Protocol C4651001

A PHASE 1, OPEN-LABEL, DOSE ESCALATION AND EXPANSION STUDY EVALUATING THE SAFETY AND PHARMACODYNAMICS OF PF-07263689, EITHER ALONE OR IN COMBINATION WITH AN ANTI-PD-1 ANTIBODY, IN PREVIOUSLY TREATED PARTICIPANTS WITH SELECTED LOCALLY ADVANCED OR METASTATIC SOLID TUMORS

Statistical Analysis Plan
(SAP)

Version: **2**

Date: **29 MARCH 2023**

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1. VERSION HISTORY

Table 1 Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Rationale Specific Changes
1 21 Oct 2021	Original 20 July 2021	NA	NA
2 29 Mar 2021	2 20 July 2021	Final database lock	• Window for missing assessment for PFS censoring updated from 57 to 119 days to align with SOA. • QTcF windows corrected to align with protocol. • Supine pulse rate criteria removed as they are not applicable. • Clarified dose adjust to require planned dose to be less than assigned dose. • Other minor updates in the corresponding sections

2. INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in study C4651001. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment. This SAP was written in reference to the original version of the protocol amendment 1 dated July 20, 2021.

Note: in this document any text taken directly from the protocol is *italicized*.

2.1. Study Objectives

2.1.1. Part 1 Primary Objectives

- *Part 1A: To assess safety and tolerability at increasing dose levels of PF-07263689 in successive cohorts of participants with select locally advanced/metastatic solid tumors, until the MTD is estimated or the MFD dose is reached.*

- *Part 1B: To assess safety and tolerability PF-07263689 in combination with sasanlimab in successive cohorts of participants with select locally advanced/metastatic solid tumors, in order to estimate and select the combination RP2D/schedule.*

2.1.2. Part 1 Secondary Objectives

- *To evaluate preliminary antitumor activity.*
- *To evaluate the viral load kinetics following first and second dose of PF-07263689.*
- *To collect sasanlimab drug concentration data in Part 1B for evaluation of sasanlimab PK.*
- *To characterize the viral shedding of PF-07263689.*
- *To evaluate the immunogenicity of PF-07263689 and sasanlimab following monotherapy and combination administration.*

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2.1.4. Part 2 Primary Objectives

- *To confirm safety and tolerability of PF-07263689 at the RP2D in combination therapy in participants with selected tumor types.*
- *To evaluate preliminary evidence of antitumor activity of PF-07263689 in combination therapy in participants with selected tumor types.*

2.1.5. Part 2 Secondary Objectives

- *To further evaluate the viral load kinetics following PF-07263689 administration.*
- *To collect sasanlimab drug concentration data in Part 2 for evaluation of sasanlimab PK.*

- *To characterize the viral shedding of PF-07263689.*
- *To further evaluate the immunogenicity of PF-07263689 and sasanlimab.*
- *To evaluate preliminary antitumor activity through time to event time points.*
- *To assess overall survival of participants treated with PF-07263689.*

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2.1.7. Primary Estimand(s)

The primary estimand for incidence of DLTs in Part 1 is DLT rate estimated based on data from DLT-evaluable participants during the DLT evaluation period, which is the first 28 days after the first dose of study intervention. The attributes of this estimand are provided in Section of 9 of the protocol.

- Population: DLT evaluable set will be used.
- Variable: Safety and DLT data collected;
- Intercurrent event(s): Administration of rescue medication. All data collected (after rescue medication or after discontinuation of treatment) are included.
- Population-level summary: Summary of AE and DLT rates by cohorts, study part and total.

The primary estimand in Part 2 is to evaluate the treatment effect of PF-07263689 in combination with PF-06801591 assessed by the ORR, based on investigator assessment per RECIST 1.1, in the response evaluable analysis population.

- Population: Response evaluable set will be used for all response related analysis including ORR and DOR;
- Variable: Best Overall Response for patient as assessed by RECIST 1.1;

- Intercurrent event(s): Administration of rescue medication. All data collected (after rescue medication or after discontinuation of treatment) are included.

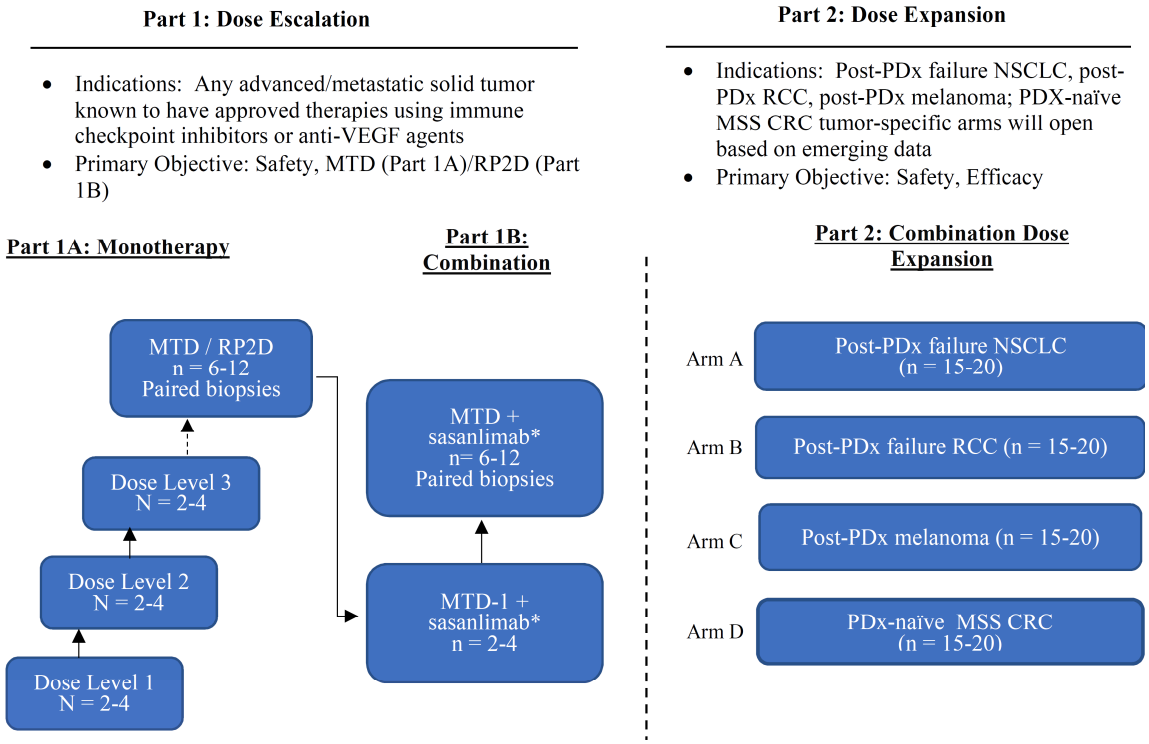
- Population-level summary: Summary table for ORR by cohorts, arm and total.

