and to establish an RP2D of PLX9486 in combination with sunitinib in patients with advanced solid tumors (including GIST)

2.2.2 Secondary Objectives

The secondary objectives of Part 2b and Part 2e are:

- To determine the pharmacokinetics (PK) of PLX9486 as a single agent and in combination with PLX3397 (Part 2b) or sunitinib (Part 2e).
- To estimate the following: ORR (using RECIST 1.1), clinical benefit rate (CBR), Overall Survival (OS) and 12-month OS rate, PFS and 6-month PFS rate, and DOR.

2.2.3 Exploratory Objectives

The exploratory objective of Part 2 of this study is to assess biomarkers in peripheral blood and in archival tumor tissue.

3. STUDY DESIGN AND PLAN

This Phase 1b and 2a, open-label, multicenter study includes a dose-evaluation portion (Part 1) in which the safety profile and RP2D of PLX9486 as a single oral agent, administered daily in 28-day dosing cycles will be evaluated in patients with solid tumors (including GIST), followed by signal-seeking expansion cohorts (Part 2, consisting of Part [redacted] 2b, [redacted] 2e and [redacted] as described in the protocol). This document covers the analysis plan for Part 1 Dose Escalation of PLX9486, Part 2b and Part 2e only that were planned in the protocol as follows:

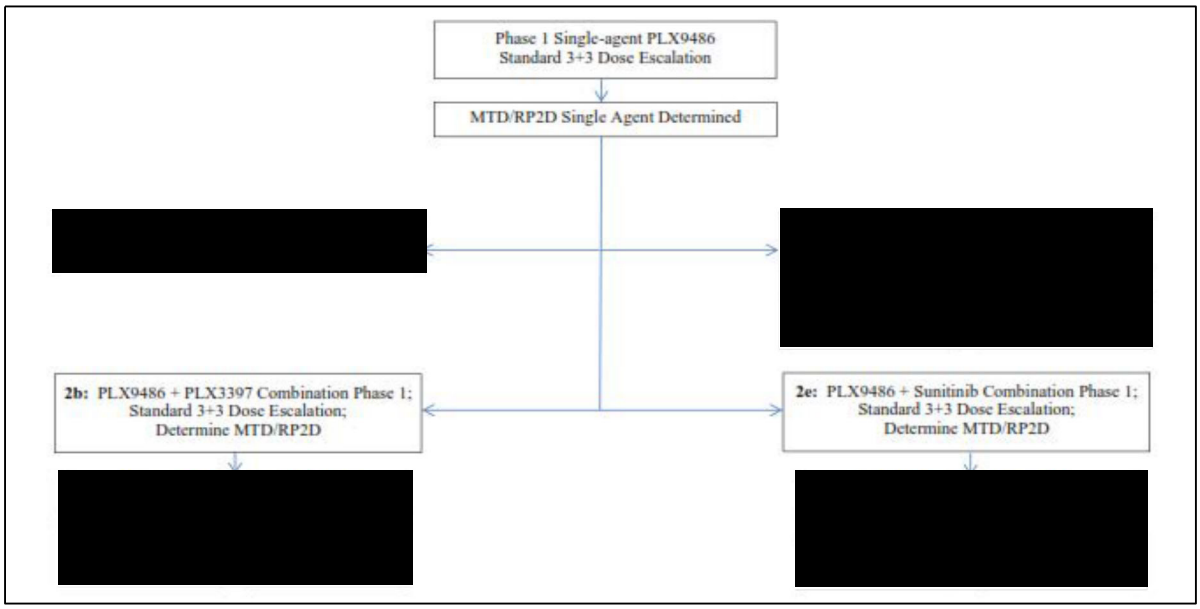
Part 1 (dose escalation) will enroll approximately 30 solid tumor patients in a standard “3+3” design. Additional patients may be required depending on the number of cohorts and evaluable patients needed.

Part 2b will be the open-label, sequential cohort dose-finding study of PLX9486 combined with PLX3397 in up to approximately 30 patients with solid tumors (including GIST) in a 3+3 design.

Part 2e will be the open-label, sequential cohort dose-finding study of PLX9486 combined with sunitinib in up to approximately 30 patients with solid tumors (including GIST) in a 3+3 design.

Figure 1 provides an overview of the study design.

Figure 1: Overview of Study PLX121-01



In the absence of Grade ≥2 toxicity that is considered "possibly" or "probably" related to the study agent or dose-limiting toxicity (DLT) and in conjunction with review of the pharmacokinetic data, dose escalation in each study part (Part 1, 2b and 2e) is planned to occur as shown in the table below.

PLX9486 Administration in Part 1: Initial and Potential Dose- escalation Cohorts

Cohort Number	PLX9486 Dose Level (mg/day)[a]	Number and Unit Strength
[redacted]		
4	1000	20 x 50 mg
5	500 (BID)	10 x 50 mg (BID)
6	1500	30 x 50 mg
7	2000	40 x 50 mg

[a]Dosing interval/frequency will be QD unless otherwise specified (e.g., BID dosing).

PLX9486 and PLX3397 Administration in Part 2b: Initial and Potential Dose-escalation Cohorts

Cohort Number	**PLX9486 Dose Level (mg/day)[a]**	**PLX3397 Dose Level (mg/day)**
1	Approximately 50% of Part 1 RP2D	600 (200 mg in AM and 400 mg in PM)

2	Approximately 100% of Part 1 RP2D	600 (200 mg in AM and 400 mg in PM)
3	100% of Part 1 RP2D	400 mg QD (Cycles 1 and 2)
		600 mg QD (Cycle 3 +)[b]
4 +	TBD[c]	TBD[c]

RP2D = recommended phase 2 dose; TBD = to be determined

[a] PLX9486 administered once-daily (QD) or for higher total daily doses, as split doses (e.g., twice-daily [BID]).

[b] At the discretion of the investigator and in the absence of clinically significant drug-related toxicity (Section 9.3 in the protocol) during Cycles 1 and 2.

[c] Based on a review of the data by the Study Committee.

PLX9486 and Sunitinib Administration in Part 2e: Initial and Potential Dose-escalation Cohorts

Cohort Number	PLX9486 Dose Level (mg/day)[a]	Sunitinib Dose Level (mg/day)
1	Approximately 50% of Part 1 RP2D	25
2	100% of Part 1 RP2D	25
3	100% of Part 1 RP2D	37.5

RP2D = recommended phase 2 dose

[a] Dosing interval/frequency will be QD unless otherwise specified (e.g., BID dosing).

Patients who are considered in dose-escalation decisions are not allowed dose reductions during the DLT assessment window. Patients who withdraw from the study prior to completing Cycle 1 for any reason other than a DLT will be replaced. A patient who experiences a DLT may remain in the trial and continue receiving study drug at a lower dose per the investigator's decision in consultation with the Medical Monitor. Further dose escalation and de-escalation rules can be found in the protocol Section 9.2.

The screening period for the study will be 21 days with the exception of tumor burden assessment [i.e., CT scan], which may be performed within 28 days of dosing. The treatment period will occur in 28-day (± 7 days) cycles until patient discontinuation or withdrawal or study termination. Patients will be monitored throughout the study for adverse reactions to the drug formulation and/or study procedures. Safety and tolerability assessments will include physical examinations, vital signs, 12-lead electrocardiograms (ECGs), ECOG score, adverse events (AEs), hematology, complete chemistry panel, coagulation, and urinalysis.

An end of study visit must occur ≥30 days after the last dose of PLX9486 and prior to starting any new anti-cancer therapy. A post-study follow-up contact by phone by site staff will be conducted every 3 months during Year 1, then every 6 months thereafter to obtain information on any new anti-cancer therapy received, response, and survival status.

For more information on scheduled assessments and procedures, see Trial Flow Charts (Table 1, Table 3, and Table 6 in the protocol).

3.1 Dose Limiting Toxicities

For Part 1, 2b and 2e, in the absence of a DLT, patients must complete the first cycle of treatment (28 days) in order to be considered evaluable for DLT. Patients who discontinue for

any reason other than a DLT or Grade ≥2 toxicity and have received less than 21 of 28 days of dosing will not be considered evaluable for DLT and will be replaced; however, their data will be reviewed by the study committee and a decision will be made based on their review.

Dose Limiting Toxicities (DLTs) are defined as AEs occurring during the first 28 days of study drug administration (Cycle 1) that are classified as possibly or probably related to the study drug, and meet one of the following Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria.

Hematologic Toxicities

- Grade 4 neutropenia lasting >7 days
- Grade ≥ 3 neutropenia with fever
- Grade 4 thrombocytopenia
- Grade ≥ 3 thrombocytopenia lasting more than 7 days or associated with clinically significant bleeding
- Grade 4 anemia

Other Toxicities

Any ≥ Grade 3 (AE or laboratory) toxicity despite adequate supportive care except for the following.

- Grade ≥ 3 nausea, vomiting, or diarrhea that resolves to Grade ≤ 2 within 72 hours, with or without medical intervention or prophylaxis because this would not be considered treatment-limiting in an oncology population
- Grade 3 fatigue that resolves to ≤ Grade 2 within 14 days because this would not be considered treatment-limiting in an oncology population
- Grade ≥ 3 asymptomatic changes in alkaline phosphatase, hypomagnesemia, hyperglycemia, or hypophosphatemia that are felt by the investigator to be clinically insignificant
- Grade 3 asymptomatic increases in transaminases (AST, ALT) confirmed upon repeat testing which resolves to ≤Grade 2 within <5 days

Any other Grade ≥ 3 toxicity (except those noted above) for which either the Principal Investigator or Sponsor deems further dose escalation inappropriate

Dose escalation will continue unless there are dose-limiting toxicities in ≥2 of at least 6 patients (i.e., 33%) in one cohort within the first 28 days. In the absence of a DLT, patients must complete the first cycle of treatment (28 days) in order to be considered evaluable for DLT. Patients who discontinue for any reason other than a DLT or Grade ≥2 toxicity and have received less than 21 of 28 days of dosing will not be considered evaluable for DLT and will be replaced. Further dose escalation or de-escalation may be considered depending upon safety and PK findings and discussion between the Sponsor and the investigators. If no DLT is observed, the recommended dose for further evaluation may be established based on toxicity, PK, and convenience of dosing in approximately 3-6 patients treated at that dose.

3.2 Schedule of Events

The Schedules of Events can be found in the corresponding Trial Flow Charts in the protocol (Table 1 for Part 1, Table 3 for Part 2b, and Table 6 for Part 2e).

4. DETERMINATION OF SAMPLE SIZE

The sample sizes of the different parts of the study are based on clinical rather than statistical considerations. The dose escalation cohorts (Part 1 and Parts 2b and 2e) follow a typical 3 + 3 design.

The following table shows the probability of escalating to the next higher dose—after either 3 or 6 patients—given the true DLT incidence rate.

True Incidence of DLTs	10%	20%	30%	40%	50%	60%	70%
Probability of Escalating Dose	0.91	0.71	0.49	0.31	0.17	0.08	0.03

From the table we see that, when the likelihood of a DLT is low (e.g., if the true DLT incidence rate is 10% or less), the probability of escalating to the next higher dose is high (> 90%), However, when the likelihood of a DLT is high (e.g., if the true DLT incidence rate is 60% or higher), the probability (or risk) of escalating to the next higher dose is low (< 10%).

5. GENERAL ANALYSIS CONSIDERATIONS

5.1 Data Summaries

The statistical analyses will be reported using summary tables, figures, and data listings. The International Conference on Harmonisation numbering convention will be used for all tables, listings, and figures. All statistical testing will be two-sided and will be performed at the 0.05 significance level. All confidence intervals (CIs) will be constructed at the two-sided, 95% confidence level. If there is intra-patient dose escalation, summary for these patients will be presented under their original cohorts.

Continuous variables will be summarized with means, standard deviations, medians, minimums, and maximums. Categorical variables will be summarized by counts and by percentages of patients in corresponding categories. Time-to-event variables will be summarized using the Kaplan-Meier method. All summary tables will be presented by study part, dose cohorts, and overall. Baseline summaries will also include a total summary column.

Individual patient data obtained from the case report forms (CRFs), PK data, and pharmacodynamics data, will be presented by cohort, patient, and time point (if applicable) in data listings. Data from all assessments, whether scheduled or unscheduled, will be included in the listing. Listings will present the dates in their original format (without any imputation).

Some patients in Part 1b were given a low dose of PLX9486 at study day -10 for use in the PK analysis. For the purposes of safety analyses this dose will be considered the date of first dose. For the purposes of efficacy analyses the date of first dose will be considered C1D1.

The analyses described in this plan are considered a priori, in that they are defined prior to database lock. Post-hoc analyses will be identified in the CSR.

All analyses and tabulations will be performed using SAS® v9.4 on a SAS server platform. Tables and listings will be presented in rich text format. Upon completion, all SAS programs will be validated by an independent programmer. In addition, all program output will undergo two independent statistical reviews, one of which is a senior level statistical review. The validation process will be used to confirm that statistically valid methods have been implemented and that all data manipulations and calculations are accurate. Checks will be made to ensure accuracy, consistency with this plan, consistency within tables, and consistency between tables and corresponding data listings. Upon completion of validation and quality review procedures, all documentation will be collected and filed by the project statistician or designee.

5.2 Data Handling

5.2.1 Baseline Values

Unless otherwise specified, the baseline value is defined as the last non-missing value obtained prior to the first dose of any study drug (PLX9486 for Part 1, PLX9486 or PLX3397 for Part 2b, and PLX9486 or sunitinib for Part 2e). Post-baseline values are defined as values obtained after the first dose of any study drug. Change from baseline is defined as a post-baseline value minus the baseline value.

Baseline weight is defined as the value obtained at Cycle 1 Day 1 (C1D1), if this value is missing the last value obtained before the date and time of the first dose of any study drug will be used.

5.2.2 Conventions

Percentages are routinely based on the total category count excluding missing values if not otherwise mentioned. Percentages showing a rate relative to the total number of patients in this group are given in special tables (e.g., AE tables). Table footnotes will specify the basis for percentages.

The precision of the original measurements will be maintained in summaries and listings, when possible. Generally, means, medians and standard deviations will be presented with an increased level of precision; 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.

Summaries of continuous variables that have some values recorded using approximate values (e.g. < or >) will use imputed values. That is, approximate values will be imputed using the closest exact value for that measurement. Listings will present the data in the original format.

For tables where rounding is required, rounding will be done to the nearest round-off unit. For example, if the round-off unit is the ones place (i.e., integers), values ≥ XX.5 will be rounded up to XX+1 while values < XX.5 will be rounded down to XX.

Conventions for handling partial dates for AEs and prior and concomitant medications are given in Appendix 1.

Listings will present the dates in their original format (without any imputation). In listings, durations of AEs and concomitant medications will not be derived using imputed dates but, rather, be set to missing when an event has a partially or completely missing start date or end date.

For frequency counts of categorical variables, categories whose counts are zero will be displayed for the sake of completeness. For example, if none of the patients 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.

6. ANALYSIS POPULATIONS

The Efficacy Evaluable population will include all patients who have taken at least one dose of study drug and have had at least one post-baseline tumor assessment or discontinue study medication early due to disease progression or death.

The Safety population will include all patients treated with at least one dose of any study drug.

The PK and PD analysis populations will consist of all patients who have adequate PK and PD data.

7. STUDY POPULATION

7.1 Patient Disposition

Patient disposition information will be summarized by study part, dose cohort and overall. Summaries will include the number of enrolled patients, the number of patients in each analysis population, and the primary reason for discontinuation.

7.2 Demographic and Baseline Characteristics

Demographic variables include age, gender, ethnicity, and race.

Descriptive statistics will be presented for age. Frequency counts and percentages will be presented for gender, ethnicity, and race. Demographic and baseline characteristics will be summarized by study part and overall. All demographic and baseline characteristics will be presented in a data listing.

7.3 Medical History

The number and percentage of patients will be summarized by study part, dose cohort and overall for each body system.

Primary Cancer History and Prior Treatment for Primary Malignancy will be listed.

7.4 Concomitant Medications (and Procedures)

Verbatim terms on CRFs will be mapped to Anatomical Therapeutic Chemical (ATC) class and Generic Drug Names using the World Health Organization (WHO) Drug Dictionary Enhanced B2 format, March 1, 2015 release.

Prior medications are those that begin prior to the administration of study drug which have a stop date prior to the date of first dose. Concomitant medications are those which are taken at any time between the date of first dose and the date of last dose of any study medication. See Appendix 1 for handling of partial dates for medications. In cases where it is not possible to determine if a medication is concomitant, the medication will be classified as concomitant.

Prior and concomitant medications will be summarized separately, by WHO ATC class and generic drug name for the Safety Population. Summaries will be presented for each study part, dose cohort, and overall. The number and percentage of patients using each medication will be presented. Patients may have more than one medication per ATC class and generic drug name. At each level of patient summarization, a patient is counted once if he/she reported one or more medications at that level. Each summary will be ordered by descending order of incidence of ATC class and generic drug name within each ATC class.

7.5 Protocol Deviations

A listing of protocol deviations will be provided.

8. EFFICACY ANALYSES

Several efficacy variables will be derived based on the collected data and will be summarized. All efficacy summaries (or analyses) will be based on Efficacy Evaluable population. This study will utilize the definition of tumor response as described in RECIST 1.1.

8.1 Tumor Response

8.1.1 Overall Timepoint Response

The investigator's assessment of a patient's target lesion response, non-target lesion response, and appearance of new lesions (collected from the CRF) will be used to determine the overall tumor response at each time point as shown in Table 1 (for patients with target lesions (with or without non-target lesions)) and Table 2 (for patients with non-target lesions only).

The possible overall tumor responses at a time point, from best to worst, are as follows.

- Complete Response (CR)
- Partial Response (PR)
- Stable Disease (SD)
- Progressive Disease (PD)

If no assessment was done or a response cannot be determined, overall timepoint response is designated as Not Evaluable (NE).

Table 1. Time Point Response: Patients with Target (+/- Non-Target) Disease

Target Lesion	Non-Target Lesions	New Lesions	Overall (Time point) Response
CR	CR	No	CR
CR	Non-CR/non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-PD or not all evaluated	No	PR
SD	Non-PD or not all evaluated	No	SD
Not all evaluated	Non-PD	No	NE
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

Table 2. Time Point Response: Patients with Non-Target Disease Only

Non-Target Lesions	New Lesions	Overall Response
CR	No	CR
Non-CR/Non-PD	No	Non-CR/non-PD[1]
Not all evaluated	No	NE
Unequivocal PD	Yes or No	PD
Any	Yes	PD

CR = Complete Response; PR = Partial Response; SD = Stable Disease; PD = Progressive Disease; NE = Not Evaluable.
Note: 'Non-CR/non-PD' is preferred over 'stable disease' for non-target disease since SD is increasingly used as endpoint for assessment of efficacy in some trials so to assign this category when no lesions can be measured is not advised.

The date of the assessment of tumor response for a time point is the earliest date of target, non-target or new lesion assessment dates. If all of these dates are missing, the date of tumor response assessment is used.

8.1.2 Best Response

The best responses for pairs of time point responses (when confirmation of CR and PR are required) are determined as shown in Table 3. Table 3 is an extended version of the corresponding RECIST table. The additional discussion provided here clarify how Best Responses for individual pairs of Overall Time Point Responses, i.e., paired by sequential time points, are determined. The Best Responses will then be used to determine Best Overall Response (Section 8.1.3).

In Table 3, the first and subsequent time points referenced in the column headers refer to an arbitrary pair of sequential time points. Also, as indicated in the table and in the table notes, special rules may apply when the first time point of the pair is the very first (post-treatment) assessment time point or when there is only one assessment.

Table 3. Best Response When Confirmation of CR and PR are Required

	Overall Response First Time Point	Overall Response Subsequent Time Point	Best Response for the Pair
1	CR	CR	**CR** (if minimum criteria for CR duration is met), otherwise **Best Response = NE.**
2	CR	PR	If the first time point is truly CR, any worsening at a subsequent time point—even disease meeting the PR criteria—makes the disease PD at that subsequent time point. Then **Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = PD**. However, sometimes 'CR' may still be claimed when subsequent scans suggest small lesions that were likely present and in fact, the patient had PR, not CR, at the first time point. Under these circumstances, the original CR should be changed to PR; see **Row 6 for Best Response criteria**.
3	CR	SD	**Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = PD**.
4	CR, PR, SD	PD	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = PD**.
5	CR, PR	NE	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = NE.**
6	PR	CR, PR	**Best Response = PR** provided minimum criteria for PR duration is met; otherwise, **Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = NE.**
7	PR	SD	**Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = NE.**
8	SD	SD, CR, PR	**Best Response = SD** provided minimum criteria for SD duration is met by the second time point; otherwise **Best Response = NE**.
9	SD	NE	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response = NE**.
10	SD	PD	**Best Response = SD** provided minimum criteria for SD duration is met at the first time point; otherwise **Best Response =PD.**
11	PD	CR, PR, SD, PD, NE	**Best Response = PD.**
12	NE	CR, PR, SD, NE	**Best Response = NE.**
13	NE	PD	**Best Response = PD.**
14	CR, PR, SD	No 2nd visit	**Best Response = SD** provided minimum criteria for SD duration is met at first time point; otherwise **Best Response = NE.**
15	PD	No 2nd visit	**Best Response = PD.**
16	NE	No 2nd visit	**Best Response = NE.**

CR = complete response, PR = partial response, SD = stable disease, PD = progressive disease, NE = not evaluable.

