KZR-261-101

A PHASE 1 STUDY OF KZR-261, A SMALL MOLECULE SEC61 INHIBITOR, IN SUBJECTS WITH ADVANCED SOLID MALIGNANCIES

Clinicaltrials.gov Identifier *NCT05047536*

Date of statistical analysis plan: *05 August 2024*

STATISTICAL ANALYSIS PLAN

A Phase 1 Study of KZR-261, a Small Molecule Sec61 Inhibitor, in Subjects with Advanced Solid Malignancies

SPONSOR:

Kezar Life Science, Inc.

PROTOCOL NUMBER:

Protocol KZR-261-101, Version 5.0

SAP DATE: *05 August 2024*

SAP VERSION: *Version 2.0*

A Phase 1 Study of KZR-261, a Small Molecule Sec61 Inhibitor, in Subjects with Advanced Solid Malignancies

Protocol Number: Protocol KZR-261-101, Version 5.0, dated 02 October 2023

SAP Version: Version 2.0

SAP Date: 05 August 2024

Statistical Analysis Plan Approval

[redacted] 15-Aug-2024 | 17:43 EDT

Approved by: _____ _____
[redacted] Date

[redacted] 15-Aug-2024 | 18:38 EDT

Approved by: _____ _____
[redacted]

Approved by: *See electronic signature and date* _____
[redacted] Date
Kezar Life Sciences, Inc.

Approved by: *See electronic signature and date* _____
[redacted] Date
Kezar Life Sciences, Inc.

Approved by: *See electronic signature and date* _____
[redacted] Date
Kezar Life Sciences, Inc

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
aPTT	Activated Partial Thromboplastin Time
ATC	Anatomical Therapeutic Chemical
AUC	Area Under the Plasma Concentration-time Curve
CBR	Clinical Benefit Rate
CEA	Carcinoembryonic Antigen
CL	Clearance
C_{max}	Maximum Plasma Concentration
CR	Complete Response
CT	Computed Tomography
D	De-Escalate to the Lower Dose
DLT	Dose-Limiting Toxicity
DOR	Duration of Response
DU	De-Escalate to the Lower Dose, Current Dose May Not Be Used Again Pending Advice of the Safety Review Committee
E	Escalate to the Next Higher Dose
ECG	Electrocardiogram
ECOG PS	Eastern Cooperative Oncology Performance Status
eCRF	Electronic Case Report Form
EI	Equivalence Interval
FBS	Fasting Blood Sugar
FIH	First-in-Human
ICH	International Conference on Harmonisation
IV	Intravenous
MAD	Maximum Administered Dose
mCRC	Metastatic Colorectal Carcinoma
mCRPC	Metastatic Castration-Resistant Prostate Cancer
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
MTD	Maximum Tolerated Dose
n	Number of Observations

Abbreviation	Definition
NCI CTCAE	National Cancer Institute Common Terminology for Adverse Events
ORR	Objective Response Rate
OS	Overall Survival
PAVA	Pool-Adjacent-Violators Algorithm
PCWG3	Prostate Cancer Working Group 3
PD	Progressive Disease
PFS	Progression-Free Survival
PK	Pharmacokinetics
PR	Partial Response
PSA	Prostate-specific Antigen
QTcF	QT Interval Corrected with Fridericia's Formula
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	Recommended Phase 2 dose
S	Stay at the same dose
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Stable Disease
[redacted]	[redacted]
SOC	System Organ Class
SRC	Safety Review Committee
$t_{1/2}$	Elimination Half-life
TEAE	Treatment-Emergent Adverse Event
VS	Vital Signs
V_{ss}	Volume of Distribution at Steady State
WHODrug	World Health Organization Drug Dictionary

1. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe in detail the planned analyses and reporting that may be conducted for protocol KZR-261-101, Version 5.0 dated 02 October 2023.

This SAP is being written with due consideration of the recommendations outlined in the most recent International Conference on Harmonisation (ICH) E9 Guideline entitled Guidance for Industry: Statistical Principles for Clinical Trials, the most recent ICH E9(R1) Addendum entitled Addendum on Estimands and Sensitivity Analysis in Clinical Trials to the Guideline on Statistical Principles for Clinical Trials, and the most recent ICH E3 Guideline, entitled Guidance for Industry: Structure and Content of Clinical Study Reports.

The statistical analysis methods presented in this document will supersede the statistical analysis methods described in the clinical protocol. If additional analyses are required to supplement the planned analyses described in this SAP, they may be completed and will be described in the clinical study report.

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. Study Objectives

2.1.1. Primary Objective for Part 1 (Dose Escalation)

- To evaluate the safety, tolerability, and PK of KZR-261 and identify the maximum tolerated dose (MTD) or maximum administered dose (MAD).

2.1.2. Primary Objective for Parts 2A and 2B (Dose Expansion and Dose Optimization)

- To further characterize the safety profile of KZR-261 and identify the recommended Phase 2 dose (RP2D).

2.1.3. Secondary Objectives

- To detect evidence of anti-tumor activity of KZR-261.
- To further characterize the PK of KZR-261 (Part 2A and 2B only).

2.1.4. Exploratory Objectives

- To evaluate potential pharmacodynamic biomarkers in peripheral blood based on gene expression and proteomic changes.
- To explore and identify potential predictive biomarkers in tissue (including tumor) samples based on gene expression at baseline.
- To evaluate changes in potential predictive biomarkers during treatment.

2.2. Study Endpoints

2.2.1. Primary Endpoints

2.2.1.1. Safety – Part 1

Safety endpoints include the following:

- Incidence of dose-limiting toxicities (DLTs) during the DLT assessment period. DLTs will be assessed during Part 1 using pre-specified AE criteria detailed in Protocol Section 3.2.3.
- Type, incidence, and severity of adverse events (AEs) and serious adverse events (SAEs), deaths, dose reductions, treatment interruptions and discontinuations due to toxicity, and changes from baseline in clinical laboratory parameters. Adverse events will be graded for severity per the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5.0.
- Changes from baseline in physical examination, ECG, and ocular examination findings.
- Changes from baseline in vital sign (VS) measurements and pulse oximetry.
- Identification of the MTD or MAD.

2.2.1.2. Safety – Parts 2A and 2B

Safety endpoints include the following:

- Type, incidence, and severity of AEs and SAEs, deaths, dose reductions, treatment interruptions and discontinuations due to toxicity, and changes from baseline in clinical laboratory parameters.
- Changes from baseline in physical examination, ECG, and ocular examination findings.
- Changes from baseline in VS measurements and pulse oximetry.
- Identification of the RP2D.

2.2.1.3. Pharmacokinetic

PK endpoints (if applicable) include the following:

- Plasma concentrations, including maximal plasma concentration (C_{max}).
- Area under the plasma concentration-time curve (AUC).
- Elimination half-life ($t_{½}$).
- Clearance (CL).
- Volume of distribution (V_z).

2.2.2. Secondary Endpoints

2.2.2.1. Anti-tumor Activity

The anti-tumor activity of KZR-261 will be measured by the following:

- Objective response rate (ORR) defined as the rate of partial responses (PRs) plus complete responses (CRs) according to the revised Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) guidelines (Eisenhauer et al., 2009). Subjects with mCRPC will be assessed per Prostate Cancer Working Group 3 (PCWG3) guidelines (Scher et al., 2016).
- Clinical benefit rate (CBR), defined as the proportion of subjects achieving a best response of CR/PR or SD over at least 2 consecutive response assessment time points.
- Duration of response (DOR).
- Progression-free survival (PFS).
- Overall survival (OS).

2.2.3. Exploratory Endpoints

2.2.3.1. Exploratory Biomarker Endpoints

Exploratory endpoints include the following:

- Serum biomarker levels including cytokines and other circulating proteins.
- Whole blood gene expression changes.
- Protein profiling of peripheral blood mononuclear cells (PBMCs).
- Circulating tumor-associated proteins.
- Changes in circulating tumor DNA.
- Baseline gene and/or protein expression in pre- and on-treatment (post-Cycle 2) tumor biopsies to identify a potential predictive biomarker(s).

3. STUDY DESIGN AND PROCEDURES

3.1. General Study Design

This FIH, open-label, multicenter, Phase 1 study is designed to assess the safety and tolerability, preliminary anti-tumor activity, and the PK characteristics of KZR-261, as well as identify the RP2D. KZR-261 will be administered as a 30- to 60-minute IV infusion via a central line on Days 1, 8, and 15 of a 4-week (28-day) treatment cycle. (Doses may be held up to 7 days for resolution of non-DLT toxicity.) Eligible subjects will have locally advanced or metastatic solid malignancies and no available or approved therapies, or refused such therapies if available.

The study will be conducted in 2 parts: Part 1 (Dose Escalation) and Part 2 (Part 2A –Dose Expansion and Part 2B – Dose Optimization).

In Part 1, increasing doses of KZR-261 will be administered in an "i3+3" design to approximately 70 subjects to evaluate the safety and tolerability, PK, and pharmacodynamics of KZR-261, including identifying the MTD or MAD.