2.2. Study Design

This is a Phase 1, open-label, multicenter, multiple dose, dose escalation, and dose expansion study will evaluate the safety, tolerability, viral load kinetics and shedding, PD, and antitumor activity of PF-07263689, either alone or in combination with sasanlimab (an investigational anti-PD-1 antibody), in participants with locally advanced or metastatic solid tumors who have exhausted all standard of care therapies available to them. The study consists of 2 parts: Part 1 dose escalation for PF-07263689 monotherapy (Part 1A) and combination with sasanlimab (Part 1B) and Part 2 dose expansion for the combination therapy.

The overall study design is depicted in the schema in Figure 1.

Figure 1. Overall Study Schema



PF-07263689 regimen: IV once weekly for 4 doses (Q1W x 4)
PF-07263689 dose range: 3 x 10^8 PFU (starting dose) to 4 x 10^{10} PFU (Maximum Feasible Dose)
Sasanlimab: 300mg SC Q4W; Each SC cycle = 28 days
Paired biospies: In Part 1, paired de novo tumor biopsy samples pre-treatment and on-treatment (C1D8 ± 1 day) will be required from 5 participants each in Part 1 at or below MTD and Part 1B at or below MTD + sasanlimab. In Part 2, paired de novo tumor biopsy samples will be collected from 5-8 participants in each arm unless biopsy samples cannot be obtained safely.
* The starting dose of PF-07263689 for Part 1B will be at or one dose lower than the MTD from Part 1A.

Part 1A and 1B, dosing of initial participants will be staggered by 7 days to mitigate against unexpected adverse drug reaction as follows:

- Each dose level: the first 2 participants may not begin dosing within 7 days of one another

Part 2 Dose Expansion: Initially, 3 tumor-specific arms will commence based on preliminary data from Part 1, with the option to open the fourth arm based on emerging data. For the post-PDx indications, Arms A, B, and C may be limited to participants with primary or secondary resistance after discussion with investigators.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Part 1 Primary Endpoints

- *First cycle DLTs.* The specific definitions of DLTs are provided in the protocol.
- *AEs as characterized by type, frequency, severity (as graded by NCI CTCAE version 5.0, except CRS, which will be graded by ASTCT criteria), timing, seriousness, and relationship to study treatment.*
- *Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE version 5.0), and timing.*

3.2. Part 1 Secondary Endpoints

- *ORR, as assessed using the RECIST version 1.1.* The definitions of ORR and other efficacy endpoints are provided in Section6.2.1.
- *Time-to-event endpoints: DOR, PFS, TTP by RECIST 1.1.*
- *Viral load kinetics parameters of PF-07263689 in blood, including C_{max}, T_{max} and AUC_{last}.*
- *Trough concentrations of sasanlimab for selected cycles*
- *Viral titers during 30, 45, and 60 days after the last PF-07263689 dose.*
- *Incidence and titers of ADA against PF-07263689 and sasanlimab.*
- *Incidence and titers of anti-IL2 antibodies.*

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3.4. Part 2 Primary Endpoints

- *ORR, as assessed using the RECIST version 1.1.*
- *AEs as characterized by type, frequency, severity (as graded by NCI CTCAE version 5.0), timing, seriousness, and relationship to study treatment.*
- *Laboratory abnormalities as characterized by type, frequency, severity (as graded by NCI CTCAE version 5.0), and timing.*

3.5. Part 2 Secondary Endpoints

- *Viral load kinetics parameters of PF-07263689 in blood, including C_{max}, T_{max}, and AUC_{last}.*
- *DCR, DOR, PFS, and TTP by RECIST version 1.1.*
- *Overall survival.*
- *Trough concentrations of sasanlimab for selected cycles..*
- *Viral titers during 30, 45, and 60 days after the last PF-07263689 dose.*

- *Incidence and titers of ADA against PF-07263689 and sasanlimab.*
- *Incidence and titers of anti- IL-2 antibodies.*

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3.7. Baseline Variables

Baseline characteristics will be collected according to Schedule of Activities as specified in the protocol. No baseline variable will be used for stratification or as covariates for the primary statistical analysis. Unless otherwise specified, the baseline value is defined as the value collected at the time closest to, but prior to, starting the study intervention administration in the first cycle.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population.

Table 2. Analysis Sets

Population	Description
Full analysis set	*The full analysis set includes all enrolled participants.* *"Enrolled" means a participant's, or their legally authorized representative's, agreement to participate in a clinical study following completion of the informed consent process. Potential participants who are screened for the purpose of determining eligibility for the study, but do not participate in the study, are not considered enrolled, unless otherwise specified by the protocol.*
Safety analysis set	*The safety analysis set includes all enrolled participants who receive at least one dose of study intervention. Unless otherwise specified, the safety analysis set will be the default analysis set used for all analyses.*

Population	Description
Per protocol analysis set (evaluable for MTD)	*The per protocol analysis set includes all enrolled participants who had at least one dose of study treatment and either experienced DLT or do not have major treatment deviations during the DLT observation period.* *A participant is classified as "dose limiting toxicity evaluable" (hence will be included in this analysis set) under the following conditions: 1) If the participant receives 3 of the 4 doses of PF-07263689 and has completed the scheduled safety assessments during the DLT observation period or 2) has experienced a DLT. Participants may miss a single dose, but the first dose and the last dose must occur within the 22-day window. Participants who withdraw from the study during the DLT evaluable period for reasons other than a DLT may be replaced with a new participant at the same dose level. The sole exception to criterion 1) is if the participant has missed a minority of safety assessments due to emergency situations (eg, site accessibility issues, inability to go to an external lab, etc.). In such cases, the DLRM Committee may judge the participant evaluable, depending on the abundance of the available data. Participants that experience any DLT at any dose level in Part 1 and Part 2 of the study will not be replaced.*
Blood viral load Kinetics Analysis Set	*All enrolled participants treated who do not have protocol deviations influencing viral load kinetics assessment, and have sufficient information to estimate at least 1 of the parameters of interest.*
Vector Shedding Analysis Set	*All enrolled participants who are treated and have at least 1 analyte concentration above the lower limit of quantitation.*
Efficacy Modified Intent to Treat (mITT) Analysis Set	*Includes all subjects who have received at least one dose of study treatment. If the FAS is same as the mITT, the analysis should be run on FAS.*
Response evaluable set	*The response evaluable population will include all participants who received at least one dose of study treatment and had baseline disease assessment [or measurable disease at baseline, if applicable] and at least one post-baseline disease assessment.*
[redacted]	CCI [redacted]

Population	Description
Immunogenicity analysis set	*The immunogenicity analysis set includes all enrolled participants who receive at least one dose of study treatment and have at least one sample tested for ADA.*

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Hypotheses and Decision Rules

There will be no formal hypothesis testing in this study.