Note: If response = SD, CR, or PR at the initial post-treatment assessment then, in meeting the minimum criteria for SD duration (only SD, not CR or PR), duration is measured from the treatment start date rather than the date of the assessment.

Note: In some situations, it may be necessary to check across more than two sequential time points in order to determine whether or not a minimum duration criteria has been met. The same logic as used for the pairs of time points should be applied. For example, for the triplet SD CR SD, duration is calculated from the first assessment date (or from the treatment start date if these are the initial assessments) to the third assessment date, if needed, to determine whether the minimum criteria for SD duration has been met.

Per the RECIST guidance and as indicated in the first table note, for patients with SD at the first time point: in determining whether the minimum criteria for SD duration is met, duration is measured from the treatment start date to that first assessment date. Then, if the duration meets the minimum interval requirement for SD, **Best Response = SD**, otherwise **Best Response = NE**. Further, as indicated in the note, this same rule is also applied to patients with a response better than SD at the first time point.

In some situations, it may be necessary to check across more than two sequential time points in order to determine whether or not a minimum duration criteria has been met. The same logic as used for the pairs of time points should be applied. For example, note the following examples.

- For the triplet SD CR/PR/SD SD, duration is calculated from the first assessment date (or from the treatment start date if these are the initial assessments) to the third assessment date, if needed, to determine whether the minimum criteria for SD duration has been met. If it is met, then **Best Response = SD**. Otherwise, **Best Response = NE.**
- For the triplet CR NE CR, if the minimum criteria for CR duration is met for the interval between the two CR assessments, then **Best Response = CR**. Otherwise **Best Response = NE**.
- For the triplet PR NE PR, if the minimum interval criteria for PR is met for the interval between the two PR assessments, then **Best Response = PR**. Otherwise **Best Response = NE**.
- For the triplet SD NE SD, **Best Response = NE**.

The minimum interval for confirmation of CR and PR is 4 weeks—the minimum of the range suggested in RECIST. The minimum interval for duration of SD is 8 weeks (i.e. 49 days taking visit window of +/-7 days into consideration).

8.1.3 Best Overall Response

A Best Response is determined for each sequential pair of post-treatment time points (and in some cases, triplets of sequential time points) as indicated in the previous section, Section 8.1.2. Then, the Best Overall Response for a patient (when confirmation of CR and PR are required) is the best of these Best Responses.

8.2 Efficacy Variables

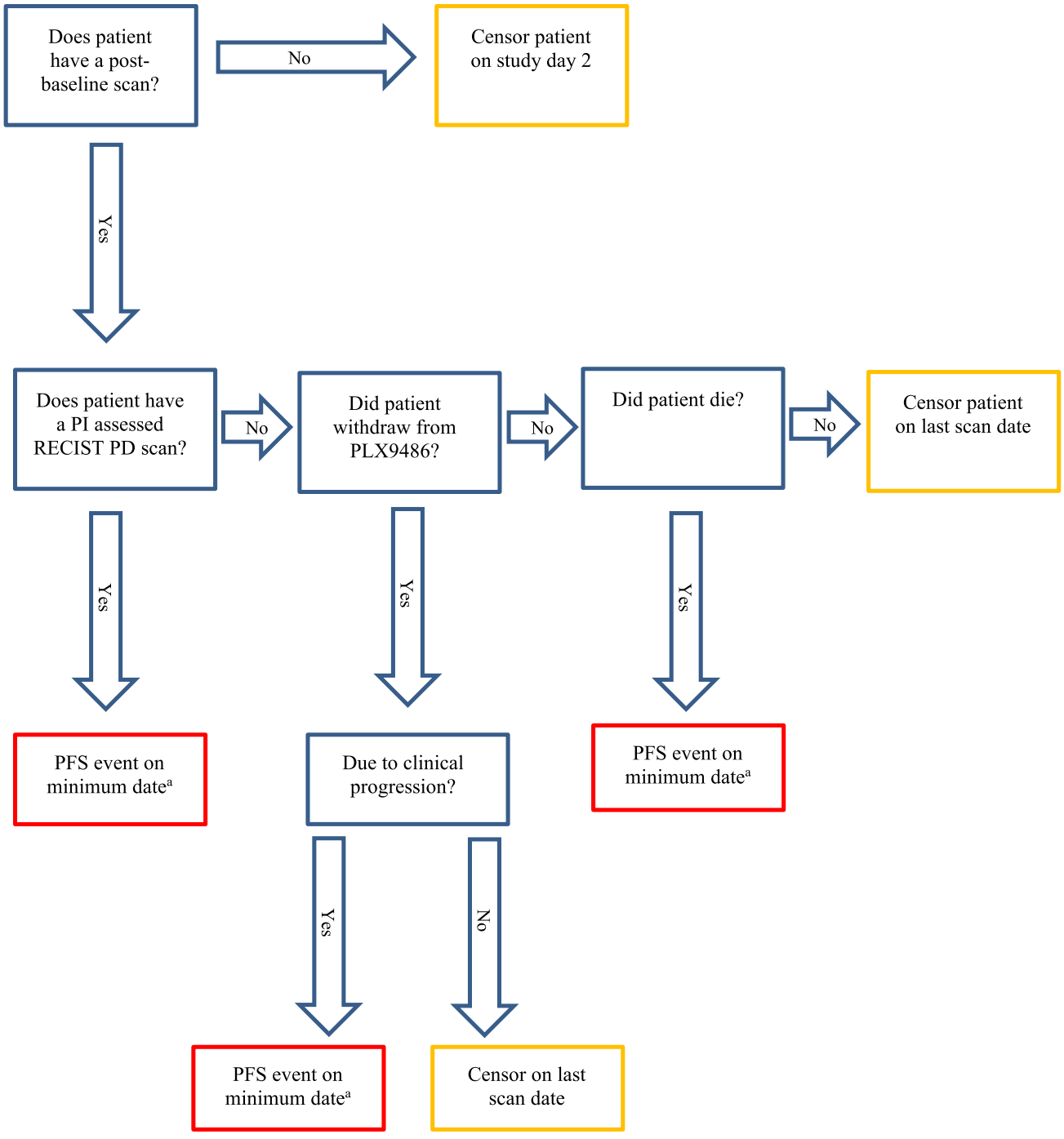
The efficacy variables for Part 1, Part 2b, and Part 2e are as follows.

- Response to treatment according to RECIST version 1.1.

- Best Overall Response is the best of the best responses (with confirmation), as detailed in the previous section
- ORR, defined as the number of patients who have a Best Overall Response of CR or PR divided by the total number of patients in the efficacy evaluable population.
- Progression-free Survival (PFS), defined as the number of days from the first day of treatment (C1D1) to the first documented PI assessment using RECIST criteria of disease progression/relapse or date of death prior to discontinuing treatment of PLX9486, whichever occurs first. The date of disease progression is earliest overall timepoint response of PI assessed PD as defined in Section 8.1.1. Patients without an assessment of disease progression/relapse who discontinue PLX9486 or discontinue from the study and indicate progressive disease or clinical progression as the primary reason for ending PLX9486 or study discontinuation will be counted as having progressed on their last dose date (if primary reason for ending treatment is progressive disease or clinical progression or death) or on their study exit date (if the primary reason for study exit is progressive disease or clinical progression or death). Patients who discontinue from the trial without having a post-baseline scan will be censored at study day 2. If disease progression/relapse/death does not occur and the patient does not discontinue PLX9486 due to clinical progression, PFS is censored as of the date of patient's last imaging exam of target or non-target lesions. See Figure 1 for a decision flowchart.
- 6-month PFS rate, defined as the number of patients with PFS of at least 180 days divided by the total number of patients in the efficacy evaluable population.
- DOR is calculated for every patient with a response to therapy and is defined as the number of days from the date of first response (PR or CR confirmed at least 28 days later) to the date of first documented disease progression/relapse or death, whichever occurs first. For the date of disease progression and the date censored, the same rules described as above for PFS are used.
- Clinical Benefit Rate: Patients are considered to experience clinical benefit if they have a Best Overall Response of SD that lasted for at least 16 weeks, or confirmed Best Overall Response of PR or CR. The Clinical Benefit Rate (CBR) is defined as the number of patients who have CBR divided by the total number of patients in the efficacy evaluable population.
- Overall Survival (OS), defined as the number of days from the first day of treatment (C1D1) until the date of death. If a patient is lost to follow-up, OS is censored at the date of last contact. Date of last contact is the latest dates among the visit dates recorded in the following CRF forms: Hematology, Chemistry, Coagulation, Urinalysis, Vital Signs, ECG, Physical Exam, Tumor Assessments (Target, Non-Target), and study drug dosing logs (PLX9486, PX3397, Sunitinib), Study Exit Status, Phone Interview where patient status is recorded as alive.
- 12-month OS rate, defined as the number of patients alive at 12 months (365 days) divided by the total number of patients in the efficacy evaluable population.
- Biomarkers in peripheral blood, in archival tumor tissue and in available tumor biopsies

Biomarker descriptive statistics is not in the scope of this SAP, except for the summary of tumor markers.

Figure 1 – PFS Decision Flowchart



PFS = Progression free survival; PI = Primary investigator; PD = Progressive disease.
Red boxes indicate PFS decision events. Magenta boxes indicate censored decision events.
[a] For events using a minimum date, the minimum of the dates of PD, withdrawal from PLX9486, and the death date if they exist is used as the date of the event.

8.3 Adjustments for Covariates

No adjustments for covariates are planned.

8.4 Handling of Dropouts or Missing Data

No imputations will be made for missing values except as noted in considering a NE response for determining timepoint response and Best Overall Response.

8.5 Interim Analysis and Data Monitoring

There are no planned interim analyses.

8.6 Examination of Subgroups

There are no planned subgroup efficacy analyses.

8.7 Multiple Comparison/Multiplicity

No adjustments for multiplicity or multiple testing will be made.

8.8 Multicenter Studies

There are no analyses planned to compare differences in response by site.

8.9 Methods of Efficacy Analysis

Patients' target lesion response, non-target lesion response, and appearance of new lesions at each time point, the overall tumor response at each time point and the Best Overall Response will be shown in listings. The target lesion assessment listing will also include change and percent change from baseline of the sum of the longest diameter from the target lesions. Nadir (the smallest sum of longest diameters of target lesions recorded since treatment started), change from nadir and the percent change from nadir will also be provided in this listing.

The number and percent of patients in each category of best overall response (CR, PR, SD, PD, and NE) will be summarized along with the ORR and CBR. Exact two-sided binomial 95% confidence intervals (CIs) will be provided for each category response and the ORR and CBR. 6-month PFS rate and 12-month OS rates will be summarized by dose cohorts and overall and the two-sided, exact binomial 95% confidence interval for these rates will be provided.

OS, PFS and DOR (in days) will be estimated using Kaplan-Meier method. The number and percentages of patients who progressed or died and who did not, will be summarized by cohort and overall. The Kaplan-Meier estimate of the 25th, median and 75th percentiles and their two-sided 95% confidence intervals will be presented by study part, dose cohort and overall. Range of DOR and PFS for all patients and for patients who progressed or died will also be presented by study part, dose cohort and overall.

Cox proportional hazards regression may be used to perform exploratory post-hoc analyses to investigate the contributions of various factors to OS, PFS and DOR.

A figure of PFS by Study Part and Cohort will also be provided.

9. PHARMACOKINETIC ANALYSES

A separate formal PK report will be written for inclusion in the final study report. Synteract is not responsible for PK analysis.

10. PHARMACODYNAMIC ANALYSES

Exploratory PD parameters will be analyzed appropriately (if samples are available). No formal statistical analysis of pharmacodynamics endpoints will be performed.

The exploratory PD endpoints of Part 1, Part 2b, and Part 2e of this study includes biomarkers in peripheral blood, in archival tumor tissue, and in available tumor biopsies. Patients with collected tumor marker sample will be listed by cohort and patient and display the collection date, collection time, test type, and result (in units).

Synteract is not responsible for PD analysis.

11. SAFETY ANALYSES

All safety analyses will be based on the safety population and summarized for each dose escalation cohort Safety variables to be assessed will include AEs, laboratory test results (hematology, serum chemistry, and urinalysis), ECGs, weight, and vital signs.

11.1 Extent of Exposure

Summary of duration for each study drug and total dose taken (mg) will be summarized by study part, cohort, and overall. Duration of treatment for each study drug (PLX9486, PLX3397 and sunitinib) is defined as the last dose date of that study drug minus the first dose date of that study drug plus 1. The overall duration of treatment is defined as the last dose date of any study drug (PLX9486, PLX3397, sunitinib) minus the first dose date of any study drug (PLX9486, PLX3397, sunitinib) plus 1.

Drug administration and accountability will be presented in data listings.

11.2 Adverse Events

An adverse event (AE) is any untoward medical occurrence in a patient administered a pharmaceutical product, which does not necessarily have a causal relationship with the treatment. An AE can be any unfavorable and unintended sign (e.g., including an abnormal laboratory finding), symptom, or disease temporally associated with the use of the study drug, whether or not it is considered to be study drug related. This includes any newly occurring event or previous condition that has increased in severity or frequency since the administration of study drug. An AE includes, but is not limited to, the following:

- Any clinically significant worsening of a preexisting condition.

- An AE occurring from overdose (i.e., a dose higher than that indicated in the protocol) of a test article, whether accidental or intentional.
- An AE occurring from abuse (e.g., use for nonclinical reasons) of a study drug.
- An AE that has been associated with the discontinuation of the use of a study drug.

A serious adverse event (SAE) is an AE that:

- Results in death.
- Is life-threatening.
- Requires inpatient hospitalization longer than 24 hours or prolongation of existing hospitalization (see clarification in the protocol on planned hospitalizations). An emergency room visit without hospitalization is not considered a hospitalization.
- Results in persistent or significant disability or incapacity. Disability is defined as a substantial disruption of a person's ability to conduct normal life functions.
- Is a congenital anomaly or birth defect.
- Is an important medical event. An important medical event is an event that may not result in death, be life-threatening, or require hospitalization but may be considered an SAE when, based upon appropriate medical judgment, it may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes listed in the definitions for SAEs.

All AE summaries will be restricted to TEAEs, which are defined as those AEs that occurred on or after dosing, and those existing AEs that worsened during the study. Furthermore, an AE is not considered treatment emergent if it is not treatment related and its onset is more than 28 days after the last dose of study drug. If it cannot be determined whether the AE is treatment emergent due to a partial onset date then it will be counted as such. See Appendix 1 for handling of partial dates for AEs. Verbatim terms on case report forms will be mapped to preferred terms and system organ classes using the Medical Dictionary for Regulatory Activities (MedDRA) v18.0.

Each AE summary will be displayed by cohort and overall. Summaries that are displayed by system organ class and preferred terms will be ordered by descending order of incidence of system organ class and preferred term within each system organ class. Summaries of the following types will be presented.

Summaries of treatment-related TEAEs include all events reported as "Possibly Related" or "Probably Related" to any of Study Treatment (PLX9486, PLX3397, and sunitinib). At each level of patient summarization, a patient is classified according to the closest relationship if the patient reported one or more events. AEs with a missing relationship are not included.

For summaries of TEAEs by highest severity, at each level of patient summarization a patient is classified according to the highest severity if the patient reported one or more events. AEs with missing severity are not included.

Summary tables will be produced for the following:

- Overall Summary of TEAEs, including summaries of total number of TEAEs, number of patients with at least one TEAE, number of patients with at least one treatment-emergent SAE, number of patients with at least one related TEAE, number of patients with at least one treatment-emergent related SAE, and number of patients with at least one TEAE leading to permanent withdrawal of study product (any of PLX9486, PLX3397, and sunitinib) or discontinuation from the study.
- Patient incidence of TEAEs by MedDRA system organ class and preferred term.
- Patient incidence of TEAEs by preferred term and highest severity grade orderd by descending order of the overall count of TEAEs
- Patient incidence of treatment-related TEAEs by preferred term and highest severity grade.
- Patient incidence of PLX9486-Related TEAEs by preferred term (Safety Population) and highest severity grade.
- Patient incidence of PLX3397-Related TEAEs by preferred term (Safety Population) and highest severity grade.
- Patient incidence of Sunitinib-Related TEAEs by preferred term (Safety Population) and highest severity grade.

AEs leading to permanent withdrawal of study drug or discontinuation from the study are defined as those having an action of "Drug Withdrawn" for any of study drugs (PLX9486, PLX3397, and sunitinib), or primary AEs associated with records from the CRF forms 'End of Treatment' or 'Study Exit Status' where the reason for end of treatment or for study exit is 'Adverse Event'. Listings of all AEs, SAEs, AEs leading to changes in study treatment, AEs leading to death, and dose limiting toxicity will be provided. Summary listing of deaths will also be provided.

11.3 Clinical Laboratory Evaluation

Laboratory results (hematology and coagulation tests, serum chemistry) will be summarized by study part, cohort and overall using descriptive statistics at baseline and at each scheduled post-baseline time point. Changes from baseline of laboratory results will also be summarized by study part, cohort and overall.

Select laboratory analytes will be graded according to National Cancer Institute CTCAE as shown in Appendix 2. The worst scheduled post-baseline CTCAE grade for each analyte will be summarized by study part, cohort and overall in shift tables to assess changes from baseline for applicable hematology and coagulation analytes (WBC, hemoglobin, lymphocytes, platelets, ANC, aPTT and INR) and applicable chemistry analytes (ALT, AST, alkaline phosphatase, direct bilirubin, total bilirubin, creatinine and phosphorus). In the hematology shift table, the following analytes will have a shift table for high and low grading: WBC, hemoglobin, and lymphocytes. Laboratory results (hematology, serum chemistry, urinalysis, and coagulation tests) will be presented in data listings. Abnormal values will be flagged as high or low relative to the local lab normal ranges, where applicable. Values that are deemed as abnormal, clinically significant (as collected on the CRF) will also be flagged. CTCAE v4.03 grades are included in these listings where applicable. In addition, listings of hematology results and chemistry results with CTCAE grade 3 or higher will be provided.

11.4 Vital Signs

The baseline value is defined as the last non-missing value obtained before the date and time of the first dose of any study drug or on pre-dose timepoint of the first dose date of any study drug.

Vital signs (heart rate, respiratory rate, blood pressure, temperature and weight) will be summarized by cohort using descriptive statistics at baseline and at each scheduled post-baseline time point. Changes from baseline will also be summarized.

A listing of vital signs will be provided.

11.5 Physical Examination

Physical examination findings will be included in a data listing only.

11.6 Electrocardiogram

The ECG data analysis will be conducted based on methodology recommended in the International Conference on Harmonization E14 guidance, The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-antiarrhymic Drugs [2].

To compensate for the effect of heart rate on QT interval, heart rate corrections will be computed for each observed QT interval using Fridericia's correction (QTcF) and will be included in the data listings. QT is the unadjusted QT interval in milliseconds and RR is the RR interval in milliseconds. The RR interval will be calculated from heart rate using the following formula:

- RR (milliseconds) = 60*1000 / [heart rate in beats per minute]

Then, the definitions of the heart-rate corrected QT intervals (in milliseconds) are:

- $QTcF = QT / [(RR/1000)^{1/3}]$ or, equivalently, $QT / [(60/\text{heart rate})^{1/3}]$

where, again, heart rate is in beats per minute.

Triplicate ECG measurements are collected. The average value of the ECG triplicates for ECG parameters (heart rate, pulse rate, RR, QRS, QT, and QTcF) will be summarized using descriptive statistics at baseline and at each scheduled post-baseline time point. Changes from baseline of the average values of the ECG triplicates will also be summarized. The derived RR and QTcF will be used in this summary. A one-sided upper 95% CI will be included for each change from baseline time point for QTcF.

The derived RR and QTcF values and the collected values in the eCRF for other ECG parameters will be displayed in a data listing. In addition, change from baseline in the derived QTcF will also be included in this listing. Outlier QTc values are those that meet at least one of the following criteria: (1) QTcF $\geq$ 450 msec (for males) or $\geq$ 470 msec (for females) or (2) increase from baseline in QTcF >30 msec. A summary of the number and percentage of patients who experience outlier QTc values will be summarized by cohort. The individual patient QTc data meeting the outlier criteria described above flagged in the data listing.

11.7 Eastern Cooperative Oncology Group (ECOG)

Eastern Cooperative Oncology Group (ECOG) performance data will be summarized using a shift table to assess changes from baseline for each cohort. ECOG data will be presented in a patient listing for all patients.

11.8 Other Collected Samples

Other selected disease related samples which were collected will be slisted including circulating DNA samples, tumor marker samples, archival tumor tissue collection, and optional paired tumor biopsy collection

8. CHANGES TO PROTOCOL-SPECIFIED ANALYSES

The Efficacy Evaluable population will include patients that discontinued treatment due to disease progression or died prior to having a post-baseline assessment.