The Dose Expansion phase will commence following determination of the MTD/MAD and a review of the totality of safety data from Part 1. Part 2A will further characterize the safety profile of KZR-261 at the MTD or MAD and evaluate the anti-tumor activity of KZR-261 in subjects who have select malignancies. Up to 175 subjects may be enrolled in up to 4 tumor-specific cohorts (such as malignant melanoma [including uveal melanoma], mesothelioma, mCRPC, and mCRC) and 1 "All-Tumors" cohort. Additional or different tumor-specific cohorts may be investigated at the Sponsor's discretion. Each tumor-specific cohort will enroll 15 subjects during Stage 1, expanding up to 35 subjects (Stage 2) as determined by a prespecified futility analysis and as long as the tumor type is not selected for investigation in Part 2B (see below). If futility is not rejected after Stage 1 (ie, prespecified criteria for futility are met), subsequent enrollment to that Part 2A cohort will cease. The All-Tumors cohort may enroll up to 35 biopsy-evaluable subjects.

Dose optimization in tumor-specific cohorts may be initiated at the Sponsor's discretion based on the totality of data after the MTD/MAD has been determined. The Sponsor may choose to cease enrollment in the Part 2A tumor-specific cohort and initiate enrollment of that tumor type in Part 2B. Approximately 30 subjects within each tumor-specific cohort will be randomized in a 1:1 ratio to receive KZR-261 at the MTD/MAD or a lower clinically active dose of KZR-261 in Part 2B. Based on additional safety data from Part 2A, the Sponsor may convene an SRC meeting to determine whether a lower dose than the MTD/MAD as determined in Part 1 should be evaluated in Part 2B. Part 2B will further characterize the safety profile of KZR-261 to support determination of the RP2D and further evaluate the anti-tumor activity of KZR-261 in subjects with select malignancies. The number of tumor-specific cohorts to be investigated in Part 2B will be at the Sponsor's discretion.

3.2. Schedule of Visits and Assessments

The Schedule of Visits and Assessments are provided in Appendix A Schedule of Events for Cycles 1 & 2 and Appendix B Schedule of Events for Cycle 3+.

4. STUDY TREATMENTS

KZR-261 is a small molecule protein secretion inhibitor formulated for clinical use as [redacted] KZR-261 for Injection is a lyophilized drug product that is supplied in vials delivering 75 mg of KZR-261 [redacted]. Each vial is reconstituted with sterile Water for Injection prior to administration. For all subjects, KZR-261 will be administered as an IV infusion via a central line on Days 1, 8, and 15 of a 4-week (28-day) treatment cycle. An IV infusion pump or syringe pump will be used for treatment of all subjects.

4.1. Dose Level Determination

4.1.1. Part 1 Dose Escalation Administration

The first cohort of subjects will be initiated with KZR-261 administered at 1.8 mg/m^2. Subjects will receive 3 doses in a 28-day cycle. Dose-escalation decisions for KZR-261 will be guided by the i3+3 design with the targeted DLT rate pT=0.3 and the equivalence interval (EI) = [0.25, 0.35]. The number of subjects that will be enrolled at each dose level for KZR-261 varies, with a minimum of 2 subjects per cohort, with a typical cohort size of 2-4, and with 6 to approximately 12 subjects dosed at potential MTD or MAD. Safety data from all subjects enrolled in each cohort will be reviewed to confirm occurrence of any DLTs experienced during the first cycle (DLT assessment period) to determine whether to expand the current cohort or to initiate enrollment into the next cohort as described in Table 1.

The columns in Table 1 represents the number of subjects enrolled at the dose, and the row represents the number of subjects experiencing any DLTs at the same dose.

Table 1: Dose Escalation Decision Matrix for Part 1 Dose Escalation

	Number of Subjects												
Number of Subjects with DLTs		1	2	3	4	5	6	7	8	9	10	11	12
	0	E	E	E	E	E	E	E	E	E	E	E	E
	1	S	S	S	S	E	E	E	E	E	E	E	E
	2		DU*	D	D	S	S	S	S	E	E	E	E
	3			DU	DU	D	D	D	D	S	S	S	S
	4				DU	DU	DU	D	D	D	D	D	S
	5					DU	DU	DU	DU	DU	D	D	D
	6						DU	DU	DU	DU	DU	DU	D
	7							DU	DU	DU	DU	DU	DU
	8								DU	DU	DU	DU	DU
	9									DU	DU	DU	DU
	10										DU	DU	DU
	11											DU	DU
	12												DU

The dose-escalation decisions are as follows: E: Escalate to the next higher dose; S: Stay at the same dose; D: De-escalate to a lower dose; DU: De-escalate to a lower dose, the current dose may not be used again pending advice of the Safety Review Committee.

The initial dose cohort will receive KZR-261 1.8 mg/m^2. Subjects will receive 3 doses in a 28-day cycle. Dose administration is planned for Days 1, 8, and 15 of each cycle. Doses may be held up to 7 days for resolution of non-DLT toxicity.

A minimum of 2 subjects will be enrolled at each dose level of KZR-261. The number of subjects that will be enrolled at each dose level varies, with a typical cohort size of 2-4, and with 6 to approximately 12 subjects dosed at the MTD/MAD. Dose levels for cohorts and the percent increase in dose can be found in Table 2.

Table 2: Dose level by cohort

Cohort	Dose Level (mg/m^2)	Percent Increase from Previous Cohort's dose (%)
1	1.8	NA
2	3.6	100
3	7.2	100
4	12.0	67
5	18.0	50
6	27.0	50
7	40.0	50
8	60.0	50
9*	80.0	33

*Additional dose cohort(s) may be needed to reach MTD/MAD

Definition of DLT

A DLT is defined as an AE or abnormal laboratory value that occurs during the first 28 days of treatment and meets the criteria listed below, unless it is assessed to be related to disease, disease progression, intercurrent illness, or concomitant medications.

Toxicities will be assessed by the Investigator using the NCI CTCAE Version 5.0. AEs that are not listed on the NCI CTCAE are to be assessed using the criteria in Protocol Section 9.1.2. The attribution of an AE to KZR-261 is to be assessed by the Investigator using the criteria in Protocol Section 9.1.3.

DLTs will be assessed in Cycle 1. Subjects who experience a DLT after the first, second, or third dose of KZR-261 will be counted as having a DLT but must be withdrawn from the study and will not be replaced. For subjects receiving study drug beyond Cycle 1, any late toxicities that occur after the DLT period (Cycle 1) will be assessed to determine the final MAD/RP2D to be carried forward in the dose expansion phase.

Subjects who do not experience a DLT in Part 1 Cycle 1 (Dose Escalation) must receive all of their scheduled doses (Days 1, 8, and 15) during the DLT assessment period with completed follow-up data available through 28 days of Cycle 1 to be eligible for DLT assessment (ie, DLT-assessable). Subjects in Part 1 Cycle 1 who miss a dose for non-AE-related reasons may be included in the DLT assessment period upon review by the Medical Monitor.

Definition of MTD, MAD, and RP2D

The estimated MTD is the dose level associated with approximately 30% of DLT-evaluable subjects experiencing a DLT. The target interval for the DLT rate is 25%-35%. Due to the discreteness of the dose levels and in the interest of the safety of subjects, the estimated MTD is the highest tested dose level with DLT rate $\leq$35% in at least 6-12 DLT-evaluable subjects. In general, the MTD will equal the RP2D unless one or more of the following suggest that an alternate dose below the MTD would be preferable:

- Clinically significant anti-tumor effect.
- The MTD is not achieved, in which case the MAD may become the RP2D.
- The occurrence of late and relevant AEs that occur after the DLT period.
- Cumulative toxicity of the MTD or MAD, reflecting that the administration of multiple cycles at the MTD or MAD is not feasible.
- AEs observed beyond Cycle 1 that would require setting the RP2D below the MTD level.

The SRC will evaluate the totality of the events and consider whether they could result from a cumulative toxicity or are significant for the determination of the RP2D.

The MAD is declared without an MTD based on a dose level with an observed DLT rate <25% (the lower bound of the MTD range) and where sufficient safety and efficacy signals have been observed.

The RP2D is the dose chosen for further study based on Phase 1 study results. The RP2D will take into account late and relevant toxicities that occur after the DLT period and/or the cumulative tolerance of multiple cycles of treatment. If the MTD or MAD proves to be clinically feasible for long-term administration in a reasonable number of subjects, then this dose usually becomes the RP2D. Further experience with the MTD/MAD may result in a RP2D dose lower than the MTD/MAD (eg, if in the expansion part >25% of subjects require a dose reduction due to toxicity, then the sponsor may convene an SRC to determine if a lower RP2D needs to be determined).

4.1.2. Part 2A Tumor-Specific Dose Expansion Administration

Following determination of the MTD/MAD in Part 1 Dose Escalation, separate tumor-specific cohorts of 15 subjects will be treated with KZR-261 using the identified MTD/MAD or SRC recommended dose. Following an interim analysis of the first 15 subjects in each cohort, the SRC will decide whether to enroll an additional 20 subjects into the respective tumor-specific cohort for a total of 35 enrolled subjects per tumor-specific cohort.