Decision Rules for Part 1:

Dose escalation or de-escalation decisions will be made based on the following. The provisional dose levels in dose escalation are provided in Section 4.3.2 of the protocol.

For Part 1, determination of MTD is achieved prior to the MFD will be performed using the DLT Evaluable set.

The dose escalation in the Part 1 of the study will be guided by a Bayesian analysis of DLT data for PF-07263689 using a 2-parameter BLRM (Part 1A) or for the combination of PF-07263689 and sasanlimab using a 5-parameter BLRM (Part 1B). Weakly informative prior distributions based on preclinical/expert opinion information will be chosen for the logistic parameters in Part 1A; the observed DLT data in Part 1A and DLT data of sasanlimab will be used to form prior distribution for the BLRM in Part 1B (see Appendix 9 of the protocol).

After each cohort of participants, the posterior distribution for the risk of DLT for new participants at different doses of interest for PF-07263689 will be evaluated. The posterior distributions will be summarized to provide the posterior probability that the risk of DLT lies within the following intervals:

Under-dosing: [0, 0.16]

Targeted dosing: [0.16, 0.33]

Overdosing: [0.33, 1]

The interpretation of the 3 intervals is:

- Under-dosing: escalate to next higher dose;
- Proper dosing: stay at current dose;
- Overdosing: de-escalate to a lower dose.

Dosing decisions are guided by the EWOC principle (Rogatko 2007). A dose may only be used for newly enrolled participants if the risk of excessive toxicity at that dose is less than

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25%. Initially, dose escalation increases will be limited to no more than a half log increase from the previous dose level, which is a common approach for biologic compounds (Saber et al. 2017; Saber et al. 2016). Following the observation of a DLT in the current cohort, subsequent dose escalation increases will be limited to no more than 100%. A return to half log dose increases may be permitted at the discretion of the sponsor if no DLT are seen at the following dose level.

The dose escalation will be stopped when the following criteria are met:

- *At least 6 participants have been treated at the recommended MTD/RP2D.*
- *The dose $\tilde{\mathbf{d}}$ satisfies 1 of the following conditions:*
    1. *The probability of target toxicity at dose $\tilde{\mathbf{d}}$ exceeds 50%, ie, $Pr(0.16 \leq \pi_{\tilde{d}} < 0.33) \geq 50\%$.*

    2. *A minimum of 15 participants have been treated in the study.*

In the event that all doses explored appear to be overly toxic and the MTD cannot be determined, the study will stop.

Additionally, when any of the following safety criteria are met, enrollment and study intervention administration will be paused, all available clinical safety data will be reviewed by the Sponsor together with the Investigators prior to determining next steps:

- *Any death that is not related to disease progression occurring within 30 days of receiving IP or does not have a determined alternative etiology.*
- *Occurrence of 2 Grade $\geq$4 DLTs in 2 study participants at the starting dose.*
- *For subsequent dose levels after the starting dose, a criterion guiding pause on enrollment at the current cohort is defined based on Bayesian posterior probabilities using a non-informative Beta (0.5, 0.5) prior distribution. The probabilities will be calculated for total number of participants in the current cohort. The safety criterion is met if the number of evaluable participants observed to have a DLT due to Grade 4 or higher AE results in a posterior probability that the true rate of such event exceeding 30% is $\geq$0.80.*
- *Any Grade 4 hypersensitivity reaction/anaphylaxis observed.*

To mitigate the risk of misclassifying DLTs, a sensitivity that uses weighted DLT/AE data (in equivocal cases) within the BLRM may be performed. If all investigators and the sponsor agree on the equivocal DLT/AE data, the DLT weighting approach could be the primary dose escalation method.

Decision Rules for Part 2:

The main objective is to evaluate the doses selected (RP2Ds) for PF-07263689 in combination with sasanlimab at the preliminary combination RP2D from Part 1B. Summary

statistics will be provided for safety and efficacy endpoints, without formal hypothesis testing.

Sample Size Consideration:

Part 1

Approximately 40 DLT evaluable participants will be enrolled in Part 1 of the study (Parts 1A and 1B). In general, the cohort size for the dose escalation will be 2 to 4 DLT evaluable participants before the estimated MTD dose level; for the dose level that is estimated to be the MTD, at least 6 (approximately 6-12) DLT evaluable participants will be treated. The total number of participants will depend on the number of dose levels needed to determine the MTD and number of participants evaluable for DLT at each dose level.

Part 2

In Part 2 dose expansion, approximately 15 to 20 participants will be enrolled for each tumor-specific cohort. Participants will receive PF-07263689 at the RP2D (as determined from Part 1) in combination with sasanlimab. The sample size is not based on statistical hypothesis test; rather it is based on clinical consideration that the stated sample size will provide sufficient evidence of preliminary efficacy of PF-07263689 in combination with sasanlimab.

A Bayesian approach will be used to estimate the ORR in the study indications. Assuming a non-informative prior (ie, Jeffrey's prior) if 5 out of 20 participants have tumor response, this would translate into a posterior probability (Beta Binomial) of 72.5% that the true response is not inferior to 20%.

If no or minimal efficacy is observed (eg, 0 or 1 responder) in the first 10 participants of an indication, that indication specific cohort may be terminated after a comprehensive data review.

5.2. General Methods

While every effort has been made to pre-specify all analyses in this statistical analysis plan, if any additional CCI [redacted] be found to be necessary, the analyses and the reasons for them will be detailed in the clinical study report (CSR).

All data will be categorized based on the scheduled visit at which it was collected. These visit designators are predefined values that appear as part of the visit tab in the case report form (CRF).