Analyses for the exploratory objective to assess tumor response in the Part 2 cohorts by Choi's criteria will not be conducted.

PK and PD analyses (including the specification of window timing of PK and PD measurements) are not covered in this document.

The RR value derived from heart rate will be used in any derivations (eg, in the derivation of QTcF) rather than the value collected on the eCRF. Further, the derived QTcB and QTcF values rather than the QTcB and QTcF values collected in the eCRF will be used for all analyses.

REFERENCES

1. National Cancer Institute Common Terminology Criteria for Adverse Events v4.03, NCI, NIH, DHHS, June 14, 2010, NIH publication # 09-7473.
2. Guidance for Industry E14 The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-antiarrhythmic Drugs, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), October 2005.

APPENDIX 1: PARTIAL DATE CONVENTIONS

Imputed dates will NOT be presented in the listings.

Algorithm for Treatment Emergence of Adverse Events

Start Date	Stop Date	Action
Known	Known/Partial/Missing	If start date < study med start date, then not TEAE; If start date ≥ study med start date and (start date ≤ (study med end date + 28) or related), then TEAE.
Partial, but known components show that it cannot be on or after study med start date	Known/Partial/Missing	Not TEAE
Partial, could be on or after study med start date	Known	If stop date < study med start date, then not TEAE; If stop date ≥ study med start date, then TEAE.
	Partial	Impute stop date as latest possible date (i.e. last day of month if day is unknown or 31 December if day and month are unknown), then: If stop date < study med start date, then not TEAE; If stop date ≥ study med start date, then TEAE.
	Missing	Assumed TEAE
Missing	Known	If stop date < study med start date, then not TEAE; If stop date ≥ study med start date, then TEAE.
	Partial	Impute stop date as latest possible date (i.e. last day of month if day is unknown or 31 December if day and month are unknown), then: If stop date < study med start date, then not TEAE; If stop date ≥ study med start date, then TEAE.
	Missing	Assumed TEAE

Algorithm for Prior/Concomitant Medications

Start Date	Stop Date	Action
Known	Known/Partial/Missing	If start date < study med start date, then assign as prior; If start date ≥ study med start date and start date ≤ end of treatment (latest last dose of any study medication), then assign as concomitant
Partial	Known/Partial/Missing	Impute start date as earliest possible date (i.e. first day of month if day is unknown or 1st January if day and month are unknown), then: If start date < study med start date, then assign as prior; If start date ≥ study med start date and start date ≤ end of treatment, then assign as concomitant
Missing	Known	If stop date < study med start date, then assign as prior; If stop date ≥ study med start date, then assign as concomitant
	Partial	Impute stop date as latest possible date (i.e. last day of month if day is unknown or 31 December if day and month are unknown), then: If stop date < study med start date, then assign as prior; If stop date ≥ study med start date, then assign as concomitant
	Missing	Assign as concomitant

APPENDIX 2: CTCAE TOXICITY GRADES FOR LABORATORY ANALYTES

CTCAE Toxicity Grades: Hematology and Coagulation

Analyte	Standard Unit	Directional Change	Toxicity Grades (CTCAE v4.03)
Hemoglobin[1]	g/dL	Decrease	Grade 1: < LLN – 10.0 g/dL Grade 2: < 10.0 – 8.0 g/dL Grade 3: < 8.0 Grade 4: Not defined
		Increase	Grade 1: > ULN – (2+ULN) g/dL Grade 2: > (2+ULN) – (4+ULN) g/dL Grade 3: > 4+ULN g/dL Grade 4: Not defined
ANC	x10^9/L	Decrease	Grade 1: < LLN – 1.5 x10^9/L Grade 2: < 1.5 – 1.0 x10^9/L Grade 3: < 1.0 – 0.5 x10^9/L Grade 4: < 0.5 x10^9/L
Platelets	x10^9/L	Decrease	Grade 1: < LLN – 75.0 x10^9/L Grade 2: < 75.0 – 50.0 x10^9/L Grade 3: < 50.0 – 25.0 x10^9/L Grade 4: < 25.0 x10^9/L
WBC	x10^9/L	Decrease	Grade 1: < LLN – 3.0 x10^9/L Grade 2: < 3.0 – 2.0 x10^9/L Grade 3: < 2.0 – 1.0 x10^9/L Grade 4: < 1.0 x10^9/L
		Increase	Grade 1: Not defined Grade 2: Not defined Grade 3: >100 x10^9/L Grade 4: Not defined
Lymphocytes	x10^9/L	Decrease	Grade 1: < LLN – 0.8 x10^9/L Grade 2: < 0.8 – 0.5 x10^9/L Grade 3: < 0.5 – 0.2 x10^9/L Grade 4: < 0.2 x10^9/L
	x10^9/L	Increase	Grade 1: Not defined Grade 2: >4.0 – 20.0 x10^9/L Grade 3: >20.0 x10^9/L Grade 4: Not defined
aPTT	sec	Increase	Grade 1: >ULN – 1.5 x ULN Grade 2: >1.5 – 2.5 x ULN Grade 3: >2.5 x ULN Grade 4: Not defined
INR	No units	Increase	Grade 1: >ULN – 1.5 x ULN Grade 2: >1.5 – 2.5 x ULN Grade 3: >2.5 x ULN Grade 4: Not defined

LLN=lower limit of normal; ULN=upper limit of normal. The LLN and ULN for each analyte will be determined from the normal range of each local laboratory.

Analyte	Standard Unit	Directional Change	Toxicity Grades (CTCAE v4.03)
[1] For increased hemoglobin results, if the baseline value is above the ULN, the baseline value will be used instead of the ULN to assess grades 1, 2, and 3.			

CTCAE Toxicity Grades: Serum Chemistry

Analyte	Standard Unit	Directional Change	Toxicity Grades (CTCAE v4.03)
Albumin	g/dL	Decrease	Grade 1: < LLN – 3.0 g/dL Grade 2: < 3.0 – 2.0 g/dL Grade 3: < 2.0 g/dL Grade 4: Not defined
Alkaline Phosphatase	U/L	Increase	Grade 1: > ULN – 2.5 x ULN Grade 2: > 2.5 – 5.0 x ULN Grade 3: > 5.0 – 20.0 x ULN Grade 4: > 20.0 x ULN
ALT (SGPT)	U/L	Increase	Grade 1: > ULN – 3.0 x ULN Grade 2: > 3.0 – 5.0 x ULN Grade 3: > 5.0 – 20.0 x ULN Grade 4: > 20.0 x ULN
AST (SGOT)	U/L	Increase	Grade 1: > ULN – 3.0 x ULN Grade 2: > 3.0 – 5.0 x ULN Grade 3: > 5.0 – 20.0 x ULN Grade 4: > 20.0 x ULN
Calcium	mg/dL	Decrease	Grade 1: < LLN – 8.0 mg/dL Grade 2: < 8.0 – 7.0 mg/dL Grade 3: < 7.0 – 6.0 mg/dL Grade 4: < 6.0 mg/dL
		Increase	Grade 1: >ULN – 11.5 mg/dL Grade 2: >11.5 – 12.5 mg/dL Grade 3: >12.5 – 13.5 mg/dL Grade 4: >13.5 mg/dL
Creatinine	mg/dL	Increase	Grade 1: > ULN – 1.5 x ULN Grade 2: > 1.5 – 3.0 x ULN Grade 3: > 3.0 – 6.0 x ULN Grade 4: > 6.0 x ULN
Creatine Phosphokinase (CPK)	U/L	Increase	Grade 1: >ULN - 2.5 x ULN Grade 2: >2.5 x ULN - 5 x ULN Grade 3: >5 x ULN - 10 x ULN Grade 4: >10 x ULN
Direct Bilirubin	mg/dL	Increase	Grade 1: > ULN – 1.5 x ULN Grade 2: >1.5 – 3.0 x ULN Grade 3: >3.0 – 10.0 x ULN Grade 4: >10.0 x ULN
Total Bilirubin	mg/dL	Increase	Grade 1: > ULN – 1.5 x ULN Grade 2: >1.5 – 3.0 x ULN Grade 3: >3.0 – 10.0 x ULN Grade 4: >10.0 x ULN
Glucose	mg/dL	Decrease	Grade 1: < LLN – 55 mg/dL Grade 2: < 55 – 40 mg/dL Grade 3: < 40 – 30 mg/dL

Analyte	Standard Unit	Directional Change	Toxicity Grades (CTCAE v4.03)
			Grade 4: < 30 mg/dL
		Increase	Grade 1: > ULN – 160 mg/dL
			Grade 2: > 160 – 250 mg/dL
			Grade 3: > 250 – 500 mg/dL
			Grade 4: > 500 mg/dL
Magnesium	mg/dL	Decrease	Grade 1: <LLN - 1.2 mg/dL
			Grade 2: <1.2 - 0.9 mg/dL
			Grade 3: <0.9 - 0.7 mg/dL
			Grade 4: <0.7 mg/dL;
		Increase	Grade 1: >ULN - 3.0 mg/dL
			Grade 2: Not defined
			Grade 3: >3.0 - 8.0 mg/dL
			Grade 4: >8.0 mg/dL
Phosphorus	mg/dL	Decrease	Grade 1: < LLN – 2.5 mg/dL
			Grade 2: < 2.5 – 2.0 mg/dL
			Grade 3: < 2.0 – 1.0 mg/dL
			Grade 4: < 1.0 mg/dL
Potassium	mmol/L	Decrease	Grade 1: < LLN – 3.0 mmol/L
			Grade 2: Not defined
			Grade 3: < 3.0 – 2.5 mmol/L
			Grade 4: < 2.5 mmol/L
	mmol/L	Increase	Grade 1: > ULN – 5.5 mmol/L
			Grade 2: > 5.5 – 6.0 mmol/L
			Grade 3: > 6.0 – 7.0 mmol/L
			Grade 4: > 7.0 mmol/L
Sodium	mmol/L	Decrease	Grade 1: < LLN – 130 mmol/L
			Grade 2: Not defined
			Grade 3: < 130 – 120 mmol/L
			Grade 4: < 120 mmol/L
		Increase	Grade 1: > ULN – 150 mmol/L
			Grade 2: > 150 – 155 mmol/L
			Grade 3: > 155 – 160 mmol/L
			Grade 4: > 160 mmol/L
Uric Acid	mg/dL	Increase	Grade 1: >ULN – 10 mg/dL
			Grade 2: Not defined
			Grade 3: Not defined
			Grade 4: >10 mg/dL

LLN=lower limit of normal; ULN=upper limit of normal. The LLN and ULN for each analyte will be determined from the normal range of each local laboratory.

APPENDICES

Appendix A: List of Tables, Figures, and Listings

List of Tables

ICH Heading	Table Number	Table Description
14.1		**Demographics**
	14.1.1	Summary of Patient Disposition (All Patients)
	14.1.2	Summary of Demographic and Baseline Characteristics (Safety Population)
	14.1.3	Summary of Medical History (Safety Population)
	14.1.4	Summary of Prior Medications (Safety Population)
	14.1.5	Summary of Concomitant Medications (Safety Population)
14.2		**Efficacy**
	14.2.1	Best Overall Tumor Response (Efficacy Evaluable Population)
	14.2.2	Duration of Response (Efficacy Evaluable Population)
	14.2.3	Progression-Free Survival (Efficacy Evaluable Population)
	14.2.4	Overall Survival (Efficacy Evaluable Population)
14.3		**Safety**
14.3.1		**Adverse Events**
	14.3.1.1	Overall Summary of Treatment-Emergent Adverse Events (Safety Population)
	14.3.1.2	Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term (Safety Population)
	14.3.1.3	Summary of Treatment-Emergent Adverse Events by System Organ Class and Severity Grade (Safety Population)
	14.3.1.4.1	Summary of Any Drug-Related Treatment-Emergent Adverse Events by Preferred Term and Severity Grade (Safety Population)
	14.3.1.4.2	Summary of PLX9486-Related Treatment-Emergent Adverse Events by Preferred Term and Severity Grade (Safety Population)
	14.3.1.4.3	Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relatedness (Safety Population)
14.3.2		**Listings of Deaths, Other Serious and Significant Adverse Events**
	14.3.2.1	Summary Listing of Deaths
	14.3.2.2	Summary Listing of Serious Adverse Events (Safety Population)
Other Safety		**Laboratory**
	14.3.4.1.1	Summary of Hematology and Coagulation by Cycle and Day (Safety Population)
	14.3.4.1.2	Summary of Hematology and Coagulation - CTCAE Shift from Baseline (Safety Population)
	14.3.4.2.1	Summary of Serum Chemistry by Cycle and Day (Safety Population)
	14.3.4.2.2	Summary of Serum Chemistry - CTCAE Shift from Baseline (Safety Population)
		Exposure
	14.3.5.1	Summary of PLX9486 Exposure (Safety Population)
	14.3.5.2	Summary of PLX3397 Exposure (Safety Population)
	14.3.5.3	Summary of Sunitinib Exposure (Safety Population)
		Other Data
	14.3.6	Summary of Vital Signs (Safety Population)
	14.3.7.1	Summary of Electrocardiogram (Safety Population)
	14.3.7.2	Summary of Electrocardiogram – Abnormal QTcF Results (Safety Population)
	14.3.8	Summary of ECOG – Shift from Baseline (Safety Population)

List of Figures

ICH Heading	Table Number	Table Description
	14.2.1	Progression-Free Survival by Study Part – Study Part 1 (Efficacy Evaluable Population)

Listings

ICH Heading	Listing Number	Listing Description	CRF Form(s)
16.2		**PATIENT DATA LISTINGS**	
16.2.1		**Discontinued patients**	
	16.2.1.1	Patient Disposition	Study Exit Status, End of Treatment, Demographics
16.2.2		**Demographics and Baseline Characteristics**	
	16.2.2.1	Demographics and Baseline Characteristics	Demographics, Vital Signs
	16.2.2.2	Medical History	Medical History
	16.2.2.3.1	Primary Cancer History – Study Part 1	Primary Cancer History
	16.2.2.3.2	Primary Cancer History – Study Part 2	Primary Cancer History – Part 2
	16.2.2.4	Prior Treatment for Primary Malignancy	Prior Treatment for Primary Malignancy
	16.2.2.5	Prior and Concomitant Medications	Concomitant Medications
	16.2.2.6	Major Protocol Deviations	
16.2.3		**Study Drug Exposure**	
	16.2.3.1.1	PLX9486 Dosing Log	PLX9486 Study Drug Dosing Log
	16.2.3.1.2	PLX3397 Dosing Log	PLX3397 Study Drug Dosing Log
	16.2.3.1.3	Sunitinib Dosing Log	Sunitinib Study Drug Dosing Log
	16.2.3.2	Study Drug Accountability	Drug Accountability
	16.2.3.3.1	PLX9486 and Overall Exposure	Derived
	16.2.3.3.2	PLX3397 Exposure	Derived
	16.2.3.3.3	Sunitinib Exposure	Derived
16.2.4		**Individual efficacy response data**	
	16.2.4.1	Tumor Assessment (Target Lesions)	Tumor Evaluation - Target Lesions
	16.2.4.2	Tumor Assessment (Non-Target Lesions)	Tumor Evaluation - Non-Target Lesions Baseline; Tumor Evaluation - Non-Target Lesions
	16.2.4.3	Tumor Assessment (New Lesions)	Tumor Evaluation - New Lesions
	16.2.4.4	Tumor Response Assessment (Target and Non-Target Lesions)	Tumor Response Assessment
	16.2.4.5	Derived Efficacy Endpoints Based on Tumor Response	Derived
16.2.5		**Adverse Events Listings**	
	16.2.5.1	Adverse Events	Adverse Events
	16.2.5.2	Adverse Events Leading Changes in Study Treatment	Adverse Events; Study Exit Status; End of Treatment
	16.2.5.3	Dose Limiting Toxicity	Dose Limiting Toxicity
	16.2.5.4	Adverse Events Leading to Death	Adverse Events; Death Detail
16.2.6		**Individual Laboratory Measurements**	
	16.2.6.1.1	Hematology	Hematology
	16.2.6.1.2	Hematology – Other Tests	Hematology
	16.2.6.1.3	Hematology Laboratory Results - Grade 3 or Higher	Hematology
	16.2.6.2.1	Chemistry	Chemistry
	16.2.6.2.2	Chemistry – Other Tests	Chemistry
	16.2.6.2.3	Chemistry Laboratory Results - Grade 3 or Higher	Chemistry
	16.2.6.3.1	Urinalysis	Urinalysis
	16.2.6.3.2	Urinalysis – Other Tests	Urinalysis
	16.2.6.4.1	Coagulation	Coagulation
	16.2.6.4.2	Coagulation – Other Tests	Coagulation
16.2.7		**Other Data**	
	16.2.7.1	Vital Signs	Vital Signs
	16.2.7.2	Physical Examination	Physical Examination

	16.2.7.3.1	12-Lead Electrocardiogram	12-Lead ECG, Pre and Post Dose 12-Lead ECG, Post Dose 12-Lead ECG, 12-Lead ECG – 3 Recordings, 12-Lead ECG (Pre/3hr Post Dose), 12-Lead ECG (Pre/Post Dose), 12-Lead ECG (Pre/3&6hr Post Dose) 3 Recordings
	16.2.7.3.2	Electrocardiogram - Patients with Outlier QTc Values	12-Lead ECG, Pre and Post Dose 12-Lead ECG, Post Dose 12-Lead ECG, 12-Lead ECG – 3 Recordings, 12-Lead ECG (Pre/3hr Post Dose), 12-Lead ECG (Pre/Post Dose), 12-Lead ECG (Pre/3&6hr Post Dose) 3 Recordings
	16.2.7.4	ECOG Performance Status Assessment	Physical Examination
	16.2.7.5	Echocardiogram/MUGA Scan	Echocardiogram/MUGA Scan
	16.2.7.6	Thyroid Stimulating Hormone (TSH) Level	Thyroid Stimulating Hormone (TSH) Level
	16.2.7.7	Pregnancy Test	Pregnancy Test
	16.2.7.8.1	Circulating DNA	Circulating DNA
	16.2.7.8.2	Tumor Markers	Tumor Markers
	16.2.7.8.3	Archival Tumor Tissue Collection	Archival Tumor Tissue Collection
	16.2.7.8.4	Optional Paired Tumor Biopsy	Optional Paired Tumor Biopsy

Appendix B: Table Layouts

Notes to programmer:

(1) Sponsor, protocol, and footnotes will appear on all pages of all Study Parts. For all tables, the mock shells outline layout for Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) if the layout is the same for all study parts. The remainder of the table will follow the same format for other Study Parts, unless specified otherwise in the mocks. For an example of a mock with all the study parts, see Table 14.1.1 – Summary of Patient Disposition. Study Parts to be presented are:

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

Column headers under Study Part 1 are: '250 mg QD PLX9486', '350 mg QD PLX9486', '500 mg QD PLX9486', '1000 mg QD PLX9486', '500 mg BID PLX9486' , 'Total'

Study Part 2b – Dose Extension Study Parts (PLX9486 Combined with PLX3397)
Column headers under Study Part 2b are:

'500 mg QD PLX9486 + 600 mg PLX3397 fasting', '500 mg QD PLX9486 + 600 mg PLX3397 non-fasting', 'Total'

Study Part 2e – Dose Extension Study Parts (PLX9486 Combined with Sunitinib)
Column headers under Study Part 2e are:

'500mg QD PLX9486 + 25mg Sunitinib', '1000mg PLX9486 + 25 mg Sunitinib', '1000mg PLX9486 + 37.5 mg Sunitinib', 'Total'

Overall (Study Part 1, 2b and 2e)
Column header under Overall is 'Total'
Note that the Overall part contains only 1 column, column 'Total'

(2) To present the results of xx (xx.x), if the count is 0, do not include the percent information, i.e. only present 0.
(3) When the percentage is 100%, display the result as "100", no decimal place, e.g. xx (100)
(4) 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.
(5) If a statistic is missing (e.g. standard deviation is missing when N=1 or 0, lmissing ower/upper bounds for confidence interval), display 'NA' for that statistics in the table and add 'NA = Not Applicable' to the abbreviation footnote (i.e. the last footnote if there is an abbreviation in the table title or body)

Table 14.1.1
Summary of Patient Disposition
All Patients

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

Description	250 mg QD ADSL.COHORTN (N = xx) n (%)	350 mg QD (N = xx) n (%)	500 mg QD (N = xx) n (%)	… (N = xx) n (%)	Total[2] (N = xx) n (%)
Patients Enrolled[1,2] ADSL.ENRLFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Safety Population[3] ADSL.SAFFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Efficacy Evaluable Population[4] ADSL.EEFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Reason for Study Discontinuation[5] ADSL.DCTERM					
Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Clinical Progression	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Non-Compliance with Study Treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physician Decision	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive Disease (Per RECIST)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol Deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Terminated by Sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Patient	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The following patients have missing primary reason for study discontinuation: patients ttt, zzz,
[1] Per protocol amendment 7, 30 patients were planned for Part 1, [redacted] 30 patients were planned for Part 2b, [redacted] 30 patients were planned for Part 2e [redacted]
[2]. Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column with reason for discontinuation based upon their second enrollment.
[3] All patients who received study medication.
[4] All patients who have taken at least 1 dose of study drug and have had at least 1 post-baseline tumor assessment or who discontinued study medication early due to Clinical Progression or Progressive Disease (Per RECIST).
[5] Based on primary reason for study completion/discontinuation from Study Exit Status form.
Reference: Listing 16.2.1.1.