4.1.3. Dose Modification Guidelines

Dose modifications may only be considered in cycles after Cycle 1 during Part 1 (Dose Escalation). Dose modifications may be considered during any cycle in Part 2A and 2B (Dose Expansion and Dose Optimization). In the circumstance that a subject enrolled in Part 1 has experienced an event that qualifies as a DLT the subject must be discontinued from the study and followed for resolution of AEs. Following the DLT assessment period, doses may be held or modified for specific AEs and/or laboratory abnormalities in Cycles 2+ for subjects participating in the dose escalation part and in all cycles for subjects in the dose expansion part.

4.1.3.1. Dose Reductions and Interruptions

Subjects who experience an AE at any time during the study are permitted to undergo approved dose interruptions; subjects must continue to fulfill the Dosing Criteria in Protocol Section 6.1.2 and Protocol Section 6.1.3 prior to each dose.

Subjects are not permitted to undergo dose reductions during the DLT assessment period other than temporary study discontinuation of study medication as provided in Individual Stopping Rules.

Additional dose modification instructions are found in the Protocol Section 6.1.4.

4.2. Method of Assigning Subjects to Treatment Groups

4.2.1. Subject Assignment in Part 1 Dose Escalation

Subjects who successfully complete the inclusion/exclusion screening phase and provide informed consent will be enrolled into the currently available dose cohort within 28 days of completing the screening. Inclusion and exclusion criteria are described in the Protocol Section 4.2.

4.2.2. Subject Assignment in Part 2A and 2B Tumor-Specific Dose Expansion and Dose Optimization

Subjects who successfully complete the inclusion/exclusion screening, including the additional Part 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization) inclusion screening criteria, and provide informed consent will be enrolled into the respective tumor-specific cohort at the MTD/MAD or SRC recommended dose. Additional screening criteria are described in the Protocol Section 4.2.2.

4.3. Blinding and Unblinding

This is a FIH, open-label, multicenter, Phase I study in which all subjects receive the investigational product, KZR-261, without randomization. As such, the study is unblinded.

5. SAMPLE SIZE AND POWER CONSIDERATIONS

The sample size for Part 1 will be approximately 70 subjects, but the actual sample size will depend on the number of dose levels of KZR-261, number of subjects per dose level, and the number of subjects treated at the MTD or the MAD(s) of KZR-261.

Dose escalation will continue accruing until one of the three stopping conditions below is triggered:

- The maximum sample size has been achieved,
- MTD/MAD has been identified with sufficient accuracy: data from 6 to approximately 12 subjects have been accumulated at a dose that is deemed to be the MTD/MAD, or
- All doses explored appear to be overly toxic and the MTD cannot be determined.

Due to binomial data variability in small samples, DLTs may be observed in a first cohort(s) by chance even when the true probability (DLT) is fairly low. This could result in the estimated posterior DLT rate exceeding the targeted 30% very early in the trial, triggering an early stop when very few subjects (2-4) have been treated. To prevent stopping the trial prematurely in such cases, a step-down option with a lower dose of 0.9 mg/m^2 is added to the dose grid. This dose

will be explored only if a high DLT rate occurs in the first cohort assigned to 1.8 mg/m^2, ie, it will not be used as a starting dose.

Upon identification of the MTD/MAD at the conclusion of Part 1, the study will continue with up to 4 tumor-specific expansion cohorts and 1 All-Tumors cohort in Part 2A. As previously noted, the tumor-specific cohorts (n = 15 at interim) may be increased up to 35 subjects per cohort to more precisely estimate the anti-tumor activity of KZR-261, if there is a sufficient efficacy signal at the interim analyses (Protocol Section 10.6) and if the tumor type is not selected for investigation in Part 2B (dose optimization). The All-Tumors cohort may enroll up to 35 biopsy-evaluable subjects.

Go/No-Go futility analysis for each tumor-specific cohort in Part 2A will be based on CBR as the primary outcome measurement (as defined in Protocol Section 10.5.5) after Stage 1 enrollment of 15 subjects. Each of the expansion cohorts is based on the following assumptions:

- At the interim analysis, if there is 1 or no subject with clinical benefit (ie, CBR rate <7%), further enrollment into the cohort will be stopped for futility. If futility is rejected at the interim analysis (ie, 2 or more of 15 subjects with clinical benefit), the final analysis will be based on a total 35. Note: Outcomes (ie, presence or absence of clinical benefit) for subjects enrolled in Part 1 with the same tumor type and who received the same dose of KZR-261 as evaluated in the corresponding Part 2A, tumor-specific cohort may be included among the initial 15 subjects at the interim analysis, as described above.

The operating characteristics of this design are presented in Table 3. If the true CBR is less than 5%, there is an 83% probability to reach the futility criterion at interim. On the other hand, if the true CBR is 20% or higher, the probability to stop for futility is 17%.

Table 3: Operating Characteristics of Dose Expansion Phase (Part 2A)

	Interim Analysis (N=15)	Final Analysis (N=35)		
True CBR	Pr(Futility*)	Pr(obs. CBR ≥15% 6 or more subjects with CBR)	Pr(obs. CBR ≥20% 7 or more subjects with CBR)	Pr(obs. CBR ≥25% 9 or more subjects with CBR)
5%	83%	<1%	<1%	<1%
10%	55%	11%	5%	<1%
15%	32%	39%	25%	7%
20%	17%	67%	54%	25%
25%	8%	86%	78%	52%
30%	4%	95%	92%	76%
35%	1%	98%	97%	91%

CBR=clinical benefit rate; obs.=observed; Pr=probability
* 1 or fewer subjects with CBR among the first 15 subjects.

In Part 2B (Dose Optimization), up to 120 subjects may be enrolled into up to 4 tumor-specific cohorts (30 per each tumor-specific cohort [15 per dose level]) based on the totality of data after data from Parts 1 and 2A has been assessed. The sample size for Part 2B is based on clinical considerations.

6. ANALYSIS POPULATIONS

6.1. Safety Population

The Safety Population consists of all subjects who receive at least 1 dose of study treatment (KZR-261) and will be used for the safety analyses.

6.2. Response Evaluable Population

The Response Evaluable Population is defined as all subjects who receive at least 1 dose of study treatment (KZR-261) and who have a baseline and at least 1 post-baseline anti-tumor response assessment using RECIST v1.1 or PCWG3 in the case of mCRPC. The Response Evaluable Population will be used for the efficacy analyses.

6.3. DLT Evaluable Patients

The DLT Evaluable Population consists of all subjects who either meet the following minimal exposure criteria and have sufficient safety evaluations without having a DLT, or have experienced a DLT during the DLT assessment period.

Subjects who do not experience a DLT in Part 1 Cycle 1 (Dose Escalation) must receive all of their scheduled doses (Days 1, 8, and 15) during the DLT assessment period with completed follow-up data available through 28 days of Cycle 1 to be DLT-assessable.

6.4. Pharmacokinetic Analysis Population

The PK Analysis Population consists of all subjects who receive at least 1 dose of KZR-261 and who have at least one measured post-dose concentration of KZR-261. Any protocol deviations affecting PK analyses may result in exclusion from summaries for individual time point concentrations, complete PK profiles, and/or PK parameters. These exclusions will be reviewed before database lock and confirmed with the Sponsor before implementation. The PK population is more exhaustively detailed in the PK analysis plan.

7. GENERAL STATISTICAL CONSIDERATIONS

7.1. Unit of Analysis

There are several units of analysis in this study. For select efficacy summaries based on the RECIST v1.1 criteria, specifically in the melanoma, mesothelioma, mCRC, and all-tumors cohorts in Part 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization), the unit of analysis will be the tumor, however, the overall response will be evaluated at the subject level. The tumor is defined as any target, non-target, or new lesions, including metastases, identified

during screening and follow-up imaging. In the case of mCRPC, the study unit will be the subject for efficacy summaries based on the PCWG3 modification of RECIST v1.1 which includes PSA and bone lesion assessments. Slit lamp and visual acuity summaries will be at the eye level. Additionally, AEs, SAEs, clinical laboratory data, physical examination findings, ECG, ECOG PS, biomarker data, and medical history will be presented at the subject level.

7.2. Missing or Inconclusive Data Handling

In general, there will be no imputation of missing data other than for partial or missing dates where complete dates are required to identify data as treatment-emergent or concomitant with treatment. Partial/missing birth dates, start and end dates for AEs and concomitant medications will be imputed such that if the missing part of the date causes ambiguity in the temporal relationship to treatment, it will be assumed to be treatment emergent or concomitant. Specifically, dates will be imputed as follows:

7.2.1. Partial/missing start date:

- Dates with missing day only will be imputed as the 1st of the month unless the month and year are the same as the month and year of first dose of study medication, in which case the missing day will be imputed as the first dose day of study medication.
- Dates with both day and month missing will be imputed as 1 Jan unless the year is same as the year of first dose of study medication, in which case the missing day and month will be imputed as the first dose day and month of study medication.
- Completely missing dates will be imputed as the first dose date of study medication unless the end date is on or before the first dose date of study medication, in which case missing date will be imputed as 1 Jan of the same year as the end date.