The data will be summarized by dose level, defined by the initial dose of the study intervention administered to participants. If a dose level has more than 1 cohort, data from these cohorts will be combined. DLT rates at the study dose levels will be presented via mean and medians and a Bayesian credible interval based on the posterior density from the

full probability model. This information will also be used for the dose level review meetings (DLRM) to guide the dose escalation.

For Part 1, when there are multiple dose levels, in addition to data presentation by dose level, the overall summary combining all dose levels will also be presented. For Part 2, data will be primarily summarized by tumor type, an overall summary combining all tumor types may be presented for adverse event.

5.2.1. Analyses for Binary Endpoints

Binary data will be summarized using number of unique participant incidence, proportion in the analysis set, and the 2-sided 95% exact confidence interval for the proportions, if the sample size per cohort permits. The confidence interval will be based on the Clopper-Pearson exact method.

Binary data in this study include complete response (CR), partial response (PR), stable disease (SD), progressive disease (PD), and objective response rate (ORR), based on RECIST 1.1.

5.2.2. Analyses for Continuous Endpoints

Continuous data will be summarized with the mean, median, minimum, maximum, standard deviation, and 2-sided 95% confidence interval of the mean if the sample size permits and deemed necessary.

Continuous data in this study include, but not limited to, certain laboratory measurements, vital signs, ECG, certain PK/ viral load kinetics parameters or biomarkers.

5.2.3. Analyses for Categorical Endpoints

Categorical data will be summarized by number of unique participant incidence and proportion of participant in each category, and 2-sided 95% confidence interval of the proportion if the sample size permits and deemed necessary.

An example of categorical data presentation is adverse events or laboratory abnormalities graded by NCI CTCAE v5.0, where each grade is considered as a category.

5.2.4. Analyses for Time-to-Event Endpoints

The time-to-event endpoints will be summarized using the Kaplan-Meier method and estimated survival curves may be displayed graphically when needed. Graphs will describe the number of participants at risk over time. The median, quartiles, and probabilities of an event at particular points in time will be estimated by the Kaplan-Meier method, when possible based on the number of observed events. Confidence intervals for medians and quartiles, based on the Brookmeyer-Crowley method (Brookmeyer and Crowley, 1982), may be presented. Confidence intervals for the estimated probability of an event at a particular time point may be generated using the Greenwood formula.

Time to event endpoints include duration of response(DoR), progression-free survival (PFS), time to progression (TTP) in Part 1, and additionally overall survival (OS) in Part 2.

5.2.5. Special Notes on Data Analyses When Intraparticipant Escalation Occurs

Intraparticipant dose escalation is allowed in the dose escalation phase of the study (Part 1). The intraparticipant dose escalation may occur after the 2nd scheduled tumor scan and as early as when Cycle 5 treatment starts provided a participant stayed on treatment through Cycle 4 and met other criteria as specified in Section 4.3.2 of the Protocol. If the planned/assigned dose, as reported in the dosing page of the case report form, at a cycle when intraparticipant escalation may possibly occur (e.g. Cycle 5 or higher) is the next higher dose (e.g. 450 mg) than the initially assigned dose at Cycle 1 Day 1 (e.g. 150 mg), then that participant would be identified as having an intraparticipant dose escalation. The first dose date of the higher dose will be used as an "anchor" date in the following analyses:

1) **For ORR:** when the best overall response (BOR) is determined at participant level, two "BOR" will be determined: one with tumor scans that occurred prior to the anchor date, if available; the second one with all available tumor scans without considering intraparticipant dose escalation. Both "BOR" will be presented under the dose level initially assigned at Cycle 1 Day 1. In the second one, a footnote indicating the number of participants who underwent intraparticipant dose escalation will be added.

2) **For DOR, TTP, and PFS:** only one set of analyses will be performed using all available participant level data without considering intraparticipant dose escalation.

3) **For all safety summaries:** all safety data (e.g. AE etc.) that occurred after the anchor date will be attributed and presented toward the newly assigned higher dose. This is consistent with the "as-received" principle.

4) A listing of participants who underwent intraparticipant dose escalation will be created, in which the initially assigned dose level at Cycle 1 Day 1, the newly assigned higher dose, the cycle number when the intraparticipant dose escalation occurred will be included, along with few other variables such as age, tumor type, the visit-based (e.g. week 8, or week 16) overall tumor evaluation. Further ad-hoc efficacy analyses may be initiated upon reviewing this listing.

5.3. Methods to Manage Missing Data

For the analysis of safety endpoints, the sponsor data standard rules for imputation will be applied based on the Safety Rulebook.

5.3.1. Missing Dates

In compliance with Pfizer standards, if the day of the month is missing for any date used in a calculation, the 1st of the month will be used to replace the missing date unless the calculation results in a negative time duration (eg, date of onset cannot be prior to day one date). In this case, the date resulting in 0 time duration will be used. Pfizer standards are

also used if both month and day are missing (Jan 1 unless negative time duration). This excludes the pharmacokinetic and ECG analyses, which will only use the actual date collected or if date not available deem the data missing.

5.3.2. Efficacy Analysis

For tumor assessment that will be used in the binary efficacy endpoint, every effort will be made to retrieve data in the CRF, however missing data will be left as is, no imputation will be performed. The reasons for missing tumor assessment will be collected

For the time-to-event endpoints, the missing data handling method will be censoring. Censoring rules for time-to-event endpoints are detailed in Section 6.2.2.

5.3.3. Sasanlimab Pharmacokinetics

In all data presentations (except listings), sasanlimab concentrations below the limit of quantification (BLQ) will be set to zero. (In listings BLQ values will be reported as "<LLQ", where LLQ (i.e. lower limit of quantification) will be replaced with the value for the LLQ.)

5.3.4. Viral Load Kinetics and Vector Shedding Analysis

Whole blood, saliva, urine and skin swab samples for viral shedding kinetics will be collected according to the protocol schedule. Viral shedding results below the limit of quantification (BLQ) for each matrix are considered "undectable" and will be imputed as zero for summary statistics and graphical presentation.

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5.3.6. QTc

For the corrected QT (QTc) analyses, no values will be imputed for missing data.