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Table 14.1.1
Summary of Patient Disposition
All Patients

Study Part 2 ADSL.PARTN=3 and 6

Description	Part 2b[1] ADSL.PARTN=3 500 mg QD PLX9486 + 600 mg PLX3397 Fasting (N = xx) n (%)	Part 2b[1] ADSL.PARTN=3 500 mg QD PLX9486 + 600 mg PLX3397 Non-fasting (N = xx) n (%)	Total[1] (N = xx) n (%)
Patients Enrolled[1,2] ADSL.ENRLFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)
Safety Population[3] ADSL.SAFFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)
Efficacy Evaluable Population[4] ADSL.EEFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Reason for Study Discontinuation[5] ADSL.DCTERM	xx (xx.x)	xx (xx.x)	xx (xx.x)
Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)
Clinical Progression	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)
Non-Compliance with Study Treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physician Decision	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive Disease (Per RECIST)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol Deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Terminated by Sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Patient	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The following patients have missing primary reason for study discontinuation: patients ttt, zzz,
[1] Per protocol amendment 7, 30 patients were planned for Part 1, [redacted] 30 patients were planned for Part 2b, [redacted] 30 patients were planned for Part 2e [redacted]
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
[3] All patients who received study medication.
[4] All patients who have taken at least 1 dose of study drug and have had at least 1 post-baseline tumor assessment or who discontinued study medication early due to Clinical Progression or Progressive Disease (Per RECIST).
[5] Based on primary reason for study completion/discontinuation from Study Exit Status form.
Reference: Listing 16.2.1.1.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Table 14.1.1
Summary of Patient Disposition
All Patients

Study Part 2 ADSL.PARTN=3 and 6

Description	Part 2e ADSL.PARTN=6			
	500 mg QD PLX9486 + 25 mg Sunitinib (N = xx) n (%)	1000mg PLX9486 + 25 mg Sunitinib (N = xx) n (%)	1000mg PLX9486 + 37.5 mg Sunitinib [1] (N = xx) n (%)	Total[1] (N = xx) n (%)
Patients Enrolled[1,2] ADSL.ENRLFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Safety Population[3] ADSL.SAFFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Efficacy Evaluable Population[4] ADSL.EEFL=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Primary Reason for Study Discontinuation[5] ADSL.DCTERM	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Adverse Event	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Clinical Progression	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Death	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to Follow-up	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Non-Compliance with Study Treatment	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Physician Decision	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Progressive Disease (Per RECIST)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol Deviation	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Study Terminated by Sponsor	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Withdrawal by Patient	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The following patients have missing primary reason for study discontinuation: patients ttt, zzz,
[1] Per protocol amendment 7, 30 patients were planned for Part 1, [redacted] 30 patients were planned for Part 2b, [redacted] 30 patients were planned for Part 2e [redacted]
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
[3] All patients who received study medication.
[4] All patients who have taken at least 1 dose of study drug and have had at least 1 post-baseline tumor assessment or who discontinued study medication early due to Clinical Progression or Progressive Disease (Per RECIST).
[5] Based on primary reason for study completion/discontinuation from Study Exit Status form.
Reference: Listing 16.2.1.1.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Plexxikon Inc. **Page 4 of 4**
Protocol PLX121-01

Table 14.1.1
Summary of Patient Disposition
All Patients

Overall (Study Parts 1, 2b and 2e) ADSL.PARTN=1,3,6

Description	Total[1] (N = xx) n (%)
Patients Enrolled[1,2] ADSL.ENRLFL=Y	xx (xx.x)
Safety Population[3] ADSL.SAFFL=Y	
Efficacy Evaluable Population[4] ADSL.EEFL=Y	xx (xx.x)
Primary Reason for Study Discontinuation[5] ADSL.DCTERM	
Adverse Event	xx (xx.x)
Clinical Progression	xx (xx.x)
Death	xx (xx.x)
Lost to Follow-up	xx (xx.x)
Non-Compliance with Study Treatment	xx (xx.x)
Physician Decision	xx (xx.x)
Progressive Disease (Per RECIST)	xx (xx.x)
Protocol Deviation	xx (xx.x)
Study Terminated by Sponsor	xx (xx.x)
Withdrawal by Patient	xx (xx.x)
Other	xx (xx.x)

Note: The following patients have missing primary reason for study discontinuation: patients ttt, zzz,
[1] Per protocol amendment 7, 30 patients were planned for Part 1, [redacted] 30 patients were planned for Part 2b, [redacted] 30 patients were planned for Part 2e [redacted]
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
[3] All patients who received study medication.
[4] All patients who have taken at least 1 dose of study drug and have had at least 1 post-baseline tumor assessment or who discontinued study medication early due to Clinical Progression or Progressive Disease (Per RECIST).
[5] Based on primary reason for study completion/discontinuation from Study Exit Status form.
Reference: Listing 16.2.1.1.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.1.2
Summary of Demographic and Baseline Characteristics
Safety Population ADSL.SAFFL=Y

Description	Part 1 (N = xx) (n %)	Part 2b (N = x) (n %)	Part 2e (N = xx) (n %)	Overall [3] (N = xx) (n %)
Mean Age of Patients (years) [1] ADSL.AGE	xx.x	xx.x	xx.x	xx.x
Sex of Patients ADSL.SEX				
Female	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Male	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race of Patients [2] ADSL.RACE				
White	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or African American	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
American Indian or Alaska Native	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Multiple	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Unknown	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnic Origin of Patients ADSL.ETHNIC				
Not Hispanic or Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hispanic or Latino	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Unavailable	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: N = the number of patients assigned to the cohort.
[1] Age is calculated as of the date the informed consent is signed as (Date informed consent signed minus the date of birth (in days) divided by 365.25) rounded down to the closest year.
[2] Patients could mark more than one race.
[3] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
Reference: Listing 16.2.2.1.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.1.3
Summary of Medical History
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

Body System ADMH.MHCAT	250 mg QD ADSL.COHORTN (N = xx) n (%)	350 mg QD (N = xx) n (%)	500 mg QD (N = xx) n (%)	… (N = xx) n (%)	Total [1] (N = xx) n (%)
Ears/Nose/Throat	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Cardiovascular	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Respiratory	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Dermatological	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Musculoskeletal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Gastrointestinal	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Endocrine/Metabolic	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hepatic	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lymphatic	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Immunological	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Neurological	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Genitourinary/Reproductive	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Psychiatric	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Patients could mark more than one body system.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
Reference: Listing 16.2.2.2

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) ***Repeat for Study Part 2b, Study Part 2e, Overall (ADSL.PARTN=2, PARTN=3 for overall PARTN=1,3,6)***
2) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.1.4
Summary of Prior Medications ADCM.PRIORFL=Y
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

ATC Class / Generic Drug Name	250 mg QD ADSL.COHORTN (N = xx) n (%)	350 mg QD (N = xx) n (%)	500 mg QD (N = xx) n (%)	(N = xx) n (%)	Total [1] (N = xx) n (%)
Patients Receiving any Prior Medications ADCM.PMANYFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC Class 1 ADCM.PMATCFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 1 ADCM.PMGENFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
.					
ATC Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…					

Note: Prior medications are those that begin prior to the administration of study drug, even if they continue after dosing.
Note: Patients could report multiple medications; at each level of summation (overall, ATC class, generic drug name), patients reporting more than one medication are counted only once.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
Reference: Listing 16.2.2.5

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) ***Repeat for Study Part 2b, Study Part 2e, Overall (ADSL.PARTN=2, PARTN=3 for overall PARTN=1,3,6)***
2) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.1.5
Summary of Concomitant Medications ADCM.CONCOMFL=Y
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

ATC Class ADCM.CMCLAS / Generic Drug Name ADCM.CMDECOD	250 mg QD ADSL.COHORTN (N = xx) n (%)	350 mg QD (N = xx) n (%)	500 mg QD (N = xx) n (%)	(N = xx) n (%)	Total [1] (N = xx) n (%)
Patients Receiving any Concomitant Medications ADCM.CMANYFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
ATC Class 1 ADCM.CMATCFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 1 ADCM.CMGENFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
.					
ATC Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Generic Drug Name 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…					

Note: Concomitant medications are those which are taken at any time between the date of first dose and the date of last dose of any study medication. In cases where it is not possible to determine if a medication is concomitant, the medication is classified as concomitant.
Note: Patients could report multiple medications; at each level of summation (overall, ATC class, generic drug name), patients reporting more than one medication are counted only once.
Note: Concomitant medications are coded according to the 01 March, 2015 WHODrug Dictionary.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
Reference: Listing 16.2.2.5

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) ***Repeat for Study Part 2b, Study Part 2e, Overall (ADSL.PARTN=2, PARTN=3 for overall PARTN=1,3,6).***
2) ***Order by descending count of the Overall summary ATC and by descending count of generic drug name within ATC class in the Overall summary.***
3) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***

Plexxikon Inc.
Protocol PLX121-01

Table 14.2.1
Best Overall Tumor Response ADRS.PARAMCD=CBEST
Efficacy Evaluable Population ADSL.EEFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

	250 mg QD ADSL.COHORTN (N = xx) n (%)		350 mg QD (N = xx) n (%)		… (N = xx) n (%)		Total[4] (N = xx) n (%)	
	Response Rate	95% C.I [3]	Response Rate	95% C.I [3]	Response Rate	95% C.I [3]	Response Rate	95% C.I [3]
Best Overall Tumor Response [1]								
Complete Response (CR)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Partial Response (PR)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Stable Disease (SD)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Progressive Disease (PD)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Not Evaluable (NE)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Not Done [2]	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Best Overall Response Rate (CR or PR)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%
Best Clinical Benefit Rate (CR, PR or SD at 16 weeks)	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%	n (%)	xx.x%, xx.x%

[1] Response based on RECIST (Response Criteria Evaluation in Solid Tumors) guideline (version 1.1), with confirmation of CR and PR required.
[2] Three patients withdrew from the trial due to clinical progression without having a post-baseline scan. They are included in this row.
[3] The CI is the two-sided exact binomial 95% Confidence Interval.
[4] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. BOR for re-enrolled patients is included in their initial cohort analysis and the Overall analysis but not in the Part 2e analysis.
Reference: Listing 16.2.4.4

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) ***Repeat for Study Part 2b, Study Part 2e, Overall (ADSL.PARTN=2, PARTN=3 for overall PARTN=1,3,6)***
2) ***Include index [4] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
3) ***For the BOR analysis only include re-enrolled patients in the initial cohort they enrolled in. Do not include them in the Part 2e analysis or the Overall analysis.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.2.2
Duration of Response ADTTE.PARAMCD=DOR
Efficacy Evaluable Population ADSL.EEFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

	250 mg QD ADSL.COHORTN (N = xx)	350 mg QD (N = xx)	500 mg QD (N = xx)	(N = xx)	Total[2] (N = xx)
Total number of responders [n (%)]	n (%)	n (%)	n (%)	n (%)	n (%)
Number of responders who progressed or died [n (%)]	n (%)	n (%)	n (%)	n (%)	n (%)
Number of responders who did not progress or die (censored) [n (%)]	n (%)	n (%)	n (%)	n (%)	n (%)
Percentiles [95% CI] of DOR (days)[1]					
25th	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]
Median	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]
75th	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]
Range of DOR (All patients with response)	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
Range of DOR (All patients who Progressed or Died)	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x

Note: Responders are patients with best overall response of CR or PR. Response based on RECIST guideline (version 1.1), with confirmation of CR or PR required.
Note: DOR is calculated for every patient with a response to therapy as the number of days from the date of initial response (PR or CR) to the date of first documented disease progression or death, whichever occurs first. If disease progression or death does not occur, DOR is censored as of the date of their last post-baseline tumor response evaluation. Patients without a tumor response evaluation after responding to therapy have their event censored on the day after response with a duration of one day.
[1] Kaplan-Meier product-limit estimates.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. DOR for re-enrolled patients is included in their initial cohort analysis and the Overall analysis but not in the Part 2e analysis.
CR = Complete Response; DOR = Duration of Response; N/A = Not Applicable; PR = Partial Response; NE = Not Estimable.
Reference: Table 14.3.2.1, Listings 16.2.4.5

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) ***Repeat for Study Part 2b, Study Part 2e, Overall (ADSL.PARTN=2, PARTN=3 for overall PARTN=1,3,6)***
2) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
3) ***For the DOR analysis only include re-enrolled patients in the initial cohort they enrolled in. Do not include them in the Part 2e analysis or the Overall analysis.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.2.3
Progression-Free Survival ADTTE.PARAMCD=PFS
Efficacy Evaluable Population ADSL.EEFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

	250 mg QD ADSL.COHORTN (N = xx)	350 mg QD (N = xx)	500 mg QD (N = xx)	… (N = xx)	Total[2] (N = xx)
Number of patients who progressed or died [n (%)]	n (%)	n (%)	n (%)	n (%)	n (%)
Number of patients who did not progress or die (censored) [n (%)]	n (%)	n (%)	n (%)	n (%)	n (%)
Percentiles [95% CI] of PFS (days)[1]					
25th	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]
Median	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]
75th	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]
Range of PFS for all patients (days)	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
Range of PFS for patients who progressed or died (days)	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x	xx.x – xx.x
6-month PFS [1] Percent [95% CI] CALCULATED FROM PROC LIFETEST ADTTE.PARAM="PFS" estimated at 6 months	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]	xxx [xxx, xxx]

Note: PFS is defined as the number of days from the start of therapy (i.e., C1D1) to the date of first documented disease progression/relapse or death, whichever occurs first. If disease progression/relapse/death does not occur, PFS is censored as of the date of their last evaluable tumor assessment.
[1] Kaplan-Meier product-limit estimates. The 6-month time point is defined as 180 days for this analysis.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. PFS for re-enrolled patients is included in their initial cohort analysis and the Overall analysis but not in the Part 2e analysis.
Reference: Table 14.3.2.1, Listings 16.2.4.5

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:

1) ***Repeat for Study Part 2b, Study Part 2e, Overall (ADSL.PARTN=2, PARTN=3 for overall PARTN=1,3,6).***
2) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
3) ***For the PFS analysis only include re-enrolled patients in the initial cohort they enrolled in. Do not include them in the Part 2e analysis or the Overall analysis.***

Repeat Table 14.2.3 shell for:

Table 14.2.4, Overall Survival, Efficacy Evaluable Population ADTTE.PARAM=SURV

Programming note:

1) ***Replace 6-month PFS with 12-month OS, CALCULATED FROM PROC LIFETEST ADTTE.PARAM="SURV" estimated at 12 months.***
2) ***Update footnote [1] to be "Kaplan-Meier product-limit estimates. The 12-month time point is defined as 365 days for this analysis.".***
3) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
4) ***For the OS response re-enrolled patients will have their OS calculated only for their initial cohort, however OS will use the stop date from the second cohort as this is an indication of survival. OS for re-enrolled patients is included in their initial cohort analysis and the Overall analysis but not in the Part 2e analysis.***

Plexxikon Inc. Page 1 of 1
Protocol PLX121-01

Table 14.3.1.1
Overall Summary of Treatment-Emergent Adverse Events ADAE.TRTEMFL=Y
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

Adverse Event Category	250 mg QD ADSL.COHORTN (N = xx) n (%)	350 mg QD (N = xx) n (%)	500 mg QD (N = xx) n (%)	(N = xx) n (%)	Total[2] (N = xx) n (%)
Total Number of TEAEs	xx	xx	xx	xx	xx
Patients with at least one TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with at least one TE SAE ADAE.AESER=Y	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with at least one Related TEAE[1] ADAE.AREL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with at least one Related TE SAE[1] ADAE.AESER,ADAE.AREL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with at lease one TEAE leading to any changes in study treatment ADAE.TEIRWFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Patients with at least one TEAE leading to permanent withdrawal of study product or discontinuation from the study ADAE.TEWDFL	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Patients could report multiple events; for each summation, patients reporting more than one event are counted only once.
SAE = Serious Adverse Event; TE = Treatment-Emergent; TEAE = Treatment-Emergent Adverse Event.
[1] Relatedness refers to any TEAEs reported as "Possibly Related" or "Probably Related" to any study treatment the patient received.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.

Reference: Listing 16.2.5.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) ***Include index [1] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***

Table 14.3.1.2
Summary of Treatment-Emergent Adverse Events by System Organ Class and Preferred Term ADAE.TRTEMFL=Y
Safety Population ADSL.SAFFL=Y
ADSL.PARTN, COHORTN

	Part 1					Part 2b		Part 2e			
Treatment-Emergent Adverse Events[1] System Organ Class ADAE.AEBODSYS / Preferred Term ADAE.AEDECOD	250 mg QD PLX9486 (N=) n (%)	350 mg QD PLX9486 (N=) n (%)	500 mg QD PLX9486 (N=) n (%)	1000 mg QD PLX9486 (N=) n (%)	500 mg BID PLX9486[2] (N=) n (%)	500 mg QD PLX9486 + 600 mg PLX3397 fasting[2] (N=) n (%)	500 mg QD PLX9486 + 600 mg PLX3397 non-fasting (N=) n (%)	500 mg QD PLX9486 + 25 mg Sunitinib (N=) n (%)	1000 mg QD PLX9486 + 25 mg Sunitinib (N=) n (%)	1000 mg QD PLX9486 + 37.5 mg Sunitinib[2] (N=) n (%)	Overall[2] (N=) n (%)
Patients Reporting at Least One TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…											

Note: N = the number of patients assigned to the cohort.
Note: TEAEs are those with start dates on or after the treatment start date. Treatment start date is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose date of the run-in PK period. The TEAEs of patients who escalated to a higher dose are classified according to the patient's initial dose cohort.
Note: The denominator for the percentages is the number of patients (N) in the Safety Population.
Note: Adverse Events are coded using MedDRA v 23.0.
Note: System organ classes are listed in descending order based on the Total column; within each system organ class, preferred terms are listed in descending order based on the Total column.
[1] At each level of summation (overall, system organ class, preferred term), patients reporting more than one adverse event are counted only once.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = Treatment-Emergent Adverse Event.
Reference: Listing 16.2.5.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) Sort by descending SOC and PT within PT.

Table 14.3.1.3
Summary of Treatment-Emergent Adverse Events by Preferred Term and Severity Grade ADAE.TRTEMFL=Y
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

	250 mg QD ADSL.COHORTN (N =)		350 mg QD (N =)		500 mg QD (N =)		1000 mg QD (N =)		500 mg BID[2] (N =)		Total[2] (N =)	
Preferred Term [n (%)] ADAE.AEDECOD	Any Grade ADAE.ASEV	ADAE.GR3ANYFL=Y CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3
Patients Reporting at Least One TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
….												

Note: N = the number of patients assigned to the cohort.
Note: TEAEs are those with start dates on or after the treatment start date. Treatment start date is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose date of the run-in PK period. The TEAEs of patients who escalated to a higher dose are classified according to the patient's initial dose cohort.
Note: The denominator for the percentages is the number of patients (N) in the Safety Population.
Note: Adverse Events are coded using MedDRA v 23.0.
Note: Preferred terms are listed in descending order based on the Total column.
[1] At each level of summation (overall and preferred term), patients reporting more than one adverse event are counted only once.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = Treatment-Emergent Adverse Event.
Reference: Listing 16.2.5.1

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Output Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Table 14.3.1.3
Summary of Treatment-Emergent Adverse Events by Preferred Term and Severity Grade
Safety Population

Study Part 2b – Dose Extension Study Parts (PLX9486 Combined with PLX3397) ADSL.PARTN=3

	500 mg QD PLX9486 + 600 mg PLX3397 fasting[2] (N =)		500 mg QD PLX9486 + 600 mg PLX3397 non-fasting (N =)		Total[2] (N =)	
Preferred Term [n (%)]	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3
Patients Reporting at Least One TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
….						

Note: N = the number of patients assigned to the cohort.
Note: TEAEs are those with start dates on orafter the treatment start date. Treatment start date is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose date of the run-in PK period. The TEAEs of patients who escalated to a higher dose are classified according to the patient's initial dose cohort.
Note: The denominator for the percentages is the number of patients (N) in the Safety Population.
Note: Adverse Events are coded using MedDRA v 23.0.
Note: Preferred terms are listed in descending order based on the Total column.
[1] At each level of summation (overall and preferred term), patients reporting more than one adverse event are counted only once.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = Treatment-Emergent Adverse Event.
Reference: Listing 16.2.5.1

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Output Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Table 14.3.1.3
Summary of Treatment-Emergent Adverse Events by Preferred Term and Severity Grade
Safety Population

Study Part 2e – Dose Extension Study Parts (PLX9486 Combined with Sunitinib) ADAE.PARTN=6

	500 mg QD + 25mg Sunitinib (N =)		1000 mg QD + 25mg Sunitinib (N =)		1000 mg QD + 37.5mg Sunitinib[2] (N =)		Total[2] (N =)	
Preferred Term [n (%)][1]	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3	Any Grade	CTCAE Grade ≥ 3
Patients Reporting at Least One TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
….								