7.2.2. Partial/missing end date:

- Dates with missing day only will be imputed as the last day of the month unless the month and year are the same as the month and year of the last dose of study medication, in which case the missing day will be imputed as the last dose day of study medication.
- Dates with both day and month missing will be imputed as 31 Dec unless the year is same as the year of the last dose of study medication, in which case the missing day and month will be imputed as the last dose day and month of study medication.
- If the ongoing flag is missing or “Yes” then the date will not be imputed unless death date is available, in which case the missing date will be imputed as the death date. If ongoing is “No” then the missing end date will be imputed as the last dose date.
- If the imputed date is after the date of death, then the end date will be set equal to the date of death.

The original dates will be displayed in data listings and the imputed dates will be used in derivations only (study day, treatment-emergence status, etc.).

7.3. Definition of Baseline

Baseline is defined as the last measurement prior to the dose of KZR-261 on Cycle 1 Day 1. Change from baseline will be calculated as: (Post-baseline Value – Baseline Value).

7.4. Data Analysis Conventions

All data analysis will be performed by [redacted] after the study is completed and the database has been locked. Statistical programming and analyses will be performed using SAS® version 9.4 or higher. Output will be provided in rich text format (RTF) for tables and portable document format (PDF) for tables, listings, and figures using landscape orientation. All study data will be listed by subject, dose level in Part 1 (Dose Escalation) and cohort in Part 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization), and visit (as applicable) based on all enrolled subjects unless otherwise specified. Listings will be sorted by dose level in Part 1 (Dose Escalation) and by cohort in Part 2A (Tumor-Specific Dose Expansion) and Part 2B (Dose Optimization), subject number, visit/time point, and parameter as applicable.

Summaries for continuous and ordinal variables will include the number of observations (n), arithmetic mean, standard deviation, median, minimum, and maximum. Minima and maxima will be reported with the same precision as the raw values; means and medians will be presented to one additional decimal place than reported in the raw values. Standard deviations will be presented to two additional decimal places than reported in the raw values. Summaries for discrete variables will include counts and percentages. All percentages will be rounded to one decimal place (ie, XX.X%). Changes from baseline will be calculated as follow-up visit minus baseline.

Unless otherwise specified, all data will be summarized by dose level and overall, for Part 1 (Dose Escalation), tumor-specific cohort for Part 2A (Dose Expansion), and dose and tumor-specific cohort for Part 2B (Dose Optimization).

7.5. Adjustments for Multiplicity

No multiplicity adjustments will be employed. The secondary efficacy endpoints for which hypothesis testing will be conducted will only occur after an initial pre-defined clinically relevant response has been observed at interim analysis.

8. DISPOSITION OF SUBJECTS

A listing of all enrolled subjects will include the study part (Part 1, Part 2A, Part 2B), the dose cohort in Part 1 (Dose Escalation) or tumor cohort in Part 2A and 2B, the assigned KZR-261 dose, protocol version under which the patient was consented for the trial, enrollment date, and date of informed consent, as well as dates of study treatment discontinuation and study discontinuation (and corresponding study days). For those subjects who discontinued study treatment or the study, the reason for discontinuation will be included.

Subject disposition will be presented in terms of the numbers and percentages for the following: subjects included in Safety, Response Evaluable, DLT Evaluable, and PK Populations, subjects

who discontinued from the study treatment including reason for discontinuation, and subjects who discontinued from the study including reason for discontinuation.

9. DEMOGRAPHIC, BASELINE, AND BASELINE DISEASE CHARACTERISTIC VARIABLES

9.1. Demographic and Other Baseline Variables

The Demographic and other baseline variables including age, age group (<65 years and ≥65 years), sex at birth, race, ethnicity, weight, height, body mass index, body surface area, ECOG performance status and childbearing potential, will be summarized for the Safety Population.

Age will be calculated using the following formula:

Age = (Informed Consent Date – Date of Birth) / 365.25, truncated as an integer

A subject listing of these data will also be presented.

9.2. Disease Characteristic Variables

Subject listings that include primary and any secondary cancer diagnoses, tumor measurements, and type (target, non-target) at Screening will be provided.

Baseline disease characteristics, including anatomical location of primary cancer, time since initial-diagnosis, stage at initial diagnosis, stage at study entry, and sites of metastatic disease, will be summarized for the Safety Population. Time since initial diagnosis is calculated as:

Time since Initial Diagnosis (days) = Informed Consent Date – Initial Diagnosis Date + 1

A subject listing that includes the aforementioned disease characteristics will be provided.

10. MEDICAL HISTORY AND CONCOMITANT MEDICATIONS

10.1. Medical History

Medical history will be coded using MedDRA Version 26.0 or higher. Medical history terms will be listed but not summarized. The listings will also include the onset date, and resolution date (if applicable).

10.2. Prior and Concomitant Medications/Therapy

Prior and concomitant medications/Therapy will be coded using World Health Organization Drug Dictionary (WHODrug) Global, B3, September 2021 or higher and summarized for the Safety Population based on the therapeutic drug class (Anatomical Therapeutic Chemical [ATC] 4 classification) and preferred name If the ATC 4 classification is not provided, then the next lowest classification that is provided in the coding dictionary will be used.

Prior and concomitant medications/therapy will be summarized separately. Subjects may have more than one medication per ATC classification and per preferred name. A subject will be

counted once within the ATC classification or preferred name if he/she reports one or more medication at each level. Percentages will be based on the number of subjects in each group.

A listing of subjects who received pegfilgrastim or any other bone marrow stimulant will also be provided.

10.3. Prior Cancer Therapy Regimen

A listing of all cancer therapies that includes the treatment or medication name, start date and end date if available, the dose with units, the line of therapy number, and best overall response will be provided.

10.4. Prior Radiotherapy

Prior radiotherapy site, start and end dates, and total dose will be listed.

10.5. Prior Cancer-Related Surgery

A listing of all prior cancer-related surgeries will be provided and include the type, the date and the intent of the surgery (diagnostic or therapeutic).

11. DOSING COMPLIANCE AND TREATMENT EXPOSURE

11.1. Dosing Compliance

All doses of KZR-261 are administered in-clinic, therefore dosing compliance is not expected to be an issue.

11.2. Treatment Exposure

KZR-261 administration will be listed and summarized for the Safety Population in terms of the total number of cycles and doses of KZR-261, cumulative dose administered as well as the number of interruptions and dose reductions. The reasons for dose interruptions and reductions will be summarized.

Cumulative dose will be summarized with continuous descriptive statistics for the Safety Population. A subject listing of cumulative doses of KZR-261 will be generated.

The cumulative dose will be calculated as the sum in mg of KZR-261 administered per subject over the entire course of study. Let x represent total KZR-261 dose, in mg, administered to a subject at the i^{th} dosing event out of k doses administered in cycle j of l cycles, then the cumulative dose is given by:

$$\sum_{j=1}^{l}\sum_{i=1}^{k} x_{ij}$$

Relative dose intensity will also be listed and summarized. The relative dose intensity will be the cumulative dose divided by the total planned dose, where the planned dose represents the total amount of KZR-261 in mg that would have been delivered to a subject if there were no dose modifications. The planned dose will be included in listings and summaries.

12. MTD ESTIMATION AND DLT ANALYSES

In the dose escalation part, (x_d, n_d) will be observed for $d=1, \ldots, K$, where d represents dose levels and K represents the total number of dose levels. Assuming n_d subjects have been treated at dose d, and x_d of them experienced DLTs, let $x_d|p_d \sim Bin(n_d, p_d)$ and $p_d \sim Beta(0.005,0.005)$. The posterior mean toxicity probability at dose d is estimated as,

$$\hat{p}_d = \frac{x_d + 0.005}{n_d + 0.01}$$

Isotonic regression will then be applied to the posterior mean DLT rates. Let $\tilde{p}_d$ represent the isotonic-transformed posterior means for all the doses. The MTD will be the dose that satisfies $\tilde{p}_d \leq 0.35$ and is closest to the target rate of 0.30. If multiple such doses satisfy the criteria, MTD will be the highest dose level that is $\tilde{p}_d \leq 0.30$. If no such doses, MTD will be the lowest dose that is $\tilde{p}_d > 0.30$. $\tilde{p}_d$ is estimated using Pool-Adjacent-Violators Algorithm (PAVA), a solution to isotonic regression.

DLTs will be listed and summarized by MedDRA system organ class and preferred term. The DLT analysis set will be used for summaries.

13. EFFICACY ANALYSES

All efficacy analyses will be performed on the Response Evaluable Population.

All efficacy data will be listed and summarized with descriptive statistics.

13.1. Disease Response Criteria

Evaluation of response and disease progression will be made by the Investigator according to RECIST v1.1 (Eisenhauer et al., 2009) guidelines except for mCRPC which will follow the PCWG3 modified RECIST v1.1 guidelines (Scher et al., 2016).

13.1.1. Evaluation of Target Lesions

For target lesions, classifications of disease response include Complete Response (CR), Partial Response (PR), Stable Disease (SD), and Progressive Disease (PD).

- **CR:** Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. In the case of mCRPC, PSA levels must also decline to <0.2 ng/ml (undetectable).
- **PR:** At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum of longest lesion diameters. In the case of mCRPC, PSA levels must also decline by ≥50% from baseline and the absolute decrease must be at least 2 ng/ml from baseline.
- **SD:** Neither sufficient decrease to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of longest diameters while on study, and in the case of mCRPC, the PSA level.