5.4. Statistical Considerations of COVID-19 Impacted Data

In March 2020, the World Health Organization (WHO) announced a global pandemic of the virus SARS-CoV-2 and the resulting disease COVID-19. During the conduct of this trial, if any participant's data is impacted by this pandemic, the following considerations will be given in the data analyses:

a. If a participant dropped out of the study during the DLT evaluation window in Part 1 due to COVID-19, a replacement participant may be added.

b. Death caused by COVID-19 is still considered as an "event" in the analysis of PFS and OS. If deemed necessary, a sensitivity analysis may be performed where COVID-19 driven death is censored at the death date.

c. If a scheduled tumor radiographic scan is *delayed* out of the Schedule of Activity allowable window, or is *missing* (i.e. participant skipped a scheduled tumor

radiographic scan) due to any reasons related to the pandemic, this delay or missingness does not alter the censoring rules for PFS or TTP. A censoring reason of "COVID-19" may be added to the PFS or TTP summary if the specific reason of tumor scan delay or missing can be attributed to COVID-19. If deemed necessary, a sensitivity analysis may be performed where participants would be censored on the date of COVID-19 diagnosis.

In the confirmed ORR analysis, if a response can't be confirmed by a subsequent tumor scan because of the pandemic (i.e. the subsequent tumor scan wasn't performed), then the initial response will be considered as unconfirmed. This is a conservative approach. No sensitivity analysis will be performed.

d. Any COVID-19 related symptoms are to be captured as adverse events in the case report form. Those adverse events will be summarized in the same manner as other adverse events. If COVID-19 related adverse events can be identified, then a separate AE listing may be provided for just the COVID-19 related events.

e. If identifiable, the COVID-19 related data points, including missing data where the reason of missing is identified as COVID-19 related (site closure hence data could not captured; participants skipped a visit because of concern over the pandemic), protocol deviations driven by COVID-19, safety events caused by COVID-19 may be separately listed.

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoints for Part 1

6.1.1. Dose-Limiting Toxicities (DLTs)

- Analysis set: Per protocol analysis set.

- Analysis methodology:

  For the purpose of dose escalation, the DLT observation period will be during the first cycle (28 days after the start of PF-07263689 monotherapy [Part 1A] and PF-07263689 combination with sasanlimab [Part 1B]) in each participant.

  Whether an adverse event a participant experienced during the DLT window is determined as a DLT or not is based on the DLT definitions provided in Section 4.3.3 of the protocol. A DLT yes/no checkbox will be provided in the case report form, where the investigator provides his/her judgement if an event is a DLT or not. However, the final determination will be reached between the investigators and the sponsor during the dose level review meeting (DLRM). These final decisions will be documented.

  The DLT events will be summarized by dose level. A listing of the DLTs events will also be provided in which the participant primary diagnosis (malignancy), dose level the participant was enrolled to, DLT event start day and stop day relative to the cycle 1

day 1 dose date, the DLT event term, NCI CTCAE grade, relatedness to the investigational product (PF-07263689), outcome of the event, along with other variables deemed important, will be included.

Note that the BLRM analysis results for the DLT data is for DLRM only. Those results will not be included in the clinical study report. Instead, they will be archived along with other DLRM materials.

- Missing data: All enrolled participants in Part 1 should have an indicator variable derived to be either 1 (yes) or 0 (no) based on the DLT definitions (provided in Section 4.3.3 of the protocol) and participant's safety data during the DLT observation window. If a participant fails to have a value on the indicator variable because the participant being non-DLT-evaluable, the participant may be replaced.

6.1.2. Adverse Events

- Analysis set: Safety analysis set.

- Analysis methodology: Adverse Events (AEs) will be graded by the investigator according to NCI CTCAE version 5.0 and coded using the MedDRA. The focus of AE summaries will be on Treatment Emergent Adverse Events (TEAEs). TEAE is defined as any adverse event that occurs during the on-treatment period, on or after the first dose of study treatment, and on or before the last dose of study treatment + 35 days, or before the start of any other anti-cancer therapy, whichever is earlier. AEs that occurs after the on-treatment period may still be recorded in the clinical database and will be included in the AE listings, but will not be included in the AE summaries.

  The number and percentage of participants who experienced any AE, serious AE (SAE), treatment related AE, and treatment related SAE will be summarized by system organ class (SOC) and preferred terms (PT) according to worst toxicity grades. The summaries will present AEs for the entire on-treatment period, by dose level for Parts 1, and by tumor type for Part 2. AE summaries will not be presented by treatment cycle. In the summary tables for Part 1, a "Total" column, summarizing data across all dose levels, will be presented; similarly in Part 2, a "Total" column, summarizing data across all indications will be presented. Additionally summaries of adverse events leading to death and premature withdrawal from study treatment will be provided.

  Missing data: If AE start or stop date is missing, impution will be performed according to Section 5.3. The imputed dates will be used to determine whether the AE is to be included in the TEAE summary. The missing AE start or stop dates will be listed as is in AE listings. When the CTCAE grade is missing for an AE, the AE will be excluded from the CTCAE grade summary table.

6.1.3. Laboratory abnormalities

- Analysis set: Safety analysis set.

- Analysis methodology:

  Laboratory tests in this study include several panels: hematology, chemistry, serology, coagulation, urinalysis, and pregnancy test.

  The frequency and percentage of participants who experienced laboratory test abnormalities will be summarized according to worst toxicity grade (based on NCI CTCAE version 5.0) observed for each laboratory assay. Summaries of laboratory tests results by visit may be provided. Summaries for change from baseline and percent change from baseline for the laboratory tests may be provided. Shift tables may be provided for selected laboratory tests, if deemed necessary.

  The summaries will be presented for the entire on-treatment period and for the various parts of the study (by dose level for Part 1, by tumor type for Part 2), and will not be presented by treatment cycle.

  Hematology, serology, and coagulation lab results can be combined into one summary output. Separate summaries will be created for chemistry tests. Urinalysis and pregnancy tests will not be summarized and will only be listed in data listings. Shift tables may be provided for selected laboratory tests.

- Missing data: Intermediate missing values (ie, values collected between baseline and the last study measurement) will not be imputed.

6.2. Secondary Endpoints for Part 1

6.2.1. Efficacy Endpoints

In Part 1, efficacy endpoints, including objective response rate (ORR) per RECIST 1.1, duration of response (DOR), progression-free survival (PFS), and time to progression (TTP), are secondary endpoints.

The efficacy endpoints that will be analyzed in this study are defined as follows:

- ORR is defined as the percentage of participants with a best overall response of CR or PR relative to the appropriate analysis set.

- DOR is defined as the time from first documentation of CR or PR to date of first documentation of PD or death due to any cause.

- PFS is defined as time from start date of treatment to the date of first documentation of PD or death due to any cause.