Note: N = the number of patients assigned to the cohort.
Note: TEAEs are those with start dates on or after the treatment start date. Treatment start date is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose date of the run-in PK period. The TEAEs of patients who escalated to a higher dose are classified according to the patient's initial dose cohort.
Note: The denominator for the percentages is the number of patients (N) in the Safety Population.
Note: Adverse Events are coded using MedDRA v 23.0.
Note: Preferred terms are listed in descending order based on the Total column.
[1] At each level of summation (overall and preferred term), patients reporting more than one adverse event are counted only once.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = Treatment-Emergent Adverse Event.
Reference: Listing 16.2.5.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time
Output Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Table 14.3.1.3
Summary of Treatment-Emergent Adverse Events by Preferred Term and Severity Grade (Safety Population)
Safety Population

Overall (Study Part 1, 2b and 2e) ADSL.PARTN=1,3,6

	Overall[2] (N =)	
Preferred Term [n (%)]	Any Grade	CTCAE Grade ≥ 3
Patients Reporting at Least One TEAE	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)
Preferred Term 3	xx (xx.x)	xx (xx.x)
Preferred Term 4	xx (xx.x)	xx (xx.x)
….		

Note: N = the number of patients assigned to the cohort.
Note: TEAEs are those with start dates on orafter the treatment start date. Treatment start date is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose date of the run-in PK period. The TEAEs of patients who escalated to a higher dose are classified according to the patient's initial dose cohort.
Note: The denominator for the percentages is the number of patients (N) in the Safety Population.
Note: Adverse Events are coded using MedDRA v 23.0.
Note: Preferred terms are listed in descending order based on the Total column.
[1] At each level of summation (overall and preferred term), patients reporting more than one adverse event are counted only once.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column.
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = Treatment-Emergent Adverse Event.
Reference: Listing 16.2.5.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time
Output Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Repeat Table 14.3.1.3 shell for:

Table 14.3.1.4.1 Summary of Any Drug-Related Treatment-Emergent Adverse Events by Preferred Term and Severity Grade, Safety Population INCLUDE AE IN TABLE IF EITHER ONE OF ADAE.AREL OR AREL2 OR AREL3 IS RELATED.

Programming note:

1) ***Add the following note: Note: Relatedness refers to any TEAEs reported as "Possibly Related" or "Probably Related" to study treatment.***

Table 14.3.1.4.2, Summary of PLX9486-Related Treatment-Emergent Adverse Events by Preferred Term and Severity Grade, Safety Population INCLUDE AE IN TABLE IF AREL=RELATED

Programming note:

1) ***Add the following note: Note: Relatedness refers to any TEAEs reported as "Possibly Related" or "Probably Related" to study treatment.***

Plexxikon Inc.
Protocol PLX121-01

Table 14.3.1.4.3
Summary of Treatment-Emergent Adverse Events by System Organ Class, Preferred Term and Relatedness ADAE.TRTEMFL=Y
Safety Population ADSL.SAFFL=Y

ADSL.PARTN, ADSL.COHORTN

System Organ Class ADAE.AEBODSYS / Preferred Term ADAE.AEDECOD	Part 2b 500 mg QD PLX9486 + 600 mg PLX3397 fasting (N = xx) n (%)			Part 2b 500 mg QD PLX9486 + 600 mg PLX3397 non-fasting (N = xx) n (%)			Part 2e 500 mg QD PLX9486 + 25 mg Sunitinib (N = xx) n (%)			Part 2e 1000 mg QD PLX9486 + 25 mg Sunitinib (N = xx) n (%)			Part 2e 1000 mg QD PLX9486 + 37.5 mg Sunitinib (N = xx) n (%)		
	Related to 9486 ADAE.AREL	Related to 3397 ADAE.AREL2	Related to both	Related to 9486	Related to 3397	Related to both	Related to 9486	Related to sunitinib ADAE.AREL3	Related to both	Related to 9486	Related to sunitinib	Related to both	Related to 9486	Related to sunitinib	Related to both
Patients Reporting at Least One TEAE	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
.															
System Organ Class 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Adverse Events are coded using MedDRA v 23.0.
Note: TEAEs are those with start dates on or after the treatment start date. Treatment start date is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose date of the run-in PK period. The TEAEs of patients who escalated to a higher dose are classified according to the patient's initial dose cohort.
Note: Patients could report multiple events. At each level of summation (overall, system organ class, preferred term), patients reporting more than one adverse event are counted only once. System organ classes are listed in descending order based on the total count; within each system organ class, preferred terms are listed in descending order based on the total count.
Note: The denominator for the percentages is the number of patients (N) in the Safety Population.
Note: Relatedness refers to any TEAEs reported as "Possibly Related" or "Probably Related" to Study Treatment.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in.
MedDRA = Medical Dictionary for Regulatory Activities; TEAE = Treatment-Emergent Adverse Event.
Reference: Listing 16.2.5.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) Split by study part if needed.

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.3.2.1
Listing of Deaths ADSL.DTHDT or DTHCAUS IS NON MISSING

DATASETS:ADSL, DD

Study Part PARTN	Planned Dose TRT01P	Patient No. USUBJID	Death Period[1] DTTPC	Date of Death DTHDT/ Study Day[2]	Date of Last Dose of PLX9486/Study Day	Autopsy Performed? DDATPERF	Death Certificate Obtained? DDDTHCRT	Cause of Death DDPRCDTH, DDAENO	Comments DDCOM
1	250 mg QD PLX9486	xxxxx	During Study/During Post-Study Follow-up	[redacted] 88	[redacted]/80	Yes/No	Yes/No	Disease for which Patient was given Study Treatment SAE: Primary AE number Unknown Other, Specify: xx	

[1] Patient Death Period: "During Study" if Death is the reason given for ending treatment on End of Treatment form or for ending study on the Study Exit Status form. Patients that complete treatment and study for any other reason are considered to have died during "Post-Study Follow Up".
[2] Study Day is relative to the date of the first dose of study medication.
[3] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) ***If patient's death was due to a SAE, provide primary AE number in column 'Cause of Death'***
2) ***If death date is partial, add # follows the study day value in column 'Date of Death / Study Day'***
3) ***Footnote [3] is only needed if [redacted] appear. In which case, place footnote on the Patient No.***

Plexxikon Inc.
Protocol PLX121-01

Table 14.3.2.2
Listing of Serious Adverse Events ADAE.AESER=Y
Safety Population ADSL.SAFFL=Y

DATASETS: ADS, ADAE

Study Part	Planned Dose	Patient No.	MedDRA System Organ Class// Preferred Term	Verbatim Term	AE#	Start Date (Study Day)	End Date	Serious	DLT	Severity (CTCAE Grade)	Relationship to: PLX9486/ PLX3397/ Sunitinib-	Action Taken w/: PLX9486/ PLX3397/ Sunitinib	Other Action Taken	Outcome
1		xxxx	Respiratory, thoracic and mediastinal disorders//Acute respiratory failure	ACUTE HYPOXIC RESPIRATORY FAILURE	27	[redacted] (351)		Yes		Grade 4	Unlikely\ Possibly\ Unlikely	Drug Permanently Withdrawn/ None/ None	Medication, Hospitalization	Recovered/Resolved
		xxxx	Infections and infestations//Bacterial sepsis	ALCALIGENES FAECALIS SEPSIS	1	[redacted] (8)		Yes		Grade 3	Unlikely\ Possibly\ Unlikely	Drug Permanently Withdrawn/ None/ None	Medication, Hospitalization	Recovered/Resolved
2b		xxxx	Renal and urinary disorders//Renal failure acute	ACUTE KIDNEY INJURY	9	[redacted] (208)		Yes		Grade 3	Unlikely\ Possibly\ Unlikely	Drug Temporarily Withdrawn/ None/ None	Medication, Hospitalization	Recovered/Resolved
		xxxx	Neoplasms benign, malignant and unspecified (incl cysts and polyps)//Renal cell carcinoma	NEW MALIGNANCY - RENAL CELL CARCINOMA	43	[redacted] (1051)		Yes		Grade 3	Unlikely\ Possibly\ Unlikely	Dose Not Changed/ None/ None	Hospitalization	Recovered/Resolved

[1] Study Day is relative to the date of the first dose of study medication.
[2] Not Applicable for Study Parts in study Part 1, relationship to and action take with PLX3397 for Study Parts in study Part 2b, relationship to and action take with sunitinib for Study Parts in study Part 2e.
[3] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
AE= Adverse Event; SAE = Serious Adverse Event.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:

1) ***Remove duplicates from SAE raw dataset.***
2) ***Sort by SAE Case ID within each patient.***
3) ***For column 'Investigator/Reporter…', if one component in the concatenation is missing, display 'Missing' for that component.***
4) ***Footnote [3] is only needed if the listed patient ids appear. In which case, place footnote on the Patient No.***
5) ***Obtain AESTDTC from ADAE by combining raw SAE datset with ADAE by SUBJID and AECASEID***

Table 14.3.4.1.1
Summary of Hematology and Coagulation by Cycle and Day
Safety Population

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

		250 mg QD PLX9486 (N = xx) n (%)		350 mg QD PLX9486 (N = xx) n (%)		(N = xx) n (%)		Total [1] (N = xx) n (%)	
Laboratory Parameter	Time Point	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
Hemoglobin (g/dL)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
	CxDy								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
	…								
Hematocrit (%)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
…	…								
WBC (high)[1]									

Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column. The Overall analysis includes the Part 1 or Part 2b result for re-enrolled patients.
Max = Maximum; Min = Minimum; SD = Standard Deviation.

Reference: Listing 16.2.6.1.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Table will continue with hematology parameters including Hemoglobin, Hematocrit, Platelets, RBCs, WBCs, Abs.Neutrophils, Abs.Lymphocytes, Abs. Eosinophils, Abs. Monocytes, Abs. Basophils, etc. (i.e. all the hematology parameters in ADLB), excluding 'Other Tests', followed by coagulation parameters ANC, aPTT, and INR).***
2) ***Repeat for Parts 2b, 2e and Overall (across all cohorts).***
3) ***Include index [1] on column headers 500 mg BID PLX9486 in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
4) ***For the re-enrolled patients, include their initial cohort result (Part 1 or Part 2b) in the Overall summary.***

Plexxikon Inc.
Protocol PLX121-01

Page 1 of 1

Table 14.3.4.1.2
Summary of Hematology and Coagulation – CTCAE Shift from Baseline ADLB.LBCAT=Hematology
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

	250 mg QD (N = xx) ADSL.COHORTN					… (N = xx)					Total [2] (N = xx)				
Laboratory Parameter/	Worst Post-Baseline ADLB.ATOXGR					Worst Post-Baseline					Worst Post-Baseline				
Baseline CTCAE Grade ADLB.BTOXGR	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
ANC (10^9/L)			(n=xx)					(n=xx)					(n=xx)		
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Hemoglobin (%)															
			(n=xx)					(n=xx)					(n=xx)		
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
WBC (high)[1] ADLB.SHIFT1															
			(n=xx)					(n=xx)					(n=xx)		
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
WBC (low) [1] ADLB.SHIFT2															
			(n=xx)					(n=xx)					(n=xx)		
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…															

Note: Lab values are coded using CTCAE v 4.03; Grade 0 indicates normal. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug.
Note: The lower case "n" for a lab parameter is the number of patients in the Study Part who have a baseline and a worst post-baseline CTCAE grade, and it is the denominator for the percentages.
[1] High grading is for values increased from normal, low grading is for values decreased from normal.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column. The Overall analysis includes the Part 1 or Part 2b result for re-enrolled patients.
CTCAE = Common Terminology Criteria for Adverse Events.
Reference: Listing 16.2.6.1.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:

1) ***Table will continue with hematology parameters given in Section 11.3 of SAP (WBC, hemoglobin, lymphocytes, platelets, ANC, aPTT, and INR).***
2) ***Repeat for Parts 2b, 2e and Overall (across all cohorts).***
3) ***The following parameters will have a shift table for high and low grading – please attach superscript [1] to the parameter name in column 1: WBC, Hemoglobin, and Lymphocytes.***
4) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
5) ***For the re-enrolled patients, include their initial cohort result (Part 1 or Part 2b) in the Overall summary.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.3.4.2.1
Summary of Serum Chemistry by Cycle and Day
Safety Population

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

		250 mg QD PLX9486 (N = xx) n (%)		350 mg QD PLX9486 (N = xx) n (%)		(N = xx) n (%)		Total [1] (N = xx) n (%)	
Laboratory Parameter	Visit	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
Albumin (g/dL)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
	CxDy								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Alkaline Phosphatase (U/L)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
	CxDy								
	…								

Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column. The Overall analysis includes the Part 1 or Part 2b result for re-enrolled patients.
Max = Maximum; Min = Minimum; SD = Standard Deviation.
Reference: Listing 16.2.6.2.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Table will include all serum chemistry parameters -- ALT (SGPT) (U/L), AST (SGOT) (U/L), Blood Urea Nitrogen (BUN), Calcium, Carbon Dioxide, Chloride, Creatinine, Direct Bilirubin, Creatinine Phosphatase, Glucose, LDH, Magnesium, Phosphorus, Potassium, Sodium, Total Bilirubin, Total Protein, Uric Acid, etc. excluding 'Other Tests'.***
2) ***Repeat for Parts 2b, 2e and Overall (across all cohorts).***
3) ***Include index [1] on column headers 500 mg BID PLX9486 in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
4) ***For the re-enrolled patients, include their initial cohort result (Part 1 or Part 2b) in the Overall summary.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.3.4.2.2
Summary of Serum Chemistry – CTCAE Shift from Baseline ADLB.LBCAT=Chemistry
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.COHORTN

	250 mg QD (N = xx) n (%)					… (N = xx) n (%)					Total[2] (N = xx) n (%)				
Laboratory Parameter/	Worst Post-Baseline ADLB.ATOXGR					Worst Post-Baseline					Worst Post-Baseline				
Baseline CTCAE Grade ADLB.BTOXGR	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)	Grade 0 n (%)	Grade 1 n (%)	Grade 2 n (%)	Grade 3 n (%)	Grade 4 n (%)
ALT (SGPT)			(n=xx)					(n=xx)					(n=xx)		
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
AST (SGOT)															
			(n=xx)					(n=xx)					(n=xx)		
Grade 0	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 3	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Grade 4	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…															
…															

Note: Lab values are coded using CTCAE v 4.03; Grade 0 indicates normal. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug.
Note: The lower case "n" for a lab parameter is the number of patients in the Study Part who have a baseline and a worst post-baseline CTCAE grade, and it is the denominator for the percentages.
[1] High grading is for values increased from normal, low grading is for values decreased from normal.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only counted once in the Overall column. The Overall analysis includes the Part 1 or Part 2b result for re-enrolled patients.
CTCAE = Common Terminology Criteria for Adverse Events.
Reference: Listing 16.2.6.2.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Table will continue with serum chemistry parameters given in Section 11.3 of SAP - albumin, ALT, AST, alkaline phosphatase, creatine phosphokinase, creatinine, direct bilirubin, total bilirubin, magnesium, and phosphorus.***
2) ***Repeat for Parts 2b, 2e and Overall (across all cohorts).***
3) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***
4) ***For the re-enrolled patients, include their initial cohort result (Part 1 or Part 2b) in the Overall summary.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.3.5.1
Summary of PLX9486 Exposure ADEXCOM.PARCAT1=PLX9486
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

	250 mg QD ADSL.COHORTN (N = xx)	350 mg QD (N = xx)	500 mg QD (N = xx)	… (N = xx)	Total[3] (N = xx)
Total Dose Taken ADEXCOM.PARAMN=1 (mg)[1]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Duration of Treatment (days) ADEXCOM.PARAMN=2[2]					
n	xx	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

[1] The total dose taken is derived from the duration of treatment (in days) times the assigned dose.
[2] Duration of treatment is defined as the last dose date of PLX9486 minus the first dose date of PLX9486 plus 1.
[3] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in; however, the patients are only summarized once in the Overall column with their cumulative exposure across cohorts..
Max = Maximum; Min = Minimum; SD = Standard Deviation.
Reference: Listing 16.2.3.3.1
Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) ***Continue with Study Part 2b, 2e and overall for all parts combined.***
2) ***Include index [3] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e, and the Overall column.***

Table 14.3.5.2
Summary of PLX3397 Exposure ADEXCOM.PARCAT1=PLX3397
Safety Population

Study Part 2b – Dose Extension Study Parts (PLX9486 Combined with PLX3397) PLEASE SEE TABLE 14.3.5.1 ANNOTATIONS

	500 mg QD PLX9486 + 600 mg PLX3397 fasting (N = xx)	500 mg QD PLX9486 + 600 mg PLX3397 non-fasting (N = xx)	Total (N = xx)
Total Dose Taken (mg) [1]			
n	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx
Duration of Treatment (days)[2]			
n	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx

[1] The total dose taken is derived from the duration of treatment (in days) times the assigned dose .
[2] Duration of treatment is defined as the last dose date of PLX3397 minus the first dose date of PLX3397 plus 1.
Max = Maximum; Min = Minimum; SD = Standard Deviation.
Reference: Listing 16.2.3.3.2
Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Only display Study Part 2b.

Plexxikon Inc.
Protocol PLX121-01

Table 14.3.5.3
Summary of Sunitinib Exposure ADEXCOM.PARCAT1=SUNITINIB
Safety Population

Study Part 2e – Dose Extension Study Parts (PLX9486 Combined with Sunitinib) PLEASE SEE TABLE 14.3.5.1 ANNOTATIONS

	500 mg QD PLX9486 + 25 mg Sunitinib (N = xx)	1000 mg QD PLX9486 + 25 mg Sunitinib (N = xx)	1000 mg QD PLX9486 + 37.5 mg Sunitinib (N = xx)	Total (N = xx)
Total Dose Taken (mg) [1]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx
Duration of Treatment (days)[2]				
n	xx	xx	xx	xx
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x	xx.x
Min, Max	xx, xx	xx, xx	xx, xx	xx, xx

[1] The total dose taken is derived from the duration of treatment (in days) times the assigned dose .
[2] Duration of treatment is defined as the last dose date of sunitinib minus the first dose date of sunitinib plus 1.
Max = Maximum; Min = Minimum; SD = Standard Deviation.
Reference: Listing 16.2.3.3.3
Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Only display Study Part 2e.