- **PD:** At least a 20% increase in the sum of longest diameters, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the absolute increment in the sum of longest diameters must be at least 5 mm. In the case of mCRPC, an increase in PSA ≥25% above the nadir with an absolute concentration ≥2 ng/ml at 2 time points at least 3 weeks apart constitutes PSA progression.

13.1.2. Evaluation of Non-Target Lesions

For non-target lesions or subjects with non-measurable disease, classifications of disease response include CR, non-CR/non-PD, and PD.

- **CR:** Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (<10 mm short axis).
- **Non-CR/Non-PD:** Persistence of 1 or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits.
- **PD:** Unequivocal progression of existing non-target lesions, or appearance of 1 or more new lesions. When the subject also has measurable disease, to achieve 'unequivocal progression' on the basis of non-target disease, there must be substantial worsening in nontarget disease such that, even in the presence of SD or PR in target lesions, the overall tumor burden has increased sufficiently to merit discontinuation of therapy.

13.2. Criteria for Overall Response

Listings of the various disease response parameters collected for each subject will be provided. Disease response categories include: Complete Response (CR), Partial Response (PR), Stable Disease (SD), Progressive Disease (PD), and Not Evaluable (NE). If a subject misses a disease assessment, or the Investigator is unable to assign a response category at a particular response assessment timepoint, response for this timepoint will be designated NE. Additionally, if a subject leaves the study prior to any disease assessment and is lost to follow-up, best overall response will be assigned as NE. The overall response is categorized based on the criteria in Table 4.

Table 4: RECIST 1.1 Criteria for Categorizing Target Disease Overall Response

Target Lesions	Non-Target Lesions	New Lesions	Overall 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

At the conclusion of study drug treatment, the best overall response will be determined. Best overall response is defined as the best response recorded from the start of the study treatment until the end of treatment.

13.2.1. Objective Response Rate (ORR)

Objective response is defined as a best overall response of CR or PR. The proportion of subjects with a best response of CR or PR following KZR-261 treatment will be summarized using frequencies and percentages. Only confirmed responses will be included in the calculation of ORR. Additionally, the response rates for individual categories of CR, PR, SD, PD, or NE will be summarized by frequency distributions. Two-sided 90% CIs using the Clopper-Pearson approach for ORR will be calculated using SAS® code as:

```
proc freq;
tables response / binomial (level='Yes' cl=EXACT);
exact binomial;
run;
```

13.2.2. Duration of Response (DOR)

Duration of response for subjects with CR or PR is defined as the date of first qualifying response (CR or PR) until the date of PD or death, whichever is earliest.

$$DOR\ (weeks) = \frac{([Date\ of\ PD\ or\ Death - Date\ of\ First\ CR\ or\ PR] + 1)}{7}$$

For subjects who have neither progressed nor died, DOR will be censored at the date of the last evaluable disease assessment. The median DOR will be estimated using Kaplan-Meier methods and summarized.

Separate Kaplan-Meier plots for subjects enrolled to Parts 1, 2A, and 2B will be provided.

13.2.3. Progression-Free Survival (PFS)

PFS is defined as the date of initiation of KZR-261 until the date of documented PD or death from any cause, whichever occurs first.

$$PFS\ (weeks) = \frac{([Date\ of\ PD\ or\ Death - Date\ of\ First\ Dose\ of\ KZR - 261] + 1)}{7}$$

For subjects who have neither progressed nor died, PFS will be censored at the date of the last evaluable disease assessment. The median PFS will be estimated using Kaplan-Meier methods and summarized.

Progression-Free Survival at 4 months (PFS4) is defined as the percentage of subjects alive and progression-free at 4 months (ie, 17 weeks) after the initiation of study treatment. The PFS4 responders will be summarized using frequencies and percentages. Similar to analysis of ORR, two-sided 90% CIs for PFS4 responders using the Clopper-Pearson approach will be calculated.

Progression-Free Survival at 6 months (PFS6) is defined as the percentage of subjects alive and progression-free at 6 months (ie, 26 weeks) after the initiation of study treatment. The PFS6 responders will be summarized using frequencies and percentages. Similar to analysis of ORR, two-sided 90% CIs for PFS6 responders using the Clopper-Pearson approach will be calculated.

Separate Kaplan-Meier plots for subjects enrolled to Parts 1, 2A, and 2B will be provided.

13.2.4. Overall Survival (OS)

OS is defined as the date of first dose of KZR-261 until the date of death from any cause.

$$OS\ (weeks) = \frac{([Date\ of\ Death - Date\ of\ First\ Dose\ of\ KZR - 261] + 1)}{7}$$

For subjects who have not died, OS will be censored at the date the subject is last known to be alive or the date of last contact, whichever is later. The median OS will be estimated using Kaplan-Meier methods.

Separate Kaplan-Meier plots for subjects enrolled to Parts 1, 2A, and 2B will be provided.

13.2.5. Clinical Benefit Rate (CBR)

Clinical benefit is defined as achieving a best response of CR, PR, or SD over 2 or more response assessment timepoints. Subjects meeting the criteria for clinical benefit will be summarized using frequencies and percentages. Like analysis of ORR, two-sided 90% CI using the Clopper-Pearson approach will be calculated.

13.2.6. Prostate-Specific Antigen Doubling Time

Prostate-specific antigen doubling time (PSADT) may be calculated using a published method (Scher et al., 2016).

13.2.7. Percentage Change from Baseline in Sum of Diameters of Target Lesions

Best percentage change from baseline in the sum of longest diameters of target lesions will be summarized descriptively by dose level among subjects enrolled to Part 1 and tumor cohort for Part 2A and 2B subjects. Best percentage change from baseline in sum of longest diameters will

be presented in a Waterfall Plot with corresponding dose level, best overall response, and primary cancer diagnosis identified. Individual percentage changes from baseline in sum of diameters of target lesions overtime will be presented in a spider plot with treatment identified. Scatter plot and dose response curve based on E-max model in percentage change from baseline in sum of diameters of target lesions will also be provided.

14. EXPLORATORY ANALYSES

Assessments of various pharmacodynamic study readouts as a function of dose and time post-administration may be described and related to efficacy metrics (eg, overall response, DOR, PFS), PK, and safety parameters.

Details of the planned exploratory analysis will be described in a separate Pharmacodynamic Analysis Plan.

15. SAFETY ANALYSES

All safety analyses will be conducted using the Safety Population.

15.1. Adverse Events

An AE is defined as any untoward medical occurrence in a clinical study subject administered a medicinal product, which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not it is related to the medicinal (investigational) product. This includes an exacerbation of pre-existing conditions or events, intercurrent illnesses, drug interaction or the significant worsening of the indication under investigation that is not recorded elsewhere in the eCRF under specific efficacy assessments. Anticipated fluctuations of pre-existing conditions, including the disease under study, that do not represent a clinically significant exacerbation or worsening need not be considered AEs.

It is the responsibility of the Investigator to document all AEs that occur during the study. AEs will be elicited by asking the subject a nonleading question, for example, “Have you experienced any new or changed symptoms since we last asked/since your last visit?” AEs should be reported on the appropriate page of the eCRF. All AEs will be coded using the MedDRA Version 26.0 or later.

TEAEs are defined as an event that occurred from the date of the first dose of KZR-261 administration and continuing for 30 days following the last dose administration and will include AEs that emerged during treatment having been absent pre-treatment, or worsened relative to the pre-treatment state. Adverse events recorded in the eCRF which began prior to treatment will not be included in the summary tables but will be included in the AE data listings.

Severity of AEs will be graded according to NCI CTCAE Version 5.0. If there is a change in severity of an AE, it must be recorded as a separate event. For AEs not listed in the NCI CTCAE, the Investigator should determine the severity of the AE according to the criteria in Table 5.

Table 5: NCI CTCAE Adverse Event Severity Grades

Grade 1 (Mild)	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2 (Moderate)	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living.
Grade 3 (Severe)	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.
Grade 4 (Life-threatening)	Life-threatening consequences; urgent intervention indicated.
Grade 5 (Death)	Death related to the adverse event.

The Investigator will assess the causal relationship between study drug and an AE. All AEs will be deemed related to study drug unless irrefutably determined to be related to the disease under study or another non-study drug cause.

The causal relationship between the study drug and the AE will be assessed using one of the following two categories:

1. Unrelated: An AE is not associated with study drug if any of the following is true:
    - A temporal relationship is lacking (ie, the event did not occur within a reasonable time frame after administration of the study drug).
    - Other causative factors more likely explain the event (eg, intercurrent illness, concomitant treatments, traumatic event).
    - The AE did not reoccur upon re-administration of the study drug (if applicable).
2. Related: An AE is attributed to the study drug if any of the following is true:
    - There is a positive temporal relationship (ie, the event occurred within a reasonable time frame after administration of study drug).
    - The AE is more likely explained by the study drug than by another cause and cannot be clearly assessed as “unrelated”.