- TTP is defined as the time from start date of treatment to the date of the first documentation of PD.

These efficacy endpoints will be analyzed as follows:

- Analysis set: Response evaluable set for ORR and DOR. Full analysis sest for PFS and TTP. If needed necessary PFS and TTP may be analyzed with the mITT population.

- Analysis methodology:

- ORR, both confirmed ORR and unconfirmed ORR (uORR) will be determined based on the confirmed and unconfirmed CR and PR, definitions provided below. ORR will be based on the best overall response (BOR) of a participarnt, according to RECIST 1.1. In the BOR derivation, the minimum duration of SD as the best overall response is set as 5 weeks.

  Unconfirmed CR (uCR) is defined as one objective status of CR documented before participant reached the end of the study for any reason (progressed disease, death, withdrawing consent, lost to follow-up etc) or started any other anti-cancer therapies; while confirmed CR requires two objective statuses of CR at minimum of four weeks apart documented before the scheduled end of study or the start of any other anti-cancer therapies. Sequences of CR - Non-evaluable - CR are considered confirmed CR as long as the two CR responses are observed at a minimum of 4 weeks apart. Simillarly, unconfirmed PR (uPR) is defined as one objective status of PR documented before the scheduled end of study or the start of any other anti-cancer therapies but not qualifying as uCR. Confirmed PR is defined as two objective statuses of PR or better (PR followed by PR or PR followed by CR) a minimum of four weeks apart documented before the scheduled end of study or the start of any other anti-cancer therapies, but not qualifying as CR. Sequences of PR - Stable Disease or Non-evaluable - PR are considered PRs as long as the two PR responses are observed at a minimum of 4 weeks apart. Based on these definitions, the unconfirmed ORR analysis will include both confirmed CR or PR and unconfirmed CR or PR as responders, whereas the confirmed ORR analysis will only include confirmed CR or PR as responders.

  ORR and its 95% exact confidence interval as described in Section 5.2.1 will be presented for each dose level and the total across all dose levels.

- Duration of Response (DOR). The responders who have not disease progressed at the time of analysis will be censored at the last available tumor scan date. DOR will be analyzed for the subset of participants with a confirmed objective response of CR or PR.

  In Part 1, as the sample size for each dose level is fairly small, DOR will be considered as a continuous variable. Summary statistics as described in Section 5.2.2 will be presented by dose level. No Kaplan-Meier analysis will be performed.

  Tumor response will be presented in the form of participants data listings that include, but are not limited to: tumor type, actual received day 1 dose, tumor response at each

assessment, and best overall response. Progression date, death date, date of first response, last assessment date, and date of last contact will also be listed.

Additionally, a swimmer plot will be provided to display tumor response overtime and a waterfall plot displaying the best percentage change in tumor size will be provided.

- Progression-Free Survival (PFS). PFS will be summarized using the Kaplan-Meier method, as descrbied in Section 5.2.4. And PFS may also be displayed graphically when appropriate.

  Participants without an event or with an event after 2 or more inadequate or missing tumor assessments (57 days or later) will be censored on the date of the last adequate tumor assessment that documented no progression; deaths within 17 weeks after the first dose date for participants who did not initiate new anti-cancer therapy will still be considered an event. If a new anti-cancer therapy is started prior to an event, the participant will be censored on the date of the last adequate tumor assessment that documented no progression prior to the start of the new anti-cancer therapy.

  Participants with no baseline tumor assessment (including participants with an inadequate baseline assessment) or with no adequate post-baseline tumor assessments within 17 weeks after the first dose date will be censored on the first dose date, unless the participant dies within 17 weeks of the first dose date, in which case, death will be an event on date of death.

  PFS outcome and censoring rules are summaries in Table 2. Any additional censoring rules that may affect data analysis will be documented in the Analysis Programming Specification (a separate document).

  Any tumor scan or response data impacted by COVID-19 will be handled according to Section 5.4.

Table 3. PFS and TTP Censoring Rules

Situation	Date of Event/Censoring	Outcome
No adequate baseline assessment	First dose date	Censored [a]
PD or death - after at most one missing or inadequate post-baseline tumor assessment, or - ≤ 17 weeks after the first dose date	Date of PD or death	Event
PD or death - after 2 or more missing or inadequate tumor assessments (119 days or later)	Date of last adequate tumor assessment [b] documenting no PD prior to new anti-cancer therapy or missed tumor assessments	Censored
No PD		
New anti-cancer therapy given prior to PD or death		

[a] If the participant dies ≤17 weeks after the first dose date and did not initiate new anti-cancer therapy, the death is an event with date on death date.

[b] If there are no adequate post-baseline tumor assessments prior to the PD or death, then the time without adequate assessment should be measured from the first dose date; if the criteria were met the censoring will be on the first dose date.

- Time to Progression (TTP). TTP will be summarized using the Kaplan-Meier method, as descrbied in Section 5.2.4. No graphical display will be generated for TTP. The censoring rule as described in Table 2 will be applied to TTP, where appropriate.

- Missing data: For ORR and DOR, missing data will not be imputed. For PFS and TTP, missing data will be handled by the censoring rules.

6.2.2. Viral Load Kinetics and Vector Shedding Analysis

- Analysis set: Blood viral load Kinetics and Vector Shedding Analysis set

- Analysis methodology:

Vector shedding in saliva, urine and skin swabs: Viral titers in each matrix will be summarized descriptively (n, mean, standard deviation, coefficient of variation, median, minimum, maximum, geometric mean and its associated coefficient of variation) by dose, day and nominal time.

Peak viral titer levels from shedding qPCR assay in saliva, and urine will also be summarized descriptively by dose cohort and study visit separately if sufficient data is available. Further, duration of shedding may be reported if sufficient data is available. For samples that are tested for infectious virus, descriptive statistics will be provided for each matrix by dose, day, and nominal time.

Missing data: missing concentration data or parameter data will be handled according to Sections 5.3.4.

6.2.3. Sasanlimab Pharmacokinetic Analysis in Part 1B

The concentration-time data of sasanlimab will be summarized by descriptive statistics (n, mean, standard deviation, coefficient of variation, median, minimum, maximum, and geometric mean) according to dosing cohort and time for each part of the study.