Plexxikon Inc.
Protocol PLX121-01

Table 14.3.6
Summary of Vital Signs ADVS.ANL01FL=Y
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

		250 mg QD ADSL.COHORTN (N = xx) n (%)		350 mg QD (N = xx) n (%)		… (N = xx) n (%)		Total (N = xx)[1] n (%)	
Parameter	Time Point ADVS.AVISIT	Result ADVS.AVAL	Change from Baseline ADVS.CHG	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
Systolic Blood Pressure (mmHg) ADVS.PARAM	Baseline ADVS.ABLFL=Y								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
	C1D1 – Post-dose								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
	…								
Diastolic Blood Pressure (mmHg)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
…	…								

Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug. Some patients enrolled in Part 1 participated in the run in period for the collection of PK samples were treated prior to C1D1 and have a baseline prior to study day 1. These patients have a baseline prior to C1D1 and have change from baseline displayed at C1D1 Pre-Dose.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in.
Reference: Listing 16.2.7.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:

1) ***Table will include the following vital signs: SBP, DBP (mmHg), Heart Rate (bpm), Respiration (breaths/min), Temperature (°C), weight (kg).***
2) ***Continue with Study Part 2b, and 2e.***
3) ***Include index [1] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e.***

Plexxikon Inc.
Protocol PLX121-01

Table 14.3.7.1
Summary of Electrocardiogram ADEG.ANL01FL=Y
Safety Population ADSL.SAFFL=Y

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486) ADSL.PARTN=1

		250 mg QD ADSL.COHORTN (N = xx) n (%)		350 mg QD (N = xx) n (%)		… (N = xx) n (%)		Total [2] (N = xx) n (%)	
ECG Parameter ADEG.PARAM	Time Point ADEG.AVISIT	Result ADEG.AVAL	Change from Baseline ADEG.CHG	Result	Change from Baseline	Result	Change from Baseline	Result	Change from Baseline
Ventricular Rate (bpm)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
	…								
	End of Study								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…									
QTcF(msec)	Baseline								
	n	n		n		n		n	
	Mean (SD)	xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)		xx.x (xx.xx)	
	Median	xx.x		xx.x		xx.x		xx.x	
	Min, Max	xx, xx		xx, xx		xx, xx		xx, xx	
	…								
	End of Study								
	n	n	n	n	n	n	n	n	n
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
…	Upper 95% CI[1]	xx.x		xx.x		xx.x		xx.x	

Note: The baseline value is defined as the last non-missing value of the average of the triplicate ECGs prior to the patient's first dose of study drug. Some patients enrolled in Part 1 participated in the run in period for the collection of PK samples were treated prior to C1D1 and have a baseline prior to study day 1. These patients have a baseline prior to C1D1 and have change from baseline displayed at C1D1 Pre-Dose.
[1] One-sided upper 95% confidence limit.
[2] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in.
ECG = Electrocardiogram; Max = Maximum; Min = Minimum; SD = Standard Deviation; UCL = Upper Confidence Limit.
Reference: Listing 16.2.7.3.1

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Table will continue with the following parameters: PR(msec), QRS(msec), QT(msec), QTcB (msec), and QTcF(msec) and all scheduled visits in EG/EG1/EG2 datasets. Use derived RR, QTcB, QTcF (ADEG.PARAMCD=RRINT, DQTCF, DQTCB)***
2) ***For QTcF an additional row will be added for the one-sided upper 95% confidence interval.***
3) ***Summary statistics for the end of study measurement should be included.***
4) ***For each visit, display all scheduled timepoints in ADEG.***
5) ***Continue with Study Part 2b, and 2e.***
6) ***Include index [2] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e.***
7) ***If there are not more than 2 observations in the Total column for a cohort, do not display results for that time point.***
8) ***Record raw values to whole units for min, max, one decimal for mean and median, and 2 decimal places for SD.***

Plexxikon Inc. **Page 1 of 1**
Protocol PLX121-01

Table 14.3.7.2
Summary of Electrocardiogram – Abnormal QTcF Results
Safety Population

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

ECG Parameter	250 mg QD PLX9486 (N = xx) n (%)	350 mg QD PLX9486 (N = xx) n (%)	500 mg QD PLX9486 [3] (N = xx) n (%)	(N = xx) n (%)	Total [3] (N = xx) n (%)
QTcF (Fridericia's Method)					
≥ 450 msec (for males) [1]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
≥ 470 msec (for females) [2]	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
>500 msec					
> 30 msec increase from baseline	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
> 60 msec increase from baseline	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Patients experiencing a > 60 msec event are included in the > 30 msec event summary row also.
[1] Denominator is the number of males in Safety Population.
[2] Denominator is the number of females in Safety Population.
[3] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in.
Reference: Listing 16.2.7.3.1 and 16.2.7.3.2

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) ***Continue with Study Part 2b, and 2e.***
2) ***Include index [3] on column headers 500 mg BID in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e.***
3) ***Change from baseline incidence is cumulative. That is, a patient who experiences a > 60 msec event is also counted in the > 30 msec event as well.***

Plexxikon Inc.
Protocol PLX121-01

Table 14.3.8
Summary of ECOG – Shift from Baseline
Safety Population

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

Post-Baseline Assessment/ ECOG Score	250 mg QD PLX9486 (N = xx) n (%) Baseline ECOG Score 0	1	2	3	4	5	(N = xx) n (%) Baseline ECOG Score 0	1	2	3	4	5	Total [1] (N = xx) n (%) Baseline ECOG Score 0	1	2	3	4	5
C1D8				(n =)						(n =)						(n =)		
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
C1D15				(n =)						(n =)						(n =)		
0	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
1	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
2	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
3	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
4	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
5	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
…																		

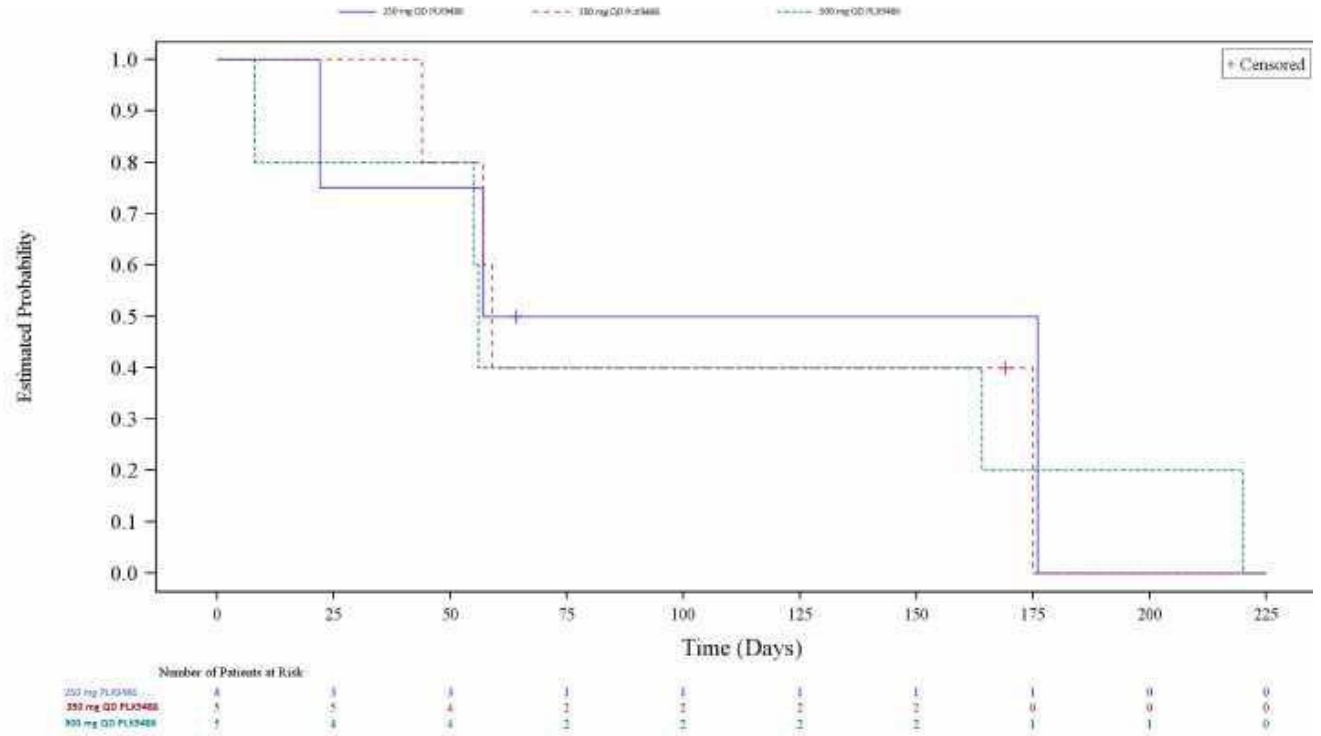
ECOG Score: 0=Fully active, able to carry on all pre-disease performance without restriction, 1=Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light housework, office work), 2=Ambulatory and capable of all self-care, but unable to carry out any work activities. Up and about more than 50% of waking hours. 3=Capable of only limited self-care, confined to bed or chair more than 50% of waking hours, 4=Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair, 5=Dead.
Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug. Some patients enrolled in Part 1 participated in the run in period for the collection of PK samples were treated prior to C1D1 and have a baseline prior to study day 1. These patients have a baseline prior to C1D1 and have change from baseline displayed at C1D1 Pre-Dose.
[1] Two patients who enrolled in Part 2b and one patient who enrolled in Part 1 completed their initial enrolment and subsequently re-enrolled in Part 2e. These patients are counted in each of the cohorts they enrolled in.
Reference: Listing 16.2.7.4

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) Continue with all study time points and Study Parts 2b, and 2e.

2) ***Include index [2] on column headers 500 mg BID PLX9486 in Part 1, 500 mg QD PLX9486 + 600 mg PLX3397 fasting and the Total columns in Part 2b, 1000 mg QD PLX9486 + 37.5 mg Sunitinib and the Total columns in Part 2e.***

Figure 14.2.1
Progression-Free Survival by Study Part - Study Part 1
(Efficacy Evaluable Population)



Reference Table 14.2.3
Note: PFS is defined as the number of days from the start of therapy (i.e., C1D1) to the date of first documented disease progression / relapse or death, whichever occurs first. If disease progression/relapse or death dose not occur, PFS is censored as of the date of their last evaluable tumor assessment.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time
Programmer notes:
1) Continue with Study Parts 2b, 2e, and Overall.

Appendix D: Listing Layouts

Notes to programmer:

(1) All listings will list Study Parts and planned dose in this order of appearance (for all Study Parts that have data relevant to the listings):

Study Part	Planned Dose
1	250 mg QD PLX9486
1	350 mg QD PLX9486
1	500 mg QD PLX9486
1	1000 mg QD PLX9486
1	500 mg BID PLX9486
2b	500 mg QD PLX9486 + 600 mg PLX3397 fasting
2b	500 mg QD PLX9486 + 600 mg PLX3397 non-fasting[2]
2e	500 mg QD PLX9486 + 25 mg Sunitinib
2e	1000 mg QD PLX9486 + 25 mg Sunitinib
2e	1000 mg PLX9486 + 37.5 mg Sunitinib

(2) For all listings, add following footnotes: (see example in Listing 16.2.1.1 – Patient Disposition)

[1] Patient numbers [redacted] completed Their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted] *(placed on patient numbers indicated)*

Number all footnotes first by their order of occurrence from left to right in the table headings, then by their order of occurrence in the body of listing itself

(3) All listings will be ordered by the following (unless otherwise indicated in the mock):

Study Part, Study Part, Patient number, Date, Visit and Time points

(4) For all listings, the mock shells outline layout for Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486). The remainder of the listings will follow the same format for other Study Parts, unless specified otherwise in the mocks. Sponsor, protocol, and footnotes will appear on all pages of all Study Parts.
(5) Display complete and partially missing dates in standard format, with no spaces.

For example:

15JUN2015
JUN2015 (if day is missing)
2015 (if month and day are missing)

Listing 16.2.1.1
Patient Disposition

Study Part	Planned Dose	Patient No.	Site	Safety Population[1]	EE Population[2]	PK Population[3]	Informed Consent Date	Date of First Dose/ Date of Last Dose/ Duration of Treatment[4] (days)	Date of Study Exit	Reason for Study Completion/Discontinuation.	Date of Last Dose of PLX9486//Date of Last Dose of PLX3397 or Sunitinib[5]	Primary Reason for Ending Treatment	Pregnancy during the study?[6]
1	250 mg QD PLX9486	[redacted]		Yes/No	Yes/No	Yes/No	[redacted]	[redacted] 29	[redacted]	Clincial Progression		Adverse Event: 2_xxxxx_14 [redacted]	Yes

Note: For Study Part column, Px-Cy = Study Part x – Study Part y. For study part 2b, patients in the first Cohort were assigned to fast for at least 8 hours prior to dosing of study drug while patients in the second Cohort were dosed in a non-fasted state. For study part 2e, patients in Cohorts 1 and 2 were dosed with food while patients in Cohort 3 were assigned to fast for at least 8 hours prior to dosing of study drug. As of Amendment 6, patients who were assigned to fasting are no longer required to fast and may take their study medication with food.

[1] All patients who received study medication.

[2] All patients who have taken at least 1 dose of study drug and have had at least 1 post-baseline tumor assessment or discontinue study medication early due to disease progression or death.

[3] All patients who have adequate PK and PD data.

[4] Duration of treatment is defined as the last dose date minus the first dose date plus 1. Date of first dose is the earliest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib), including dose dates from the run-in PK period. Date of last dose is the latest dose date of any of the study drugs (PLX9486, PLX3397, and sunitinib).

[5] Dates of last dose of study drugs are derived.

[6] If male, did the patient's partner have a pregnancy during the study?

[7] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

AE = Adverse Event; DLT = Dose Limiting Toxicity.
EE = Efficacy Evaluable; PK = Pharmacokinetic; RECIST = Response Evaluation Criteria In Solid Tumors.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.2.1
Demographics and Baseline Characteristics

Study Part	Planned Dose	Patient No.	Date of Birth	Age (years)[1]	Gender	For female, childbearing potential?[2]	Ethnicity	Race[3]	Weight (kg)	Height (cm)	BMI (kg/m^2)[4]	Is patient in single dose PK sub-study?	Optional Paired Tumor Biopsy?	Optional Fresh Tumor Biopsy?
1	250 mg QD PLX9486	xx-xxx	DDMMMYYYY	xx	[redacted]	No, Post-Menopausal/Yes, Hormonal Contraception	[redacted]	[redacted]	xxx.x	xxx.x	xx.x	Yes/No	Yes/No	Yes/No
	350 mg QD	xx-xxx			[redacted]									

[1] Age is calculated as of the date the informed consent is signed.
[2] If the answer is No, the reason is specified; if the answer is Yes, the method of contraception is specified.
[3] Patients could mark more than one race.
[4] BMI is derived as the weight in kilograms divided by the square of the height in meters.
[5] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
BMI = Body mass index.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) If there is more than one "Race" separate by "/".

Listing 16.2.2.2
Medical History

Study Part	Planned Dose	Patient No.	Any Past and/or Concomitant Diseases or Past Surgeries?	Body System	Description	Onset Date	Ongoing?	End Date
1	250 mg QD PLX9486	[redacted]	Yes/No			DDMMMYYYY Unknown	Yes/No	 Unknown

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) ***Show body system names vice body system codes.***
2) ***Sort by body system shown in the CRF then by description within each patient.***

Listing 16.2.2.3.1
Primary Cancer History – Study Part 1
Part 1 of 2

Study Part	Planned Dose	Patient No.	Anatomical Location of Primary Tumor	At Initial Histologic Diagnosis			Histologic Subtype	Histologic Degree of Differentiation	Date of Metastatic Diagnosis	Anatomical Location of Metastatic Disease	At Study Entry	
				Date	Tumor Stage	T/N/M Stage					Tumor Stage	T/N/M Stage
1	250 mg QD PLX9486	[redacted]				Tx/Nx/M0						

Part 2 of 2

Study Part	Planned Dose	Patient No.	Genomic Analysis on Tumor Tissue		KIT Mutation? If yes, specify	Other significant mutations? If yes, specify
			Performed?	Anatomical Location		
1	250 mg QD PLX9486	[redacted]	Yes: lab name/No		Yes: specify / No	Yes: specify / No

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***If there is more than one "Anatomical Location of Primary Tumor" separate by "/".***
2) ***Sort by date of initial histologic diagnosis date within each patient.***
3) ***If genomic analysis was performed on tumor tissue, specify lab performing analysis in column 'Performed'.***
4) ***For column 'T/N/M Diagnosis (under 'At Initial Diagnosis' and 'At Study Entry')) if one of the T, N, or M diagnosis is missing display 'Missing' for that diagnosis (e.g. if T diagnosis is missing and N diagnosis =Nx, and M diagnosis=M0, display 'Missing/Nx/MO')***
5) ***For column 'Anatomical Location of Metastatic Disease' combine all applicable locations separated by ";" (locations are variables MH1LOCxx in the raw datasets)***

Listing 16.2.2.3.2
Primary Cancer History – Study Part 2
Part 1 of 3

Planned Dose	Patient No.	Primary Tumor Type	At Initial Histologic Diagnosis			If Germ Cell Tumor, Specify
			Date	Tumor Stage	T/N/M Stage	
250 mg QD PLX9486	xx-xxx	Other: Specify	Date9.	IA	Tx/Nx/M0	Non-Seminoma: Specify

Part 2 of 3

Patient No.	Anatomical Location of Primary Tumor	At Initial Histologic Diagnosis			Histologic Subtype	Histologic Degree of Differentiation	At Study Entry	
		Date	Tumor Stage	T/N/M Stage			Tumor Stage	T/N/M Stage
xx-xxx				Tx/Nx/M0				

Part 3 of 3

Patient No.	Genomic Analysis on Tumor Tissue at Initial Diagnosis				Genomic Analysis on Tumor Tissue at Study Entry						
	Performed?	Anatomical Location	KIT Mutation? If yes, specify	Other non-KIT significant mutations? If yes, specify	Performed?	Anatomical Location	KIT Mutation? If yes, specify	Other non-KIT significant mutations? If yes, specify	Diagnosis Timeframe	Exon Present	Specification of Mutation Present
[redacted]	Yes: lab name/No	xxxxxx	Yes: specify / No	Yes: specify / No	Yes: lab name/No	xxxxxx	Yes: specify / No	Yes: specify / No		8 Other: Specify	xxxxxx

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***If there is more than one "Anatomical Location of Primary Tumor" separate by "/".***
2) ***Sort by date of initial histologic diagnosis date within each patient.***
3) ***If genomic analysis was performed on tumor tissue, specify lab performing analysis in column 'Performed'.***
4) ***For column 'T/N/M Diagnosis (under 'At Initial Diagnosis' and 'At Study Entry')) if one of the T, N, or M diagnosis is missing display 'Missing' for that diagnosis (e.g. if T diagnosis is missing and N diagnosis =Nx, and M diagnosis=M0, display 'Missing/Nx/MO')***
5) ***For column 'Anatomical Location of Metastatic Disease' combine all applicable locations separated by ";" (locations are variables MH1LOCxx in the raw datasets)***

Listing 16.2.2.4
Prior Treatment for Primary Malignancy

Study Part	Planned Dose	Patient No.	Any previous primary malignancy treatment?	Record #	If Yes, Type of Therapy	Description	Setting	Start Date	Stop Date	Best Response to Treatment	Primary Reason for Stopping Treatment
1	250 mg QD PLX9486	[redacted]	Yes/No	1	Surgery	Other: Specify		[redacted]	[redacted]		
	350 mg QD	[redacted]									

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) Sort by Start Date and then record number within each patient.

Listing 16.2.2.5
Prior and Concomitant Medications

Study Part	Planned Dose	Patient No.	Any Medications	Record #[1]	ATC Class // Preferred Name // Verbatim	Start Date/ Stop Date	Dose (Units)	Dose Form	Route/ Frequency	Indication
1	250 mg QD PLX9486	[redacted]	Yes	1	NATURAL OPIUM ALKALOIDS// MORPHINE SULFATE// MS CONTIN	[redacted] Ongoing	4 (mg)	Tablet	Oral / QD	MH # 21_CONSTIPATION_[redacted] Primary AE #3_INTERMITTENT DIARRHEA [redacted] Additional AE(s): #1_DIARRHEA_[redacted] / # 2_DIARRHEA_[redacted] Other: STABLE BRAIN METASTASES
				2		[redacted] [redacted]				

Note: Prior medications are those that start prior to the first dose of any study drugs, even if the medications continues after dosing. Concomitant medications are those which are taken at any time between the date of first dose and the date of last dose of any study medication. In cases where it is not possible to determine if a medication is concomitant, the medication is classified as concomitant.
Note: Only patients who reported taking any non-study medication from 14 days prior to study treatment or during the course of the study (including over-the-counter and prescription drugs) are recorded and listed.
[1] Prior medications are denoted by a P, concomitant medications are denoted by a C, prior and concomitant medications are denoted by PC following the CM #.
[2] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted].
AE = Adverse Event; ATC = Anatomical Therapeutic Chemical; MH = Medical History.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) ***Sort by start date and stop date, and then CM # within each Study Part/patient.***
2) ***Show the unit, dose form, route and frequency, not the codes.***
3) ***Use XMED dataset.***
4) ***See the footnote regarding flagging of conmeds starting after the first dose of a patient's dose escalation Study Part.***
5) ***For column 'Indiccation', concatenate if there are multiple indications. Use '/' to separate the different indications.***

Listing 16.2.2.6
Major Protocol Deviations

Study Part	Planned Dose	Patient No.	Visit	Protocol Deviation Category	Verbatim	Medical Monitor Significance Assessment Significant/ Not significant/More information needed
1	250 mg QD PLX9486	[redacted]	C1D1	Procedures/Tests	C1D1 scan lost	
	350 mg QD PLX9486	[redacted]	EOS	Study Drug	Study drug packages not returned to site	

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) Sort by Start Date, visit, category, and verbatim within each patient.

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Protocol PLX121-01

Listing 16.2.3.1.1
PLX9486 Dosing Log

Study Part	Planned Dose	Patient No.	Start Date	Stop Date	Prescribed Dose (mg) /Prescribed Daily Dose Frequency	Prescribed Total Daily Dose (mg)	Was Prescribed Dose Taken by Patient?	Actual Dose Taken (mg)[1]	Dose Reason	Dose Change due to AE		Drug Overdose		
										Dose Change?	AE Related to Dose Change	Overdose Occurred? [2]	Overdose related to AE?	Related AEs
1	250 mg QD PLX9486	[redacted]	date9.	date9.	xxx/QD	250	Yes/No		Starting Dose	Yes/No	Xxxxx xxxx	Yes/No	Yes/No	Primary AE: xxx/ Secondary AE(s): xxxxx; xxxxx
	350 mg QD	[redacted]				350			PK RUN IN Starting Dose					

[1] If prescribed dose was not taken by the patient.
[2] Patient is considered to have had overdose if Dose Reason is 'Patient Overdose'.
[3] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) ***Sort by start date and stop date within each Study Part/patient.***
2) ***For column 'If Yes, AE(s)': concatenate all AEs. Separate primary AE with Secondary AEs by '/', separate more than 1 secondary AEs by ';'***
3) ***Continue for all study parts***
4) ***If change is due to overdose there may be multiple associated AEs. Append them together with the Primary first, then the Secondary(s).***

Listing 16.2.3.1.2
PLX3397 Dosing Log

Study Part	Planned Dose	Patient No.	Start Date	Stop Date	Prescribed Dose (mg) /Prescribed Daily Dose Frequency	Prescribed Total Daily Dose (mg)	Was Prescribed Dose Taken by Patient?	Actual Dose Taken (mg)[1]	Dose Reason	Was Change in Dose due to AE?	If Yes, AE(s)	Overdose occured?[2]
1		xx-xxx	date9.	date9.	xxx/QD	250	Yes/No		Starting Dose	Yes/No	Primary AE: xxx/ Secondary AE(s): xxxxx; xxxxx	

[1] If prescribed dose was not taken by the patient.
[2] Patient is considered to have had overdose if Dose Reason is 'Patient Overdose'
[3] Patient Nos [redacted] completed Study and subsequently re-enrolled, respectively, as Patient Nos [redacted].