An overall summary that includes the number and percentage of subjects who experienced at least one TEAE, including treatment-related TEAEs, SAEs, treatment-related SAEs, TEAEs leading to treatment interruption, dose reduction, discontinuation, death, and Grade 3 or 4 TEAEs will be provided. TEAEs will be summarized by dose level in Part 1 (Dose Escalation) and by tumor cohort in Parts 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization) All verbatim TEAEs will be coded to a MedDRA system organ class (SOC) and preferred term (PT). If a subject reports the same PT multiple times within a SOC, that PT will be counted once (at the highest level of severity) within that SOC. If a subject reports multiple different PTs within the same SOC, a subject will be counted once at the SOC level. SOCs and PTs will be listed in order of descending frequency within each SOC.

Summaries of TEAEs by maximal severity will be presented.

All AEs will be presented in a subject listing.

The following will be presented as listings and summary tables:

- TEAEs leading to study treatment discontinuation
- TEAEs related to KZR-261
- TESAEs
- TESAEs related to KZR-261
- TEAEs related to KZR-261 leading to early treatment discontinuation
- TEAEs leading to dose reduction
- TEAEs leading to death by category (Death on-treatment, Death post-treatment, and all death)
- TEAEs related to KZR-261 leading to death
- Grade 3 or 4 TEAEs
- Grade 3 or 4 TEAEs related to KZR-261
- Selected TEAEs by category (such as neutropenia and neutrophil count decreased, QTc prolongation and cardiac toxicities, liver toxicity, nephrotoxicity, bone marrow toxicity, etc)

In addition, all SAEs will be presented in a separate listing.

15.2. Physical Examination

Any clinically significant abnormal physical examination results are recorded as AEs and included in the AE listings and tables accordingly.

Slit lamp and visual acuity data will be summarized.

A subject listing of slit lamp and visual acuity data will be produced.

15.3. Vital Signs, Oxygen Saturation, Height, Weight

Vital signs, including temperature (°C), systolic and diastolic blood pressure (mmHg), heart rate (bpm), and respiratory rate will be summarized using descriptive statistics, at baseline and each study day and time point by dose level in Part 1 and by tumor cohort in Parts 2A and 2B for all actively treated subjects. Oxygen saturations (%), height (cm), weight (kg), BMI (kg/m^2), and BSA (m^2) will be summarized similarly.

The following vital signs categories will also be summarized:

- Systolic pressure: for high values >= 180 and increase form baseline of >=20. Low values <=90 and decrease form baseline of >=20.
- Diastolic pressure: for high values >=105 and increased from baseline of >=15. Low values <=50 and decrease from baseline of >=15.

- Heart rate: for high values >=100 and increase form baseline of >25%. For low values: <=50 and decrease from baseline of >25%.
- Body temperature: for high values >=39.1 Celsius.

Changes from baseline will also be summarized at each post-baseline study visit.

Listings of vital signs results, oxygen saturations, height, weight, BMI, and BSA will also be produced.

15.4. Electrocardiogram

QT interval corrected for pulse rate by Fridericia's formula (TQcF) will be summarized using descriptive statistics at baseline and each day and time point by dose level in Part 1 (Dose escalation) and by cohort in Parts 2A and 2B (Tumor-specific Dose Expansion and Dose optimization). Shifts from baseline in ECG interpretation will be also summarized using frequency and percentages by dose level in Part 1 (Dose Escalation) and by cohort in Parts 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization).

To assess the frequency of QTc interval prolongation, the number and percentage of subjects having notable ECG values according to the following categories will also be summarized by dose level in Part 1 (Dose escalation) and by cohort in Parts 2A and 2B (Tumor-specific Dose Expansion and Dose optimization):

- Change from Baseline in QTcF: ≤30, >30 to ≤60, >60 msec
- Maximal QTcF:, >450 to ≤480, >480 to ≤500, >500 msec

A subject listing of ECG data will also be produced.

15.5. Clinical Laboratory Data

Continuous variables will be summarized by dose level in Part 1 (Dose Escalation) and by tumor cohort in Parts 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization) and for all actively treated subjects at each visit and time point (where appropriate) using arithmetic means, medians, minimum and maximum values. Categorical variables will be summarized by dose level in Part 1 (Dose Escalation) and by cohort in Parts 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization) using frequencies and percentages for all actively treated subjects at each visit and time point (where appropriate). Shift tables summarizing changes from baseline will also be produced by dose level in Part 1 (Dose Escalation) and by cohort in Parts 2A and 2B (Tumor-Specific Dose Expansion and Dose Optimization).

Unscheduled laboratory data will be included in subject listings and denoted as unscheduled. Summaries by visit will use the nominal visit value in the event of multiple laboratory values drawn within a visit window. However, all values drawn within a study window will be used to identify the minimal and maximal values. In the event that visit windows overlap, only the values from assessments occurring after the previous and prior to the subsequent nominal visit value will be considered for identification of the minimal and maximal values.

Summaries of abnormal laboratory results will be presented by analyte and severity grade.

A shift table consisting of changes from baseline in neutrophil counts will be produced.

A listing of tumor marker data will be produced. The tumor marker reference ranges are provided in Appendix C Tumor Marker Reference Ranges.

16. PHARMACOKINETIC ANALYSES

Details of the PK analyses are provided in a separate document.

17. PHARMACODYNAMIC ANALYSES

Details of PD analyses are provided in a separate document.

18. INTERIM ANALYSES (EXPANSION COHORTS ONLY)

In the tumor-specific expansion cohorts, the Go/No-Go procedure will be carried out at completion of Stage 1 based on the CBR exceeding a target value, or falling below a lower reference value. As previously noted, the following target values and lower reference values are defined as: CBR ≥6.7% (1/15) vs CBR <6.7% (1/15) for all Part 2A expansion cohorts.

The Go/No-Go criteria for the interim planning are presented in Table 3.

19. CHANGES FROM PROTOCOL-STATED ANALYSES

There are no changes from the protocol-stated analyses.

20. REFERENCES

Eisenhauer EA, Therasse P, Bogaerts J, et al. (2009) New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer* 45(2): 228-247.

Scher HI, Morris MJ, Stadler WM, et al. (2016) Trial design and objectives for castration-resistant prostate cancer: updated recommendations from the Prostate Cancer Clinical Trials Working Group 3. *J Clin Oncol* 34(12): 1402.

21. APPENDICES

Appendix A: Schedule of Events for Screening and Cycles 1 & 2

Appendix B: Schedule of Events for Cycle 3+

Appendix C : Tumor Marker Reference Ranges

APPENDIX A. SCHEDULE OF EVENTS FOR SCREENING AND CYCLES 1 & 2

Study Period	Screening [a]	Pre-Treatment (Baseline)	Treatment Period									Treatment Period								
Cycle			Cycle 1[q]									Cycle 2 [q]								
Day	D-28 to D-1	D0 to D1	D1	D2	D3[t]	D5[t]	D8	D15	D16	D22	D28[p]	D1[p]	D2	D3[t]	D5[t]	D8	D15	D16	D22	D28 [p]
Visit Window (days)					+1	+1	±1	±3		±3	+3	+1		+1	+1	±1	±3		±3	+3
Informed consent form	X																			
Inclusion/exclusion criteria	X																			
Hepatitis B and C testing	X																			
Medical history	X																			
ECOG PS	X	X									X	X								X
Physical examination[b]	X	X					X	X		X	X	X				X	X		X	X
Slit lamp exam and visual acuity[s]	X										X	X								X
Pregnancy test [c]	X	X									X	X								X
Vital sign measurement and oxygen saturation [d]	X	X	X	X			X	X	X	X	X	X	X			X	X	X	X	X
12-lead ECG [e]	X	X	X	X			X	X	X		X	X	X			X	X	X		X
Hematology (Protocol Table 8)	X	X					X	X		X	X	X				X	X		X	X
Serum chemistry (fasting)[g] (Protocol Table 9)	X	X					X	X		X	X	X				X	X		X	X
HgbA1c [r]		X																		
Coagulation parameters [g] (Protocol Table 10)	X										X	X								X
Urinalysis [h]	X										X	X								X
PSA [i]		X									X	X								X
Tumor markers [j]	X										X	X								X

Study Period	Screening [a]	Pre-Treatment (Baseline)	Treatment Period									Treatment Period								
Cycle			Cycle 1 [q]									Cycle 2 [q]								
Day	D-28 to D-1	D0 to D1	D1	D2	D3[t]	D5[t]	D8	D15	D16	D22	D28[p]	D1[p]	D2	D3[t]	D5[t]	D8	D15	D16	D22	D28 [p]
Visit Window (days)					+1	+1	±1	±3		±3	+3	+1		+1	+1	±1	±3		±3	+3
Tumor imaging and measurements [k]	X																			X
PK [l]																				
Part 1			X	X	X	X	X	X	X			X	X	X	X	X	X	X		
Part 2			X	X			X	X												
Pharmacodynamic & biological studies [m]			X	X			X	X	X		X	X								X
Circulating tumor DNA [n]			X								X	X								X
Tumor biopsy or submission of tumor specimen [f]	X																		X	
KZR-261 treatment [o]			X				X	X				X				X	X			
Concomitant medications		X	X	X			X	X	X	X	X	X	X			X	X	X	X	X
AE and SAEs		X	AEs collected through 30 days after last KZR-261 dose.																	

Abbreviations: AE=adverse event; aPTT=activated partial thromboplastin time; β-hCG=β-human chorionic gonadotropin; CA=cancer antigen; CEA=carcinoembryonic antigen; CT=computed tomography; DNA=deoxyribonucleic acid; ECG=electrocardiogram; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EOT=End of Treatment; INR=internal normalized ratio; mCRPC=metastatic castration-resistant prostate cancer; MRI=magnetic resonance imaging; PBMC=peripheral blood mononuclear cell; PCWG3= Prostate Cancer Working Group 3; PD= progressive disease; PK=pharmacokinetics; PSA=prostate-specific antigen; PT=prothrombin time; PTT=partial thromboplastin time; RECIST=Response Evaluation Criteria in Solid Tumors; RNA=ribonucleic acid; SAE=serious adverse event; WOCBP=woman of childbearing potential

[a] All Screening procedures must be performed prior to the Day 0 or Day 1 visit. Eligibility for this study should be assessed only after signing of informed consent.

[b] A complete physical examination including measurement of body weight will be conducted at Screening and Baseline. Height will be measured at the Screening visit only. An abbreviated physical examination including measurement of body weight will be conducted at all other study visits indicated. Subjects with skin, subcutaneous, or lymph node metastases may also have tumor evaluations (including measurements, with a ruler or calipers) by means of physical examination. Patients will be asked at each visit about mouth dryness and salivary gland pain and sensitivity, and urinary and ejaculation issues.

[c] For WOCBP, a negative serum β-hCG pregnancy test is required at Screening and a negative pregnancy test, serum or urine, at all other visits indicated. The Screening visit test should be performed within 2 weeks prior to treatment and in closer proximity to treatment start date if required by local/institutional regulations. A positive urine pregnancy test result should be confirmed by a serum pregnancy test. Pregnancy testing may occur more frequently if required by local/institutional regulations.

[d] Vital signs and oxygen saturation will be measured at all visits except Days 3 and 5. Blood pressure and pulse should be measured after the subject has had at least 5 minutes of rest in the seated position. If blood pressure is elevated on the first measurement at Screening or Baseline, it should be repeated after an additional 5 minutes of rest. It is recommended that blood pressure be obtained from the same arm at each assessment.

[e] When performed at the same time point, vital sign measurements should be performed per institutional guidelines, preferably prior to ECGs. A 12-lead ECG is performed 10 minutes after the subject has been in the supine position. ECGs will be performed on Days 1 and 15 of Cycles 1 and 2 pre-treatment, 15 minutes after the start of the infusion, at the end of the infusion, and 5 and 30 minutes, and 2, 4, 6, and 24 hours (Day 2 and Day 16) post-infusion. Additional ECGs will be performed on Day 8, 30 minutes prior to infusion, and 5 and 15 minutes and 1-hour post-infusion. ECG time points during the infusion, at the end of the infusion, and ≤1 hour post-infusion have a ±2 minute window. ECG time points >1 hour post-infusion have a ±5 minute window; the 24-hour ECG has a ±60 minute window.

[f] Tumor biopsies (fresh [preferred] or archived) will be requested pre-treatment. Although a fresh sample is preferred, submission of an adequate tumor specimen (paraffin block) collected within one year before the subject's first dose of KZR-261 will be acceptable for subjects where a fresh sample cannot be obtained. If a paraffin block is not available, a minimum of 10 and up to 20 5-µm unstained slides should be provided. For any subject who provided a tumor sample pre-treatment, an additional biopsy of accessible tumor will be requested at either the end of Cycle 2 (Days 21-28 of Cycle 2) or at PD, whichever comes first. Pre-treatment tumor biopsies (fresh only) will be required for subjects enrolled in the All-Tumors expansion cohort (exceptions to this requirement may be considered after discussion with the Medical Monitor); an additional biopsy of accessible tumor tissue will be required at either the end of Cycle 2 (Days 21-28 of Cycle 2) or at PD, whichever comes first. Blood samples for coagulation parameter tests must be collected within 24 hours prior to all biopsy procedures.

[g] Blood samples for serum chemistry tests must be collected with subject in a fasting state (ie, no food or caloric drinks for at least 6 hours before testing, or overnight). For coagulation parameter tests, either PT or INR may be measured, and either PTT or aPTT, depending on institutional standards. Blood samples for coagulation parameter tests must be collected within 24 hours prior to all biopsy procedures. It is recommended that the smallest appropriate sampling tubes be used for sample collection to curtail blood loss due to phlebotomy.

[h] Urinalysis dipstick testing is acceptable.

[i] Only subjects with mCRPC.

[j] If tumor markers in blood (eg, PSA, CA-125, CEA, CA-15.3, CA-19.9) are known to be elevated, they should be measured.

[k] All subjects must have Baseline imaging (CT scan of chest/abdomen/pelvis or MRI, as indicated) within 28 days prior to first dose of study treatment. Imaging should be repeated prior to Cycle 3 (ie, end of Cycle 2) There is a 7-day window around imaging procedures to allow time for result availability prior to the next cycle. If an imaging procedure must be scheduled to occur outside the 7-day window allowance, this should be discussed with the Medical Monitor for approval prior to the procedure. Response assessments will be conducted in accordance with RECIST 1.1 criteria. Subjects with mCRPC will be assessed per PCWG3 guidelines. All subjects with mCRPC will have bone scans at the same time points as the imaging procedures. Subjects with skin, subcutaneous, or lymph node metastases may also have tumor evaluations (including measurements, with a ruler or calipers) by means of physical examination.

[l] Plasma PK samples will be collected during Part 1 on Days 1 and 15 of Cycles 1 and 2 pre-treatment, 15 minutes post-start of infusion, end of infusion, 5 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours, and 24 hours (ie, Day 2 and Day 16) post-infusion. An additional plasma sample will be obtained in Cycles 1 and 2 at 48 hours (Day 3) and 96 hours (Day 5) post-infusion and on Day 8 at pre-treatment (30 minutes prior to infusion), 15 minutes and 1 hour after completion of the infusion.

Plasma PK samples will be collected during Parts 2A and 2B on Day 1 of Cycle 1 at the end of infusion and 24 hours post-start of infusion (Day 2). An additional plasma sample will be obtained on Days 8 and 15 prior to infusion and Day 15 at the end of infusion.

Windows for PK sampling are provided in the laboratory manual.

[m] Whole blood samples will be collected for pharmacodynamic studies Cycle 1 Day 1 pre-treatment, 6 hours post-dose, 24 hours post-dose (Day 2), Cycle 1 Day 8 pre-treatment and Cycle 1 Day 15 pre-treatment, 6 hours post-dose, 24 hours post-dose (Day 16), and Cycle 2 Day 1 pre-treatment in a [redacted] tube for RNAseq, in sodium heparin to be shipped to central laboratory for PBMC processing, and in sodium heparin processed onsite to plasma samples (as described in the laboratory manual). Samples will be collected on Cycle 1 Day 28 if treatment is halted and not proceeding to Cycle 2.

[n] Whole blood will be collected in a [redacted] tube and shipped to the central laboratory for processing to plasma samples (for circulating tumor DNA testing) and cell pellet (cellular genomic DNA) pre-treatment Day 1 of Cycle 1, pre-treatment Day 1 Cycle 2, or at time of disease progression.
[o] Subjects should remain at the study site for 6 hours following study treatment administration for observation for the first cycle, first dose (Cycle 1 Day 1) and for 2 hours for the rest of Cycle 1 dosing (Cycle 1 Days 8 and 15). For Cycle 2, subjects will be under observation for 1 hour following study treatment administration. For Cycle 3 and beyond, there will be no required monitoring following study treatment administration.
[p] Day 28 assessments of the prior cycle may be combined with Day 1 of the next cycle. Whenever possible, these evaluations should be referred to as the End of Cycle evaluation (for the earlier cycle) as opposed to the beginning of cycle evaluation for the subsequent cycle.
[q] For subjects who discontinue study treatment during or after Cycles 1 or 2, see EOT evaluations in Appendix B. Subsequent to discontinuation of study treatment, subjects will have an EOT visit as soon as possible following their last KZR-261 dose and prior to initiation of follow-on anticancer therapy. Safety follow-up by telephone will occur approximately 30 days following their last KZR-261 dose. Subjects who discontinue study treatment for reasons other than PD will be contacted by telephone approximately every 90 days for 12 months after last study treatment for evidence of PD, collection of information about subsequent anti-tumor therapy, and assessment of survival status. Subjects who discontinue study treatment for PD will be contacted by telephone approximately every 90 days for 12 months after last study treatment for assessment of survival status.
[r] HgbA1c to be measured at pre-treatment (baseline).
[s] Subjects will have monitoring for cataracts at Screening, at the end of Cycle 1 prior to the start of Cycle 2, and at the end of Cycle 2 prior to Cycle 3.
[t] Day 3 and Day 5 visits are for Part 1 only.

APPENDIX B. SCHEDULE OF EVENTS FOR CYCLE 3+

Study Period	Treatment Period					EOT/EW (as soon as possible after last dose of study treatment) [l]	Safety F/U 30 days after last dose of study treatment [l]	Long-Term F/U 12 months after last dose of study treatment [m]
Day	**D1 [k]**	**D8**	**D15**	**D22**	**D28[k]**			
Visit Window (days)	**±3**	**±1**	**±3**	**±3**	**±3**			
ECOG PS	X				X	X		
Physical examination [a]	X				X	X		
Slit lamp exam and visual acuity [b]	X				X	X		
Pregnancy test [c]	X				X			
Vital sign measurement and oxygen saturation [d]	X	X	X	X	X	X		
12-lead ECG [e]	X	X [e]	X [e]		X	X		
Hematology (Protocol Table 8)	X	X	X	X	X	X		
Serum chemistry (fasting) [f] (Protocol Table 9)	X	X	X	X	X	X		
HgbA1c [o]	X				X			
Coagulation parameters [f] (Protocol Table 10)	X				X	X		
Urinalysis [g]	X				X	X		
PSA [h]	X				X			
Tumor markers [i]	X				X			
Tumor imaging and measurements [j]					X	X		
Circulating tumor DNA [n]	X				X	X		
KZR-261 Treatment	X	X	X					
Concomitant medications	Concomitant medications through 30 days after the last dose.						X	
AE and SAEs	AEs collected through 30 days after last KZR-261 dose.						X	
Disease/survival status						X		X

Abbreviations: AE=adverse event; aPTT=activated partial thromboplastin time; β-hCG=β-human chorionic gonadotropin; CA=cancer antigen; CEA=carcinoembryonic antigen; ECG=electrocardiogram; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EOT=End of Treatment; EW=Early Withdrawal; F/U=Follow-Up; INR=internal normalized ratio; mCRPC=metastatic castration-resistant prostate cancer; PD=progressive disease; PSA=prostate-specific antigen; PT=prothrombin time; PTT=partial thromboplastin time; RECIST=Response Evaluation Criteria in Solid Tumors; SAE=serious adverse event; WOCBP=woman of childbearing potential

[a] For Cycles 3+, an abbreviated physical examination including weight, is only required prior to the start of each cycle (Day 1) and at the EOT visit. Subjects with skin, subcutaneous, or lymph node metastases may also have tumor evaluations (including measurements, with a ruler or calipers) by means of physical examination. Patients will be asked at each visit about mouth dryness and salivary gland pain and sensitivity, and urinary and ejaculation issues.

[b] Subjects will have monitoring for cataracts at Cycle 4 Day 1 ±3 days, Cycle 6 Day 1 ±3 days. Slit lamp and visual acuity examinations should be conducted at EOT.

[c] For WOCBP, a negative serum or urine pregnancy test, whichever is preferred, is required at all visits indicated. A positive urine pregnancy test result should be confirmed by a serum pregnancy test. Pregnancy testing may occur more frequently if required by local/institutional regulations.

[d] Vital signs and oxygen saturation will be measured at all visits. Blood pressure and pulse should be measured after the subject has had at least 5 minutes of rest in the seated position. If blood pressure is elevated on the first measurement at Screening or Baseline, it should be repeated after an additional 5 minutes of rest. It is recommended that blood pressure be obtained from the same arm at each assessment.

[e] When performed at the same time point, vital sign measurements should be performed per institutional guidelines, preferably prior to ECGs. A 12-lead ECG is performed 10 minutes after the subject has been in the supine position. ECGs will be performed on Day 1 pre-treatment and at the end of infusion for all cycles. For Cycle 4 only, ECGs will be performed on Days 1 and 15 at pre-treatment, 15 minutes after the start of the infusion, at the end of the infusion, and 5 and 30 minutes, and 2, 4, and 6 hours post-infusion. Additional ECGs for Cycle 4 only will be performed on Day 8, 30 minutes prior to infusion, and 5 and 15 minutes and 1 hour post-infusion. ECG time points during the infusion, at the end of the infusion, and ≤1 hour post-infusion have a ±2 minute window. ECG time points >1 hour post-infusion have a ±5 minute window. ECG time points >1 hour post-infusion have a ±5 minute window.

[f] Blood samples for serum chemistry tests must be collected with subject in a fasting state (ie, no food or caloric drinks for at least 6 hours before testing, or overnight). For coagulation parameter tests, either PT or INR may be measured, and either PTT or aPTT, depending on institutional standards. It is recommended that the smallest appropriate sampling tubes be used for sample collection to curtail blood loss due to phlebotomy.

[g] Urinalysis dipstick testing is acceptable.

[h] Only subjects with mCRPC.

[i] If tumor markers in blood (eg, PSA, CA-125, CEA, CA-15.3, CA-19.9) are known to be elevated, they should be measured.

[j] Imaging should be repeated prior to Cycle 3, prior to Cycle 5 (ie, end of Cycle 4) and every 2 cycles thereafter (ie, end of Cycles 4, 6, 8 etc.). There is a 7-day window around imaging procedures to allow time for result availability prior to the next cycle. If an imaging procedure must be scheduled to occur outside the 7-day window allowance, this should be discussed with the Medical Monitor for approval prior to the procedure. Imaging should be repeated at EOT if the last response assessment was >4 weeks prior. Tumors will be measured according to RECIST v1.1. Subjects with mCRPC will be assessed per PCWG3 guidelines. All subjects with mCRPC will have bone scans at the same time points as the imaging procedures. Subjects with skin, subcutaneous, or lymph node metastases may also have tumor evaluations (including measurements, with a ruler or calipers) by means of physical examination.

[k] Day 28 assessments of the prior cycle may be combined with Day 1 of the next cycle. Whenever possible, these evaluations should be referred to as the End of Cycle evaluation (for the earlier cycle) as opposed to the beginning of cycle evaluation for the subsequent cycle.

[l] Subsequent to discontinuation of study treatment, subjects will have an EOT visit as soon as possible following their last KZR-261 dose and prior to initiation of follow-on anticancer therapy. Safety follow-up by telephone will occur approximately 30 days after the subject's last dose of study treatment. If AEs have not resolved at that time, additional safety follow-ups will occur approximately every 30 days until AE resolution or until, in the opinion of the Investigator, the event is stabilized or determined to be chronic.

If a subject attending a Day 28 or Day 1 visit meets criteria for EOT, the EOT visit assessments should be conducted instead of Day 28/Day 1 assessments.

[m] Subjects who discontinue study treatment for reasons other than PD will be contacted by telephone approximately every 90 days for 12 months after last study treatment for evidence of PD, collection of information about subsequent anti-tumor therapy, and assessment of survival status. Subjects who discontinue study treatment for PD will be contacted by telephone approximately every 90 days for 12 months after last study treatment for assessment of survival status.

[n] Whole blood will be collected in a [redacted] tube and shipped to the central laboratory for processing to plasma samples (for circulating tumor DNA testing) and cell pellet (cellular genomic DNA) pre-treatment Day 1 of Cycles 3-6. A circulating tumor DNA sample should be collected at EOT or at time of disease progression. This collection is not required for subjects who continue to receive treatment beyond Cycle 6.

[o] HgbA1c to be measured on Day 28 every 3 cycles (ie, end of Cycles 3, 6, 9, etc.) or at Day 1 prior to treatment of the following cycles (ie, Day 1 of cycles 4, 7, 10, etc.).

APPENDIX C. TUMOR MARKER REFERENCE RANGES

Analyte	Lbtestcd	Lbtest	Unit	Reference Range
Alpha-fetoprotein (AFP)	AFP	Alpha-fetoprotein Measurement	ng/mL	<8 ng/mL
AFP-L3	AFPL3	Alpha Fetoprotein L3 Measurement	ng/mL	<8 ng/mL
Beta-human chorionic gonadotropin (Beta-hCG)	Choriogonadotropin Beta	Choriogonadotropin Beta Measurement	mUI/mL	<2 mUI/mL
Bladder Tumor Antigen (BTA)	BTA	Bladder Tumor Antigen	NA	NA
CA 15-3	CA15_3AG	Cancer Antigen 15-3	U/mL	<30 U/mL
CA 27.29	CA2729AG	Cancer Antigen 27-29	U/mL	<38 U/mL
CA 19-9	CA19_9AG	Cancer Antigen 19-9	U/mL	<37 U/mL
CA 125	CA125	Cancer Antigen 125	U/mL	<35 U/mL
Carcinoembryonic antigen (CEA)	CEA	Carcinoembryonic Antigen	ng/mL	<2.5 ng/mL
Chromogranin A (CgA)	CGA	Chromogranin A	ng/mL	<225 ng/mL
Des-gamma-carboxy prothrombin (DCP)	DCP	Des-gamma-carboxy prothrombin	ng/mL	<7.5 ng/ml
Fibrin/Fibrinogen	FIBRINO	Fibrinogen	mg/dL	200 mg/dL-400 mg/dL
Prostate-specific antigen (PSA)	PSA	Prostate Specific Antigen	ng/mL	<4 ng/mL
Soluble mesothelin-related peptides (SMRP)	SMRP	Soluble Mesothelin Related Peptides	NA	NA

Signature Page for [redacted]

Approval Task	[redacted]-2024 15:13:11 GMT+0000

Approval Task	[redacted]24 17:58:13 GMT+0000

Approval Task	[redacted]24 22:06:10 GMT+0000

Signature Page for [redacted]