CCI

[redacted]

6.2.5. Analysis of Immunogenicity Data

For the immunogenicity data, the percentage of participants with positive ADA and neutralizing antibodies each will be summarized. For participants with positive ADA or neutralizing antibodies, the magnitude (titer), time of onset, and duration of ADA or neutralizing antibodies response will also be described, if data permit. The potential impact of immunogenicity on clinical response including pharmacodynamic markers, safety/tolerability and efficacy will be explored, if warranted by the data.

CCI

[redacted]

CCI [redacted]

6.4. Primary Endpoints for Part 2

6.4.1. Efficacy Endpoint: Overall Response Rate (ORR)

ORR is considered as a primary endpoint in Part 2. This endpoint in Part 2 will be analyzed in the same manner as described in Section 6.2.2.

6.4.2. Safety Endpoints

Adverse events and laboratory tests are the safety primary endpoints for Part 2. The analysis set, analysis methodology will be same as described in Sections 6.1.2, 6.1.3 respectively.

6.5. Secondary Endpoints for Part 2

6.5.1. Efficacy Endpoints

The secondary efficacy endpoints for Part 2 include DOR, PFS, TTP, as well as overall survival (OS). DOR, PFS, and TTP will be analyzed in the same approach as described in Section 6.2.2.

DOR in Part 2, may be additionally analyzed using the Kaplan-Meier approach if there is a relatively large number of objective responder. The outcome, event dates and reasons for censoring for DOR will be the same as for those in the analysis of PFS (Table 3 in Section 6.2) except that participants will not be censored for inadequate baseline assessment or for no adequate post-baseline assessment, as only participants with an objective response are included in the analysis.

OS, defined as the time from start date of treatment to the date of death due to any cause, is an efficacy endpoint that is only applicable to Part 2 of the study, will be analyzed with the Kaplan-Meier approach. Participants last known to be alive are censored at date of last contact. The date of last contact will be derived for participants not known to have died at the analysis data cutoff date using the latest complete date (non-imputed) among AE collection date, vital sign date, tumor assessment date, date of follow up anti-cancer therpay etc. This is not an exclusive list of possible dates. Any retrievable last contact date from the clinical database will be used.

6.5.2. Pharmacokinetic, Viral load kinetics, and vector shedding Analysis

Sasanlimab Pharmacokinetic analysis, viral load kinetics and vector shedding analyses for Part 2 will be carried out in the same manner as described in Section 6.2.2 and 6.2.3.

6.5.3. Analysis of Immunogenicity Data

For the PF-07263689 immunogenicity data, the percentage of participants with anti-vaccinia virus neutralizing antibodies and positive anti-IL2 antibodies will be summarized by dose level and "Total" across all dose levels for Part 1, by tumor type for Part 2. For patients with

positive ADAs, the magnitude (titer), time of onset, and duration of ADA response will also be described, if data permit. In addition, efforts will be made if data permit, as appropriate, to examine possible correlations of the ADA response with clinical data on the PK, safety and/or efficacy. *For sasanlimab immunogenicity data, the percentage of participants with positive ADA and neutralizing antibodies will be summarized. For participants with positive ADA or neutralizing antibodies, the magnitude (titre), time of onset, and duration of ADA or neutralizing antibodies response will also be described, if data permit.*

CCI [redacted]

6.7. Other Endpoints for Part 1 and Part 2

6.7.1. Physical Examination

Participants will have physical examinations according to the study protocol. The physical examinations may include weight, vital signs, assessment of ECOG performance status and height, assessments of the cardiovascular, respiratory and gastrointestinal systems, skin, lungs etc. Physical examination generally will not be summarized or listed except vital signs or ECG. Any change from baseline considered by the investigation to be clinically significant should be recorded as an adverse event in the CRF, thus will be analyzed in the adverse events data.

6.7.2. Concomitant Medications and Nondrug Treatments

Concomitant, and further therapies (drug and non-drug treatments) will be coded by the World Health Organization (WHO) medical dictionary. This data will not be summarized. Data listings of concomitant medications and further therapies may be provided.

6.7.3. Vital Sign Abnormalities

Vital signs including temperature, pulse rate, respiratory rate, and blood pressure, will be assessed.

- Analysis set: Safety analysis set.
- Analysis methodology:

  The vital signs will be generally considered as continuous endpoints. However the summaries of vital signs as continuous variables will not be provided as they may not be clinically meaningful. Instead, vital signs during the on-treatment period will be summzried by the categories of abnormality as specified in Appendix 1. Shift tables will not be provided unless deemed necessary.

- Missing data: Intermediate missing values (ie, values collected between baseline and the last study measurement) will not be imputed.

6.7.4. Heart rate corrected QT interval

- Analysis set: Safety analysis set.

- Analysis methodology:

  Changes from baseline for the ECG parameters QT interval, heart rate, QTc interval, PR interval, and QRS complex will be summarized by dose level and visit.

  The number (%) of participants with maximum postdose QTc values and maximum increases from baseline in the following categories will be tabulated by dose level, and with a "Total" across all dose levels for Part 1; and by tumor type and cycle for Part 2:

Safety QTc Assessment

Degree of Prolongation	Mild (msec)	Moderate (msec)	Severe (msec)
Absolute value	>450-480	>480-500	>500
Increase from baseline		30-60	>60

In addition, the number of participants with uncorrected QT values >500 msec will be summarized.

If more than 1 ECG is collected at a nominal time after dose administration (for example, triplicate ECGs), the mean of the replicate measurements will be used to represent a single observation at that time point. If any of the 3 individual ECG tracings has a QTc value >500 msec, but the mean of the triplicates is not >500 msec, the data from the participant's individual tracing will be described in a safety section of the CSR in order to place the >500msec value in appropriate clinical context. However, values from individual tracings within triplicate measurements that are >500 msec will not be included in the categorical analysis unless the average from the triplicate measurements is also >500 msec. Changes from baseline will be defined as the change between the postdose QTc value and the average of the predose triplicate values on Day 1.

The analysis of ECG results will be based on participants in the safety analysis set with baseline and on-treatment ECG data.

ECG measurements (an average of the triplicate measurements) will be used for the statistical analysis and all data presentations. Any data obtained from ECGs repeated for safety reasons after the nominal time-points will not be averaged along with the preceding triplicates. Interval measurements from repeated ECGs will be included in the outlier analysis (categorical analysis) as individual values obtained at unscheduled time points.

QT intervals will be corrected for HR (QTc) using standard correction factors (ie, Fridericia's (default correction), Bazett's, and possibly a studyspecific factor, as appropriate). Data will be summarized and listed for QT interval, HR, PR interval, QRS complex, QTcF (and other correction factors, eg, QTcB as appropriate), and by dose for Part 1, and by tumor type for Part 2. *Individual QT (all evaluated corrections) intervals will be listed* by dose, time for Part 1, and by tumor type, time for Part 2. *The most appropriate correction factor will be selected and used for the following analyses of central tendency and outliers and used for the study conclusions. Descriptive statistics (n, mean, median, standard deviation, minimum, and maximum) will be used to summarize the absolute corrected QT interval and changes from baseline in corrected QT after treatment* by dose, time for Part 1, and by tumor type, time for Part 2.

- Missing data: Intermediate missing values (ie, values collected between baseline and the last study measurement) will not be imputed.

6.8. Subset Analyses

There are no planned subset analyses.

6.9. Baseline and Other Analyses for Part 1 and Part 2

The analyses defined in this section will be applicable for both Part 1 and Part 2.

6.9.1. Baseline Summaries

Baseline characteristics will be summarized and/or listed in participant level data listings:

- Demographics: will be summarized by dose level (Part 1) and overall across all dose levels, or by tumor type (Part 2). This will be based on the Full analysis set. Demographic data will also be listed in a data listing.

- Primary diagnosis: will be summarized for all enrolled participants.

- ECOG performance status: will be summarized by dose level (Part 1) or by tumor type (Part 2) using the full analysis set.

- Number of Prior regimens that were used to treat the primary diagnosed disease will be summarized.

6.9.2. Study Conduct and Participant Disposition

An accounting of the study participants will be tabulated. The participant dose level cohort will be listed. The Full Analysis Set will be used.

Participant discontinuation from treatment and study will be tabulated and listed for each participant separately with their reason for discontinuation. The Safety Analysis Set will be used.

6.9.3. Study Treatment Exposure

The Safety Analysis Set will be used for the anlaysis of treatment exposure.

Treatment exposure will be assessed with the following approaches:

- Duration of Treatment (DOT): defined as the last active dose date minus the first active dose date + 1. DOT will be summarized, as a continuous variable, by dose level for Part 1 and overall across all dose levels; or by tumor type for Part 2. DOT will also be categorized into different intervals (≥ 1 cycle; ≥ 2 cycles; ≥ 3 cycles etc.), frequency and percentage of participants for each interval will be descriptively summarized by dose level for Part 1 and overall across all dose levels; or by tumor type for Part 2

- Treatment Compliance: defined as the proportion of cumulative actually taken dose over the cumulative planned dose for cycle 1 (for the purpose of defining the per-protocol population for the MTD evaluation) and over the entire treatment period (i.e. between the first active dose date and the last active dose date) for relative dose intensity (RDI).

- Dose interruption, defined as a situation when the actual dose was less than the planned dose (as collected in the case report form) will be summarized by dose level and overall for Part 1; by tumor type and cycle for Part 2. Dose interruption data may also be listed in a data listing in which reasons for dose interruption (e.g. AE), if available, will be included.

- Listing by participant level of dosing administration data: cycle number, start date and stop date of dosing period within each cycle (including records with 0 mg), total daily dose received for each dosing period, any missed doses with unknown dates (yes/no), number of missed doses with unknown dates, reason for any dosing changes, total planned dose, total actual dose received, percentage of planned dose, dose reduction (yes/no), and dose interruption (yes/no) if data permits.

- Duration of Follow-up (DOFU): defined as the last contact date minus the first active dose +1 for participants who were alive by the end of the study, or as the death date minus the first active dose + 1 for participants who died as recorded in the clinical database. DOFU will be summarized, as a continuous variable, by dose level for Part 1 and overall across all dose levels; or by tumor type for Part 2.

7. INTERIM ANALYSES

No formal interim analysis will be conducted for this study. As this is an open-label study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessment, facilitating dose-escalation decisions, facilitating PK/PD modeling, and/or supporting clinical development.

8. REFERENCES

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9. APPENDICES

9.1. Appendix 1: Categorical Classes for ECG and Vital Signs

Clinically Relevant Categories for QTcF

QTcF (msec)	max. ≤450	450< max. ≤480	480< max. ≤500	max. >500
QTcF (msec) increase from baseline	30≤ max. < 60	max. >60		

Clinically Relevant Categories for Pulse Rate and QRS

Pulse Rate (msec)	max. ≥300	
Pulse Rate (msec) increase from baseline	Baseline >200 and max. ≥25% increase	Baseline ≤200 and max. ≥50% increase
QRS (msec)	max. ≥200	
QRS (msec) increase from baseline	Baseline >100 and max. ≥25% increase	Baseline ≤100 and max. ≥50% increase

Clinically Relevant Categories for Vital Signs

Systolic BP (mm Hg)	min. <90	≥160 max.
Systolic BP (mm Hg) change from baseline	max. decrease ≥30	max. increase ≥30
Diastolic BP (mm Hg)	min. <50	≥100 max.
Diastolic BP (mm Hg) change from baseline	max. decrease ≥20	max. increase ≥20
Pulse Rate (BPM)	min. <40	≥120 max.

Measurements that fulfil these criteria are to be listed in the study report.

9.2. Appendix 2: Abbreviations

The following is a list of abbreviations that may be used in this document.

Abbreviation	Term
ADA	antidrug antibodies
AE	adverse event
AUC_{inf}	area under the concentration-time curve from time zero extrapolated to infinite time
AUC_{last}	area under the concentration-time curve from time zero to the last quantifiable time point prior to the next dose
BLRM	Bayesian logistic regression model
BOR	best overall response
CD47	cluster of differentiation 47
CI	confidence interval
CL	clearance
CL/F	clearance after non-intravenous administration
C_{max}	maximum observed concentration
COVID-19	coronavirus disease 2019
CR	complete response
CTCAE	Common Terminology Criteria for Adverse Events
DOR	duration of response
DLT	Dose Limisting Toxicity
EWOC	escalation with overdose control
IHC	Immunohistochemistry
MTD	maximum tolerated dose
ORR	overall response rate
OS	overall survival
CC1	[redacted]
PD-1	programmed cell death 1
PD-L1	programmed death-ligand 1
PFS	progression-free survival
PK	pharmacokinetic(s)
PR	partial response
QTc	corrected QT

Abbreviation	Term
RECIST	Response Evaluation Criteria in Solid Tumors
RP2D	recommended Phase 2 dose
SAE	serious adverse event
SAP	statistical analysis plan
TEAE	treatment-emergent adverse events
TTP	Time to Progression