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) ***Sort by start date and stop date within each Study Part/patient.***
2) ***For column 'If Yes, AE(s)': concatenate all AEs. Separate primary AE with Secondary AEs by '/', separate more than 1 secondary AEs by ';'***
3) ***This listing is only relevant for Study Part 2b.***

Listing 16.2.3.1.3
Sunitinib Dosing Log

Study Part	Planned Dose	Patient No.	Start Date	Stop Date	Prescribed Dose (mg) /Prescribed Daily Dose Frequency	Prescribed Total Daily Dose (mg)	Was Prescribed Dose Taken by Patient?	Actual Dose Taken (mg)[1]	Dose Reason	Dose Change due to AE: Dose Change?	Dose Change due to AE: AE Related to Dose Change	Drug Overdose: Overdose Occurred?[2]	Drug Overdose: Overdose related to AE?	Related AEs
1	250 mg QD PLX9486	[redacted]	date9.	date9.	xxx/QD	250	Yes/No		Starting Dose	Yes/No	Xxxxx xxxx	Yes/No	Yes/No	Primary AE: xxx/ Secondary AE(s): xxxxx; xxxxx
	350 mg QD	[redacted]				350			PK RUN IN Starting Dose					

[1] If prescribed dose was not taken by the patient.
[2] Patient is considered to have had overdose if Dose Reason is 'Patient Overdose'
[3] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted].

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) ***Sort by start date and stop date within each Study Part/patient.***
2) ***For column 'If Yes, AE(s)': concatenate all AEs. Separate primary AE with Secondary AEs by '/', separate more than 1 secondary AEs by ';'***
3) ***This listing is only relevant for Study Part 2e.***

Listing 16.2.3.2
Study Drug Accountability

Study Part	Planned Dose	Patient No.	Date Dispensed	Treatment Label ID Dispensed	Amount Dispensed (Tablets)	Date Returned	Treatment Label ID Returned	Amount Returned (Tablets)	Comments
1	250 mg QD PLX9486	[redacted]	date9.			date9.			

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) Sort by dispensed date and returned date within each Study Part/patient.

Listing 16.2.3.3.1
PLX9486 Overall Exposure

Study Part	Planned Dose	Patient No.	Duration of Treatment (Days)[2]	Total Dose Taken (mg)[3]
1	250 mg QD PLX9486	[redacted]	xxx	xxx

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
[2] Duration of treatment of PLX9486, derived as the last dose date of PLX9486 minus the first dose date of PLX9486 plus 1.
[3] The total dose taken is derived from the duration of treatment (in days) times the assigned dose.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Present all study parts

Listing 16.2.3.3.2
PLX3397 Exposure

Study Part	Planned Dose	Patient No	Duration of Treatment (Days)[2]	Total Dose Taken (mg)[3]
1	500 mg QD PLX9486 + 600 mg PLX3397 fasting	xx-xxx	xx	xx

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
[2] Duration of treatment of PLX3397, derived as the last dose date of PLX3397 minus the first dose date of PLX3397 plus 1.
[3] The total dose taken is derived from the duration of treatment (in days) times the assigned dose.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Present only for Study Part 2b.

Listing 16.2.3.3.3
Sunitinib Exposure

Study Part	Planned Dose	Patient No.	Duration of Treatment (Days)[2]	Total Dose Taken (mg)[3]
1	500 mg QD PLX9486 + 25 mg Sunitinib	xx-xxx	xx	xx

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
[2] The total dose taken is derived from the duration of treatment (in days) times the assigned dose.
[3] Duration of treatment of PLX9486, derived as the last dose date of PLX9486 minus the first dose date of PLX9486 plus 1.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Present only for Study Part 2e.

Listing 16.2.4.1
Tumor Assessment (Target Lesions)

Study Part	Planned Dose	Patient No.	Visit	Assessment Date	Radiographic Evaluation Performed?	Lesion # [1]	Description	Location	Method of Assessment	Longest Diameter (cm) [2]	Sum of Longest Diameters (cm)	Change from Baseline (cm)[3]	Percent Change from Baseline (%) [3]	Nadir (cm) [4]	Change from Nadir (cm)[5]	Percent Change from Nadir (%)[5]	Any New Lesions?
1	250 mg QD PLX9486	[redacted]	SCREEN	[redacted]	Yes	1*	LIVER, SEGMENT II	Liver	Spiral Computed Tomography (CT)	3.2	6.5						Yes/No
						2*	RIGHT LIVER	Liver	Spiral Computed Tomography (CT)	Unable to Evaluate	6.5						Yes/No
			Unscheduled	[redacted]	Yes	1	LIVER, SEGMENT II	Liver	Spiral Computed Tomography (CT)	4.60	8.4	- 1.9	xx.x				Yes/No
						2	RIGHT LIVER	Liver	Spiral Computed Tomography (CT)	3.80	8.4	- 1.9	xx.x				Yes/No

[redacted]

Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug.
[1] A '*' indicates baseline. A ^ indicates assessments were collected after last dose date.
[2] If lymph node, short axis is recorded instead.
[3] Change from baseline, and percent change from baseline of the sum of longest diameters.
[4] Nadir is the smallest sum of longest diameters recorded since treatment started.
[5] Change and percentage change from nadir are shown for the assessment that produces the nadir (equal to zero there by definition) and for each subsequent assessment.
[6] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) Sort by visit and lesion number within each patient.

Listing 16.2.4.2
Tumor Assessment (Non-Target Lesions)

Study Part	Planned Dose	Patient No.	Visit	Assessment Date	Any Non-Target Lesion?/ Radiographic Evaluation Performed? [1]	If No, Reason [2]	Lesion #	Description	Location	Method	Non-Target Lesion Status[2]
1	250 mg QD PLX9486	[redacted]	SCREEN	[redacted]	Yes/No		1	LEFT UPPER LOBE LUNG	Lung	Spiral Computed Tomography (CT)	Unable to Evaluate

Note: Baseline is defined as the last value obtained on or before the date and time of the first dose of any study drug.
[1] If Baseline records, whether any non-target lesion(s) was identified at baseline. If non-baseline records, whether radiographic evaluation was performed.
[2] For non-baseline records.
[3] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) Sort by visit, date and lesion number within each patient.

Listing 16.2.4.3
Tumor Assessment - New Lesions

Study Part	Planned Dose	Patient No.	Visit	Assessment Date	Lesion #	Description	Longest Diameter (cm)	Location	Method of Assessment	Unable to Evaluate?
1	250 mg QD PLX9486	[redacted]	C3D1		1					Yes/No

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:
1) Sort by time point, date and lesion number within each patient.

Plexxikon Inc. **Page 1 of x**
Protocol PLX121-01

Listing 16.2.4.4
Tumor Response Assessment (Target and Non-Target Lesions)

Study Part	Planned Dose	Patient No.	Visit	Assessment Date	Days from First Dose[1]	Target Lesion Response[2]	Non-Target Lesion Response	New Lesion?	Investigator Assessed Overall Response[3]	Calculated RECIST Overall Response[4]
1	250 mg QD PLX9486	[redacted]	Screen	[redacted]		NE	NE		NE	NE
			Unscheduled	[redacted]		Not Done	Non-CR/Non-PD	Yes/No	PD	PD

Note: A * after Assessment Date indicates assessments after last dose date.
[1] Days from first dose of study drug is derived as the assessment date - first dose of any study drug + 1.
[2] PD is defined as ≥ 20% relative increase from nadir and absolute increase of at least 5 mm in the sum of diameters of target lesions.
[3] Overall response is determined by Investigator using RECIST v1.1, and recorded in the CRF form 'Tumor Response Assessment'.
[4] Derived programmatically using RECIST v1.1 criteria based on target, non-target responses and new lesion evaluation recorded in the database.
[5] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
CR = Complete Response; NE = Not Evaluable (Inevaluable for Response); PD = Progressive Disease; PR = Partial Response; RECIST = Response Criteria Evaluation in Solid Tumors; SD = Stable Disease.
UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by date, visit and lesion number within each patient.***
2) ***Put 'Not Done' into response columns when response assessment is Not Done (RSND1 or RSDN2 is 1).***
3) ***For column 'Reason for PD', fill in if Derived Overall Response is PD. Possible values: New Lesion(s), ≥20% relative increase [2], New Lesion(s) and ≥20% relative increase[2]***
4) ***Program for footnote 'Note: A * after Assessment Date indicates assessments after last dose date.'***

Listing 16.2.4.5
Derived Efficacy Endpoints Based on Tumor Response

			Duration of Response[1]		Progression-Free Survival[2]		Overall Survival[3]		Tumor Response	
Study Part	Planned Dose	Patient No.	Days	Censor	Days	Censor	Days	Censor	Clinical Benefit?[4]	Best Overall Response[5]
1	250 mg QD PLX9486	[redacted]							Yes/No	

[1] DOR is calculated for every patient with a response to therapy as the number of days from the date of initial response (PR or CR) to the date of first documented disease progression or death, whichever occurs first. If disease progression or death does not occur, DOR is censored as of the date of their last post-baseline tumor response evaluation.
[2] PFS is defined as the number of days from the start of therapy (i.e., C1D1) to the date of first documented disease progression or death, whichever occurs first. Patients without a post-baseline tumor response evaluation have their event censored on the first date of study drug If disease progression or death does not occur, PFS is censored as of the date of their last post-baseline tumor response evaluation.
[3] OS is defined as the number of days from the start of therapy (i.e., C1D1) to the date of death. If a patient is lost to follow-up, OS is censored at the date of last contact. For more details, see SAP Section 8.2.
[4] A patient is considered to experience Clinical Benefit if they have a Best Overall Response of CR, PR or SD that lasted for at least 16 weeks.
[5] Best Overall Tumor Response is the best overall response derived as the best of all Best Responses for each sequential pair of post-treatment time points (and in some cases, triplets of sequential time points). Best Responses for each sequential pair of post-treatment time points follow the rules for determining best response when confirmation of CR, PR, and minimum duration of SD are required. For more details, see SAP Section 8.1.2 and 8.1.3.
[6] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
CR = Complete Response; DOR = Duration of Response; NE = Not Evaluable; PD = Progressive Disease; PR = Partial Response; RECIST = Response Criteria Evaluation in Solid Tumors; SD = Stable Disease.
Reference: Listings 16.2.4.1 and 16.2.4.4

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.5.1
Adverse Events
Part 1 of 3

Study Part	Planned Dose	Patient No.	Any AE?	AE No.[1]	System Organ Class // Preferred Term // Verbatim Text[2]	Serious?	Initial Severity/Maximum Severity	Start Date/ Study Day[3]	End Date/ Study Day[3]	DLT?[4]	Relationship to PLX9486/ Action Taken with PLX9486	Relationship to PLX3397 or Sunitinib/ Action Taken with PLX3397 or Sunitinib	Other Actions Taken/ Treatment of Event	Outcome
1	250 mg QD PLX9486	[redacted]	Yes/No	1*		Yes/No	Grade 1/Grade 3	[redacted] 2	[redacted] 36	Yes/No	Possibly Related/ Dose Not Changed	Not Applicable / Not Applicable	None/xxxxx	Recovered / Resolved
				2*										

Note: More detailed information about SAE can be found in Part 2, and about subsequent increase in severity can be found in Part 3 of the listing.
[1] A * after the adverse event number indicates a treatment emergent adverse event.
[2] AEs are coded using MedDRA v 23.0.
[3] Study Day is relative to the date of the first dose of study medication. Study Day is only displayed for AE dates with complete date information.
[4] DLTs are defined as AEs occurring during the first 28 days of study drug administration (Cycle 1) that are classified as possibly or probably related to the study drug, and meet one of the following Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria listed in SAP Section 3.1
[5] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted].
AE = Adverse Event; CTCAE = Common Terminology Criteria for Adverse Events; DLT = Dose Limiting Toxicity; MedDRA = Medical Dictionary for Drug Activities, NA = Not Applicable

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.5.1
Adverse Events
Part 2 of 3

						SAE Criteria					
Study Part	Planned Dose	Patient No.	AE No.[1]	System Organ Class // Preferred Term // Verbatim Text[2]	Serious?	Congenital Anomaly/ Birth Defect	Persistent or significant disability or incapacity	Death	Initial or Prolonged Hospitalization Date of Admission/ Date of Discharge	Life-Threatening	Other Serious or Important Medical Event
1	250 mg QD PLX9486	xxxxx	1*		Yes/No	Yes/No	Yes/No	Yes/No	Yes/ DDMMMYYYY/ DDMMMYYYY	Yes/No	Yes/No
			2*								

[1] A * after the adverse event number indicates a treatment emergent adverse event.
[2] AEs are coded using MedDRA v18.0.
[3] Study Day is relative to the date of the first dose of study medication. Study Day is only displayed for AE dates with complete date information.
[4] DLTs are defined as AEs occurring during the first 28 days of study drug administration (Cycle 1) that are classified as possibly or probably related to the study drug, and meet one of the following Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria listed in SAP Section 3.1
[5] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
AE = Adverse Event; CTCAE = Common Terminology Criteria for Adverse Events; DLT = Dose Limiting Toxicity; MedDRA = Medical Dictionary for Drug Activities.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.5.1
Adverse Events
Part 3 of 3

							1st Increase in Severity			2nd Increase in Severity			3rd Increase in Severity			4th Increase in Severity		
Study Part	Planned Dose	Patient No.	AE No.[1]	System Organ Class // Preferred Term // Verbatim Text[2]	Initial Severity	Subsequent increase in Severity?	1st	Severity	Date	2nd	Severity	Date	3rd	Severity	Date	4th	Severity	Date
1	250 mg QD PLX9486	[redacted]	1*		Grade 1 (Mild)	Yes/No	Yes/No	Grade 2 (Moderate)		Yes/No	Grade 3 (Severe)		Yes/No	Grade 4 (Life Threatening)		Yes/No	Grade 5 (Fatal)	
			2*															

[1] A * after the adverse event number indicates a treatment emergent adverse event.
[2] AEs are coded using MedDRA v18.0.
[3] Study Day is relative to the date of the first dose of study medication. Study Day is only displayed for AE dates with complete date information.
[4] DLTs are defined as AEs occurring during the first 28 days of study drug administration (Cycle 1) that are classified as possibly or probably related to the study drug, and meet one of the following Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria listed in SAP Section 3.1
[5] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
AE = Adverse Event; CTCAE = Common Terminology Criteria for Adverse Events; DLT = Dose Limiting Toxicity; MedDRA = Medical Dictionary for Drug Activities.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Note to Programmer:

1) ***For columns 'Relationship to PLX3397 or Sunitinib/ Action Taken with PLX3397 or Sunitinib[5], in the column body, display 'NA/NA' for data from study part 1, display information of relationship/action taken with PLX3397 for Study Parts in study part 2b, display information of relationship/action taken with Sunitinib for Study Parts in study part 2e.***
2) ***Sort by start date and end date within each patient.***
3) ***Note that there may be more than one "other" action taken. List all, separated by '/'.***
4) ***Use XAE data set.***
5) ***Leave blanks at column 'End Date/Study Day' for observations which have completely missing AE End Date.***
6) ***If AE start date is partial date or missing, display 'DDMMYYY' only in column 'AE Start Date/Study Day'. If AE end date is partial date or missing, display 'DDMMYYY' only in column 'AE End Date/Study Day'.***
7) ***Place footnote for re-enrolling patients on the Patient ID number.***

Listing 16.2.5.2
Adverse Events Leading Changes in Study Treatment

Study Part	Planned Dose	Patient No.	AE No. [1]	System Organ Class/ Preferred Term/ Verbatim Text [2]	Start Date/ Study Day [3]	End Date/ Study Day [3]	Serious?	DLT?[4]	Initial Severity/Maximum Severity	Relationship to A/B/C[5]	Action Taken with A/B/C? [6]	Outcome
	250 mg QD PLX9486									NA/NA/Yes		
1											Withdrawl/reduced/modified	

[1] A * after the adverse event number indicates a treatment emergent adverse event.
[2] AEs are coded using MedDRA v 23.0.
[3] Study Day is relative to the date of the first dose of study medication. Study Day is only displayed for AE dates with complete date information.
[4] DLTs are defined as AEs occurring during the first 28 days of study drug administration (Cycle 1) that are classified as possibly or probably related to the study drug, and meet one of the following Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria listed in SAP Section 3.1
[5] Not Applicable for Study Parts in study part 1, relationship to and action take with PLX3397 for Study Parts in study part 2b, relationship to and action take with sunitinib for Study Parts in study part 2e.
[6] AEs whose actions taken with study drug (PLX9486, PLX3397 or sunitinib) is 'Drug Withdrawn' or if in the CRF form 'End of Treatment', a patient's primary reason for ending treatment from is 'Adverse Event' and a non-missing associated primary AE is recorded.
[7] If patient has primary reason for study discontinuation from the CRF from 'Study Exit Status' being 'Adverse Event' and a non-missing associated primary AE. In this study there were no cases which qualify for this footnote.
[8] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
AE = Adverse Event; CTCAE = Common Terminology Criteria for Adverse Events; DLT = Dose Limiting Toxicity; MedDRA = Medical Dictionary for Drug Activities, NA = Not Applicable.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer note:

1) ***Sort by start date and end date within each patient.***
2) ***Note that there may be more than one "other" action taken. List all, separated by '/'.***
3) ***Use XAE data set.***
4) ***Leave blanks at column 'End Date/Study Day' for observations which have completely missing AE End Date.***
5) ***If AE start date is partial date or missing, display 'DDMMYYY' only in column 'AE Start Date/Study Day'. If AE end date is partial date or missing, display 'DDMMYYY' only in column 'AE End Date/Study Day'.***
6) ***Include AEs if Action is "Drug Withdrawn" or datasets DS/DS2 indicate AE # led to Study Exit/ End of Study Treatmen and has an associated primary AE number.***
7) ***For columns 'Relationship to PLX3397 or Sunitinib/ Action Taken with PLX3397 or Sunitinib[5], in the column body, display 'NA/NA' for data from study part 1, display information of relationship/action taken with PLX3397 for Study Parts in study part 2b, display information of relationship/action taken with Sunitinib for Study Parts in study part 2e.***
8) ***If a patient has a primary reason for study discontinuation on the study exit status form with an non-missing AE number, append a superscript [7] to the AE verbatim term in the listing.***
9) ***If patients listed in footnote [8] appear in the listing, append the superscript [8] to the individual patient number in the listing.***

Listing 16.2.5.3
Dose Limiting Toxicity

Study Part	Planned Dose	Patient No.	DLT #	AE Associated with DLT	Date of Assessment	Patient on Study Drug at Least 28 Days?	Dose Limiting Hematologic Toxicities		Other DLT	
							Occurred?	Type [1]	Occurred? [2]	Specify [3]
1	250 mg QD PLX9486					Yes/No	Yes/No	Type 1/ Type 5	Yes/No	xxxx xxxxxxx

[1] Type 1 = Grade 4 Neutropenia; Type 2 = Grade ≥ 3 Neutropenia with fever; Type 3 = Grade 4 Thrombocytopenia, Type 4 = Grade ≥3 thrombocytopenia with clinically significant bleeding; Type 5 = Grade ≥ 3 Anemia.
[2] If Yes then any other Grade ≥ 3 toxicity (except for those listed on the CRF) for which, either the Principal Investigator or Sponsor deems further dose escalation inappropriate.
[3] If Yes, specify reason.
[4] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
AE = Adverse Event; DLT = Dose Limiting Toxicity.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programming note:
1) This can be done using EX3 dataset where the AETERM is populated. Only display the Types found in the data for a DLT, stack Type X/Type Y for each of the types a patient may have.

Listing 16.2.5.4
Adverse Events Leading to Death

Study Part	Planned Dose	Patient No.	Any AE?	AE No.[1]	System Organ Class // Preferred Term // Verbatim Text[2]	Start Date/ Study Day[3]	End Date/ Study Day[3]	Serious ?	DLT?[4]	Initial Severity/ Maximum Severity / Relationship to PLX9486/ Action Taken with PLX9486	Relationship to PLX3397 or Sunitinib/ Action Taken with PLX3397 or Sunitinib[5]	Other Actions Taken/ Treatment of Event	Outcome
1	250 mg QD PLX9486	[redacted]	Yes/ No	1*		[redacted] 5/ 2	[redacted] 5/ 36	Yes/No	Yes/No	Grade 1 (Mild)/ Grade 3 (Severe) Possibly Related/ Dose Not Changed	NA/NA	None/xxxxx	Recovered / Resolved
				2*									

[1] A * after the adverse event number indicates a treatment emergent adverse event.
[2] AEs are coded using MedDRA v 23.0.
[3] Study Day is relative to the date of the first dose of study medication. Study Day is only displayed for AE dates with complete date information.
[4] DLTs are defined as AEs occurring during the first 28 days of study drug administration (Cycle 1) that are classified as possibly or probably related to the study drug, and meet one of the following Common Terminology Criteria for Adverse Events (CTCAE) v4.03 criteria listed in SAP Section 3.1
[5] Not Applicable for Study Parts in study part 1, relationship to and action take with PLX3397 for Study Parts in study part 2b, relationship to and action take with sunitinib for Study Parts in study part 2e.
[6] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted].
AE = Adverse Event; CTCAE = Common Terminology Criteria for Adverse Events; DLT = Dose Limiting Toxicity; MedDRA = Medical Dictionary for Drug Activities, NA = Not Applicable.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by start date and end date within each patient.***
2) ***Note that there may be more than one "other" action taken. List all, separated by '/'.***
3) ***Use XAE data set.***
4) ***Leave blanks at column 'End Date/Study Day' for observations which have completely missing AE End Date.***
5) ***If AE start date is partial date or missing, display 'DDMMYYY' only in column 'AE Start Date/Study Day'. If AE end date is partial date or missing, display 'DDMMYYY' only in column 'AE End Date/Study Day'.***
6) ***Include AEs with Severity, Toxicity Grade = Fatal (Grade 5) or Death Details dataset specified AEs***

Plexxikon Inc.
Protocol PLX121-01

Listing 16.2.6.1.1
Hematology
Part 1 of 2

Study Part	Planned Dose	Patient No.	Visit	Sampling Collected?	Collection Date / Time	HGB (g/dL)	HCT (%)	Platelets ($x10^9$/L)	RBC ($x10^{12}$/L)	WBC ($x10^9$/L)
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No	[redacted] / 07:57	12.00 L [1]*	35.70 L	12.00 L (1)	430	430
			C1D1							
			C1D8							
			C1D15							
			C2D1							
			…							
			EOS							

Part 2 of 2

Study Part	Planned Dose	Patient No.	Visit	Sampling collected?	Collection Date / Time	Neutrophils (Absolute) ($x10^9$/L)	Lymphocytes (Absolute) ($x10^9$/L)	Eosinophils (Absolute) ($x10^9$/L)	Monocytes (Absolute) ($x10^9$/L)	Basophils (Absolute) ($x10^9$/L)

Note: L=Low and H=High with respect to laboratory reference ranges, where applicable. CTCAE v4.03 grades are in parentheses where applicable. * indicates abnormal, clinically significant, as reported by the investigator. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled; CTCAE = Common Terminology Criteria for Adverse Events.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by visit and analyte within each patient.***
2) ***Note that the same analyte may have different units and ranges for different patients due to test performed at difference among lab and etc.***
3) ***Convert lab results to a standard unit for each analyte (use ADLB.AVAL)***
4) ***For column 'Result', display the number of decimal places as in ADLB.AVAL***

Listing 16.2.6.1.2
Hematology – Other Tests

Study Part	Planned Dose	Patient No.	Visit	Collection Date / Time	Other Tests	Result	Unit	Reference Range Low	Reference Range High	Clinically Significant?
1	250 mg QD PLX9486	[redacted]	SCREEN	DDMMMYYYY/ HH:MM	BANDS	xx.x	xxxxx	xx.x	xx.x	Yes/No
					xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
			…							

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by visit, date/time and analyte (test name alphabetically) within each patient.***
2) ***For column 'Result', display the result as original result and in the number of decimal places as in raw data***

Listing 16.2.6.1.3
Hematology Laboratory Results: Grade 3 or Higher

Study Part	Planned Dose	Patient No.	Visit	Collection Date/Time	Lab ID	Lab Parameter (Unit)	Result	CTCAE Grade	Reference Range Low	Reference Range High
1	250 mg QD PLX9486	xx-xxx	C1D1	date9./time5.	1			Grade 3		
				date9.	1			Grade 4		
				date9.	1					
				date9.	1					
				date9.	2					
				date9.	3					
.										
.										

Note: Laboratory parameters are graded according to CTCAE v4.03. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled; CTCAE = Common Terminology Criteria for Adverse Events.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Plexxikon Inc.
Protocol PLX121-01

Listing 16.2.6.2.1
Chemistry
Part 1 of 3

Study Part	Planned Dose	Patient No.	Visit	Sampling collected?	Collection Date / Time	Alkaline Phosphatase (U/L)	ALT/SGPT (U/L)	AST/SGOT (U/T)	Total Bilirubin, (mg/dL)	Direct Bilirubin (mg/dL)	LDH (U/L)	Glucose (mg/dL)
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No	DDMMMYYYY/ HH:MM	12.00 L (1)*	35.70 L	12.00 L [1]	430	12.30 H	0.66 (2)	99 H
			C1D1									
			C1D8									
			…									

Part 2 of 3

Study Part	Planned Dose	Patient No.	Visit	Sampling collected?	Collection Date / Time	Sodium (mmol/L)	Potassium (mmol/L)	Chloride (mmol/L)	Carbon Dioxide (mmol/L)	Blood Urea Nitrogen (BUN) (mg/dL)	Creatinine (mg/dL)	Creatine Phosphokinase (U/L)

Part 3 of 3

Study Part	Planned Dose	Patient No.	Visit	Sampling collected?	Collection Date / Time	Protein, Total (g/dL)	Albumin (g/dL)	Calcium (mg/dL)	Phosphorus (mg/dL)	Uric Acid (mg/dL)	Magnesium (mg/dL)

Note: L=Low and H=High with respect to laboratory reference ranges, where applicable. CTCAE v4.03 grades are in parentheses where applicable. * indicates abnormal, clinically significant, as reported by the investigator. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled; CTCAE = Common Terminology Criteria for Adverse Events.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by visit, date/time and analyte within each patient.***
2) ***Note that the same analyte may have different units and ranges for different patients due to test performed at difference among lab and etc.***
3) ***Convert lab results to a standard unit for each analyte (use ADLB.AVAL)***
4) ***For column 'Result', display the number of decimal places as in ADLB.AVAL***

Listing 16.2.6.2.2
Chemistry – Other Tests

Study Part	Planned Dose	Patient No.	Visit	Collection Date / Time	Other Tests	Result	Unit	Reference Range Low	Reference Range High	Clinically Significant?
1	250 mg QD PLX9486	[redacted]	SCREEN	DDMMMYYYY/ HH:MM	xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
					xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
			…							

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by visit, date/time and analyte (test name alphabetically) within each patient.***
2) ***For column 'Result', display the result and number of decimal places as in raw data***

Listing 16.2.6.2.3
Chemistry Laboratory Results: Grade 3 or Higher

Study Part	Planned Dose	Patient No.	Visit	Collection Date/Time	Lab ID	Lab Parameter (Unit)	Result	CTCAE Grade	Reference Range Low	Reference Range High
1	250 mg QD PLX9486	xx-xxx	C1D1	date9./time5.	1			Grade 3		
				date9.	1			Grade 4		
				date9.	1					
				date9.	1					
				date9.	2					
				date9.	3					

.
.

Note: Laboratory parameters are graded according to CTCAE v4.03. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled; CTCAE = Common Terminology Criteria for Adverse Events.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.6.3.1
Urinalysis
Part 1 of 2

Study Part	Planned Dose	Patient No.	Visit	Sampling Collected?	Collection Date / Time	Appearance	Color	pH	Protein/ Albumin	Glucose/ Sugar	Ketones/ Acetones	Hemoglobin/ Blood	Nitrite
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No	DDMMMYYYY/ HH:MM	CLEAR	STRAW	0.66	Positive, 1+*	Positive, Trace	Not Done	Positive, +4	Positive, Trace

Part 2 of 2

Study Part	Planned Dose	Patient No.	Visit	Sampling Collected?	Collection Date / Time	Microscopic Exam Performed?	WBC (cells/hpf)	Casts
1	250 mg QD PLX9486	[redacted]	SCREEN C1D1	Yes/No	DDMMMYYYY/ HH:MM	Yes/No	50-100	Absent/Present/Not Done

Note: L=Low and H=High with respect to laboratory reference ranges for pH; * indicates abnormal, clinically significant, as reported by the investigator.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled; WBC = White Blood Cell.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by visit, date/time and analyte within each patient.***
2) ***Note that the same analyte may have different units and ranges for different patients due to test performed at difference among lab and etc.***
3) ***Convert lab results to a standard unit for each analyte (use ADLB.AVAL)***
4) ***For column 'Result', display the number of decimal places as in ADLB.AVAL***
5) ***If test result is positive, Specify will be Trace, 1+, 2+, 3+, 4+ or Unknown.***

Plexxikon Inc. **Page 1 of x**
Protocol PLX121-01

Listing 16.2.6.3.2
Urinalysis – Other Tests

Study Part	Planned Dose	Patient No.	Visit	Collection Date / Time	Other Tests	Result	Unit	Reference Range Low	Reference Range High	Clinically Significant?
1	250 mg QD PLX9486	[redacted]	SCREEN	DDMMMYYYY/ HH:MM	xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
					xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
			…							

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted].
EOS = End of study; HPF = High power field; LPF = Low power field; NA and N/A = Not applicable; RBC = White Blood Cell; UA = Urinalysis; UNK = Unknown; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) ***Sort by visit, time point and analyte (test name alphabetically) within each patient.***
2) ***For column 'Result', display the result and number of decimal places as in raw data***

Plexxikon Inc.
Protocol PLX121-01

Listing 16.2.6.4.1
Coagulation

Study Part	Planned Dose	Patient No.	Visit	Sampling Collected?	Collection Date / Time	Was Patient Fasting?	Prothrombin Time (PT) (sec)	Partial Thromboplastin Time (PTT) (sec)	International Normalized Ratio (INR)	Other, Specify/ Result/ Units
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No	DDMMMYYYY/ HH:MM	Yes/No/Unknown	9.8 (1)	23.0*	0.98	

Note: L=Low and H=High with respect to laboratory reference ranges, where applicable. CTCAE v4.03 grades are in parentheses where applicable. * indicates abnormal, clinically significant, as reported by the investigator. CTCAE grading is performed using data values only and does not consider symptomatic criteria.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled; CTCAE = Common Terminology Criteria for Adverse Events.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) Sort by Visit within each patient.

Listing 16.2.6.4.2
Coagulation – Other Tests

Study Part	Planned Dose	Patient No.	Visit	Collection Date / Time	Was patient fasting?	Other Tests	Result	Unit	Reference Range Low	Reference Range High	Clinically Significant?
1	250 mg QD PLX9486	[redacted]	SCREEN	DDMMMYYYY/ HH:MM	Yes/No/Unknown	xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
						xxxxx	xx.x	xxxxx	xx.x	xx.x	Yes/No
			…								

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by visit, time point and analyte (test name alphabetically) within each patient.***
2) ***For column 'Result', display the result and number of decimal places as in raw data***

Plexxikon Inc.
Protocol PLX121-01

Listing 16.2.7.1
Vital Signs
Part 1 of 2

Study Part	Planned Dose	Patient No.	Visit	Time Point	Vitals Collected?	Measurements Date / Measurements Time	Weight (kg) Result	Weight (kg) Change from Baseline	Temperature (°C) Result	Temperature (°C) Change from Baseline	Heart Rate (bpm) Result	Heart Rate (bpm) Change from Baseline
1	250 mg QD	[redacted]	SCREEN		Yes/No		60		37.6		60	
			C1D1	Pre-Dose	Yes/No		61*		36.6*		62*	
							62	1	36.4	-0.2	70	8
											81	
		…		…								

Part 2 of 2

Study Part	Planned Dose	Patient No.	Visit	Time Point	Vitals Collected?	Measurements Date / Measurements Time	Respiration (breaths/min) Result	Respiration (breaths/min) Change from Baseline	SBP (mmHg) Result	SBP (mmHg) Change from Baseline	DBP (mmHg) Result	DBP (mmHg) Change from Baseline	Position of Patient
1	250 mg QD	[redacted]	SCREEN		Yes/No		15		137H		83		Sitting
			C1D1	Pre-Dose	Yes/No		16*		132H*		82*		
							22	6	110	-22^	67	-15#	
													Standing
													Supine
		…		…									Prone

Note: * Baseline value. ^ indicates decrease from baseline in SBP greater than 20, # indicates decrease from baseline in DBP greater than 10.
[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
DBP = Diastolic Blood Pressure; EOS = End of study; SBP = Systolic Blood Pressure; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Combine data from VS (Vital Signs) & VS1 (Pre and Post Dose Vital Signs)***
2) ***Use ADVS.AVAL to get standardized results***

Listing 16.2.7.2
Physical Examination

Study Part	Planned Dose	Patient No.	Visit	Examination Performed?	Examination Date	Any Abnormal Findings?[1]
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No		Yes/No
			C1D1			

[1] Abnormal findings prior to treatment are documented in medical history; abnormal findings post treatments are documented as adverse events.
[2] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Plexxikon Inc.
Protocol PLX121-01

Listing 16.2.7.3.1
12-Lead Electrocardiogram

Study Part	Planned Dose	Patient No.	Visit	Time Point	ECG Performed?	ECG Date/ Time	ECG Number	Interpre-tation[1]	HR (bpm)	RR[2] (msec)	PR (msec)	QRS (msec)	QT (msec)	QTcF[2] (msec)	Change from Baseline of QTcF[2]
1	250 mg QD PLX9486	[redacted]	10-Day Run-in	xxxxx	Yes/No	Date9./ 09:25	1	Normal	xx	xx	xx	xx	xx	xx	
					No		2								
					No		3								
							4*		xx	xx	xx	xx	xx	xx	
			SCREEN				1								
							2								
							3								
							4*								
			C1D1	Pre-Dose*			1								
							2								
							3								
							4*								
				1 Hour Post-Dose			1								
							2								
							3								
							4*								

Note: * Baseline value; 4* = Average of triplicate. L=Low and H=High with respect to reference ranges for PR and QRS.
Note: The baseline value is defined as the last non-missing value of the average of the triplicate ECGs prior to the patient's first dose of study drug.
[1] If interpretation was abnormal, was the ECG clinically significant?
[2] RR and QTcF are derived.
[3] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
CS = [Abnormal] Clinically Significant; EOS = End of study; NCS = [Abnormal] Not Clinically Significant; ND = Not Done; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) Combine records from all raw ECG datasets: EG, EG1, EG2, EG3, EG4, EG5, EG7. Display RR, QTcB and QTcF from ADEG.

Listing 16.2.7.3.2
12-Lead Electrocardiogram – Patients with Outlier QTc Values

Study Part	Planned Dose	Patient No.	Gender	Visit	ECG Date	ECG Time	Parameter (msec)	Baseline Result	Actual Result [1]	Change From Baseline [1]
1	250 mg QD	xxxxxx	[redacted]	Visit 1	date9.	time5.	QTcF	xxx.x	xxx.x	xx.x
				Visit 2	date9.	time5.	xxxx	xxx.x	xxx.x	xx.x
		xxxxxx	[redacted]	Visit 1	date9.	time5.	xxxx	xxx.x	xxx.x	xx.x
				Visit 2	date9.	time5.	xxxx	xxx.x	xxx.x	xx.x
P1-C2	xxxxx	xxxxxx	[redacted]	Visit 1	date9.	time5.	xxxx	xxx.x	xxx.x	xx.x
						time5.	xxxx	xxx.x	xxx.x	xx.x

Note: The baseline value is defined as the last non-missing value of the average of the triplicate ECGs prior to the patient's first dose of study drug.
QTcF (Fridericia's method) are derived.
[1] Post-baseline outlier values considered in this listing are as follows: (1) QTcF ≥ 450 msec (for males) or ≥ 470 msec (for females), or (2) increase from baseline in QTcF >30 msec. Findings which meet any of these outlier criteria are asterisked.
[2] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.
Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Use derived RR, QTcB, QTcF (ADEG.PARAMCD=RRINT, DQTCF, DQTCB)

Listing 16.2.7.4
ECOG Performance Status Assessment

Study Part	Planned Dose	Patient No.	Visit	ECOG Performed?	Assessment Date	ECOG[1]
1	250 mg QD PLX9486	[redacted]	C1D1 C1D8 C1D15 C2D1 … TERM	Yes/No	DDMMMYYYY	0/1/2/3/4/5

[1] ECOG: 0 = Fully active, able to carry on all pre-disease performance without restriction, 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work, 2 = Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours, 3 = Capable of only limited self care, confined to bed or chair more than 50% of waking hours, 4 = Completely disabled. Cannot carry on any self care. Totally confined to bed or chair, 5 = Dead.
[2] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
ECOG= Eastern Cooperative Oncology Group; EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer Note:
1) Get ECOG data from releavant parts in CRF form 'Physical Examination' (raw dataset PE)

Listing 16.2.7.5
Echocardiogram/MUGA Scan

Study Part	Planned Dose	Patient No.	Visit	Performed?	Assessment Date	Assessment Time	% LVEF	Interpretation	Associated Primary AE[1]	Description of Abnormality
1	250 mg QD PLX9486	xx-xxx	C1D1	Yes/No	DDMMMYYYY	10:15		Normal/Abnormal, CS/Abnormal, NCS		

[1] Only recorded if the interpretation is 'Abnormal, CS'.
[2] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
MUGA = Multigatd acquisition; CS = Clinically Significant; NCS = Not Clinically Significant; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.7.6
Thyroid Stimulating Hormone (TSH) Level

Study Part	Planned Dose	Patient No.	Visit	Sample Collected?	Collection Date	Collection Time	TSH Level
1	250 mg QD PLX9486	xx-xxx	C1D1	Yes/No	DDMMMYYYY	10:15	

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.7.7
Pregnancy Test

Study Part	Planned Dose	Patient No.	Visit	Test performed?	If No, Specify Reason	Test Type	Collection Date	Result
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No		Urine Dipstick		Negative
			EOS	Yes/No		Serum		Positive

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Listing 16.2.7.8.1
Circulating DNA

Study Part	Planned Dose	Patient No.	Visit	Assessment Obtained Pre-dose?	Assessment Date	Assessment Time
1	250 mg QD PLX9486	[redacted]	C1D1	Yes/No	DDMMMYYYY	HH:MM

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted].
EOS = End of study; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) Sort by Visit within each patient.

Listing 16.2.7.8.2
Tumor Markers

Study Part	Planned Dose	Patient No.	Visit	Sample Collected?	Collection Date	Collection Time	Test Type	Result (Unit)
1	250 mg QD PLX9486	[redacted]	C1D1	Yes/No/NA	DDMMMYYYY	HH:MM	Carcinoembryonic Antigen-CEA (Colorectal) CA-125 (Ovarian) Calcitonin (Medullary Thyroid) CA19-9 (Pancreatic) Prostate-Specific Antigen-PSA (Prostate) Other, specify:	0.5 (ng/mL)

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]
EOS = End of study; NA = Not Applicable; UNS = Unscheduled.

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) Sort by Visit within each patient.

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Protocol PLX121-01

Listing 16.2.7.8.3
Archival Tumor Tissue Collection

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

Study Part	Planned Dose	Patient No.	Visit	Sample Obtained?	Collection Date	Collection Time	Anatomical Site	Tracking Number for Specimen	Date Sample Shipped
1	250 mg QD PLX9486	[redacted]	SCREEN	Yes/No	DDMMMYYYY	HH:MM	COLON	xxxxxxxxxx	DDMMMYYYY

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:

1) ***Sort by Visit within each patient.***
2) ***If tissue specimen collection date is unknown, then put 'Unknown' into collection date column.***

Listing 16.2.7.8.4
Optional Paired Tumor Biopsy

Study Part 1 – Dose Escalation Study Parts (Single-Agent PLX9486)

Study Part	Planned Dose	Patient No.	Visit	Sample Collected?	Collection Date	Type	Anatomical Site	Shipping Date	Tracking Number for Specimen
1	250 mg QD	xx-xxx	C1D1	Yes	[redacted]	Core			
			C1D15	Yes	[redacted]				
			C2D1	Yes	[redacted]				

[1] Patient numbers [redacted] completed their initial Cohort and subsequently re-enrolled, respectively, as patient numbers [redacted]

Program Location: \\xx\xxx\xxx\xxx\xxxxxx\xxxxxxxxxxxxxxxx\xxxx\xxxxx.sas date time

Programmer notes:
1) Sort by Visit within each patient.

Signature: [redacted]
Email:
Title:

Signature: [redacted]
Email:
Title:

Signature: [redacted]
Email:
Title: