Pfizer Inc.
Protocol #: TTI-621-03/C4961003

A Phase I/II Study of PF-07901800 (TTI-621) in Combination with Doxorubicin in Patients with Unresectable or Metastatic High-Grade Leiomyosarcoma

Statistical Analysis Plan

Version 2.0

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List of Abbreviations

Abbreviation	Definition
CCI [redacted]	
CCI [redacted]	
AE	Adverse Event
AESI	Adverse Event of Special Interest
ANC	Absolute Neutrophil Count
BMI	Body Mass Index
CDISC	Clinical Data Interchange Standards Consortium
CEC	Clinical Evaluation Committee
CI	Confidence Interval
CM	Concomitant Medications
CR	Complete Response
CRF	Case Report Form
CRO	Contract Research Organization
CSR	Clinical Study Report
CT	Computed Tomography
CTCAE	Common Terminology Criteria for Adverse Events
DCO	Data Cut-Off
DCR	Disease Control Rate
DES	DLT-Evaluable Set
DLT	Dose-Limiting Toxicity
DOR	Duration of Response
ECG	Electrocardiogram
ECHO	Echocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EORTC	European Organisation for Research and Treatment of Cancer
EOS	End of Study
EOT	End of Treatment
FAS	Full Analysis Set
FDA	United States Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practice

h	hour
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IgG1	immunoglobulin G1
IL	Interleukin
IP	Investigational Product
IR	Immune Response
IRB	Institutional Review Board
CCI [redacted]	
ITT	Intent-to-Treat
IU	International Units
IV	Intravenous
L	liter(s)
LVEF	Left Ventricular Ejection Fraction
m^2	meter(s) squared
mAb	monoclonal antibody
MedDRA	Medical Dictionary for Regulatory Activities
mg/mL	Milligrams per milliliter
min	minute(s)
MTD	Maximum Tolerated Dose
MUGA	Multi-gated Acquisition Scan
NA	Not Available
CCI [redacted]	
NCI	National Cancer Institute
NE	Not Evaluable
ORR	Objective Response Rate
OS	Overall Survival
PD	Progressive Disease; Pharmacodynamics
PET	Positron Emission Tomography
PFS	Progression-Free Survival
PI	Principal Investigator
PK	Pharmacokinetics
PP	Per Protocol
PR	Partial Response
PRO	Patient-Reported Outcomes

PT	Preferred Term
QA	Quality Assurance
QLQ-C30	Quality-of-Life Questionnaire Core 30
RECIST	Response Evaluation Criteria in Solid Tumors
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAS	Safety Analysis Set
SD	Stable Disease
SIRPα	Signal Regulatory Protein α
SOC	System Organ Class
SOP	Standard Operating Procedure
CCI	[redacted]
TEAE	Treatment Emergent Adverse Events
TLF	Tables, Listings, and Figures
TNFα	Tumor Necrosis Factor α
TTP	Time to Progression
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

1. Introduction

1.1 Background

Soft tissue sarcomas are a rare, heterogeneous group of mesenchymal tumors, commonly the result of complex chromosomal abnormalities that play a role in disease progression and metastasis.

Doxorubicin has been since the 1970s the standard of care for first-line treatment of patients with metastatic or advanced soft tissue sarcoma; however, doxorubicin activity is poor, with a response rate of 9 - 27% (Schoenfeld, 1982; Judson, 2001) and progression-free survival of 3-5 months (D'Ambrosio, 2020; Penel, 2012; Italiano, 2012), with cumulative cardiac toxicity that limits its use (Borden, 1987).

Ontorpacept, also known as TTI-621 or PF-07901800, is a recombinant soluble fusion protein designed to block the cell-surface protein CD47, which is found on the surface of many normal cell types and at high levels on many malignant tumor cells. CD47 binds to signal regulatory protein alpha (SIRPα) on the surface of macrophages and inhibits their phagocytic activity. This CD47-mediated inhibition of macrophage phagocytosis activity is an important mechanism through which cancer cells can escape immune-mediated clearance, and high levels of CD47 correlate with poor clinical prognosis across a number of cancer types. PF-07901800 (TTI-621) combines CCI [redacted] human SIRPα (the binding domain for CD47) with the Fc region of human IgG1, generating a decoy receptor for CD47 on the surface of tumor cells that both over-rides the CD47-mediated inhibition of phagocytosis through the SIRPα portion of the protein and provides a pro-phagocytic stimulation through the IgG1 moiety.

It is hypothesized that blockade of CD47-mediated immune evasion and concomitant activation of phagocytosis with PF-07901800 (TTI-621) will be clinically beneficial in patients with sarcoma subtypes in which CD47 is expressed and macrophage scores are increased. CCI [redacted]

Thus, the primary goals of this clinical trial are to evaluate the safety of PF-07901800 (TTI-621) administered in combination with standard-of-care doxorubicin in anthracycline-naïve patients with high-grade soft tissue sarcomas and to further evaluate clinical activity and safety in the leiomyosarcoma subpopulation.

1.2 Protocol and Amendment History

This Statistical Analysis Plan (SAP) is based on version 2.0 of Protocol TTI-621-03 (17JUN2022). This SAP will govern the analysis of data from this study. The plan for efficacy analyses may be modified prior to the clinical database lock. Any deviations from the analysis plan, will be documented as such in the clinical study report.

2. Study Objectives

2.1 Primary Objectives

- To evaluate the safety of escalating dose levels of PF-07901800 when administered in combination with 75 mg/m^2 doxorubicin in 21-day cycles and establish the maximum tolerated dose level of PF-07901800 when administered in combination with doxorubicin (Phase I Dose Escalation)

- To evaluate the safety of selected dose levels of PF-07901800 when administered in combination with 75 mg/m^2 doxorubicin in 21-day cycles and then as monotherapy in 28-day cycles until documentation of objective disease progression (Phase II Expansion)

- To investigate clinical activity assessed as overall response rate of PF-07901800 administered in combination with 75 mg/m^2 doxorubicin for up to six cycles (18 weeks) and then as monotherapy until documentation of objective disease progression (Phase II Expansion)

2.2 Secondary Objectives

- To further assess safety of the selected dose levels of PF-07901800 administered in combination with 75 mg/m^2 doxorubicin

- To describe other evidence of clinical benefit

2.3 CCI

CCI

[redacted]

3. Study Endpoints

3.1 Primary Endpoints

- Overall safety profile as assessed by the type, frequency, severity, timing and causal relationship of any adverse events, changes in vital signs, ECGs, serum chemistry or other laboratory assessment, treatment delays or discontinuations for patients enrolled into the dose escalation portion of the study

- Percentage of patients with objective response (CR + PR) as defined by RECIST v1.1 criteria

3.2 Secondary Endpoints

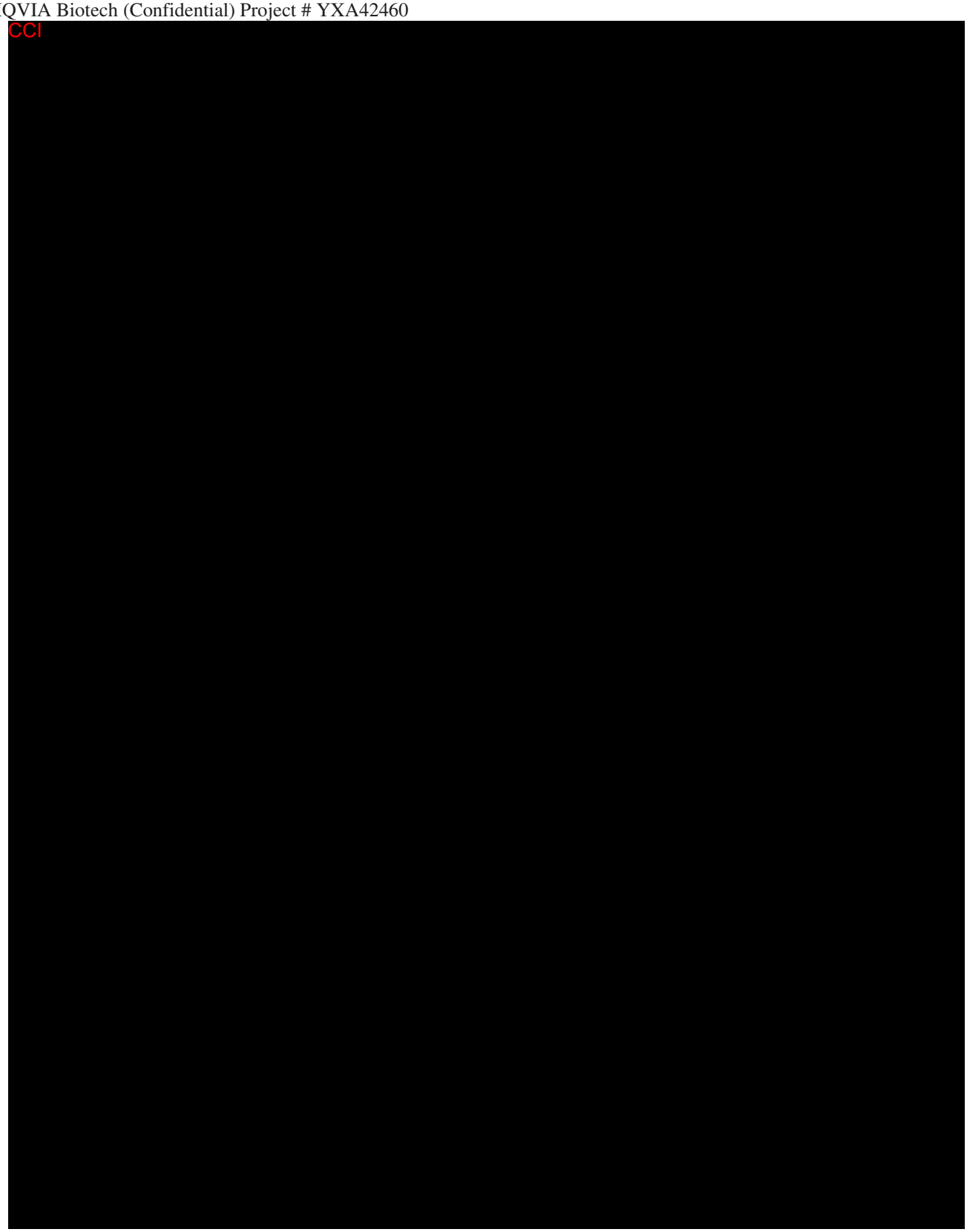
- Overall safety profile as assessed by the type, frequency, severity, timing and causal relationship of any adverse events, changes in vital signs, ECGs, serum chemistry or other laboratory assessment, treatment delays or discontinuations for patients enrolled into the selected dose level cohorts in the expansion portion of the study

- Progression-free survival (PFS), overall survival (OS), disease control rate (DCR: CR + PR + SD), duration of response (DOR), duration of disease control, time to progression and time to new metastases as defined by RECIST v1.1 criteria, time to worsening of ECOG performance status, time to worsening of patient-reported outcomes assessments

3.3 CCI

[redacted]

CCI

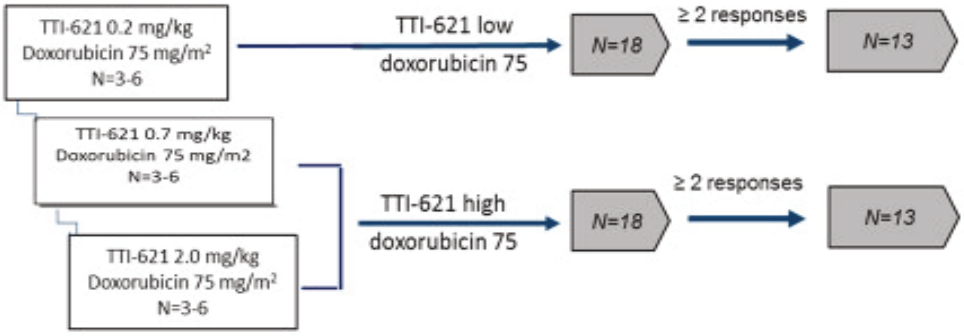


4. Study Design

4.1 Design Overview

Multi-center, open-label study designed to evaluate PF-07901800 administered in combination with doxorubicin. The first portion of the study will evaluate the safety of increasing dose levels of PF-07901800 in combination with doxorubicin at the standard dose of at 75 mg/m^2 in patients with high-grade soft tissue sarcoma. Two dose levels of PF-07901800 in combination with doxorubicin will be selected for further evaluation in an expansion phase in which patients with high-grade leiomyosarcoma.

The study will consist of a 28-day screening period, a treatment period in which patients will receive doxorubicin in combination with PF-07901800 in 21-day cycles for a maximum of six cycles, followed by continued treatment with PF-07901800 as monotherapy in 28-day cycles until documentation of objective disease progression or development of unacceptable toxicity, and a long-term follow-up period for assessment of overall survival.



4.2 Study Population

Eligible patients are those with high-grade soft tissue sarcoma who have not received more than one prior line of therapy (gemcitabine with docetaxel) and have not received an anthracycline in any setting (neoadjuvant, adjuvant or as treatment for advanced of metastatic disease). Up to approximately 80 patients are anticipated to participate in the study, with up to 18 in the dose escalation portion of the study and 31 in each of two expansion cohorts.

The protocol provides additional inclusion and exclusion criteria in its Section 6.

4.3 Sample Size Estimation

4.3.1 Dose Escalation cohorts

The number of patients will depend on the number of dose cohorts that will be enrolled before reaching the MTD. It is anticipated that three dose levels of PF-07901800 given in combination with a fixed dose of doxorubicin will be evaluated and that at least nine and up to approximately 18 patients will be enrolled to evaluate these three dose levels. On this basis of emerging safety data, additional dose levels may be added. The size and design of the dose escalation phase of the study is consistent with standard 3+3 design with the objective of determining the safety of escalating doses of PF-07901800 in combination with fixed dose doxorubicin and establishing PF-07901800 doses for further evaluation in the intended patient population.

4.3.2 Expansion cohorts

Expansion cohorts are initially planned to evaluate two PF-07901800 dose levels in combination with doxorubicin: a low dose of PF-07901800 (Cohort A) and a higher dose (Cohort B). A Simon two-stage design will be used for each dose cohort, assuming a baseline overall response rate of 10% with doxorubicin monotherapy in the Simon two-stage design and an alternative of 25%, a power of 90% and one-sided Type 1 error set at 0.20, each dose level cohort will require 18 patients enrolled and evaluable for response in Stage 1; with at least two clinical responses, an additional 13 patients will be enrolled in Stage 2. The combination will be considered worthy of further study if at least five clinical responses are observed in either 31-patient cohort.

To mitigate the risk of thrombocytopenia Grade 3 or Grade 4 observed at PF-07901800 highest dose 2mg/kg (Cohort B) on Day 8 during the combination therapy, PACL No 5 was issued to terminate enrollment into Cohort B after enrollment of the 18 patients (Stage 1) was completed. The remaining 13 patients, who were initially planned to be enrolled in Stage 2 Cohort B, were enrolled in an expansion Cohort C which was added to the study to evaluate a medium dose of PF-07901800 at 1 mg/kg. Simon's 2-stage design was not applicable for Cohort C.

4.4 Treatment Group Assignation

The dose escalation portion of the study carries a traditional 3+3 design to evaluate three dose levels of PF-07901800. Standard guidelines for enrollment for the 3+3 design will be followed, with requirement that three

patients complete the 21-day safety assessment period before the next dose cohort is open to enrollment and expansion to six patients in the case of a treatment-related dose-limiting toxicity.

However, recognizing that leiomyosarcoma is a rare disease and expecting that patients with leiomyosarcoma may be eager to participate in the study, careful modifications to the enrollment schema have been developed to avoid having to withhold enrollment for these patients.

During the dose escalation portion of the study, eligible patients will be enrolled to the cohort that is open at the time they present to the study. Based on known safety and clinical activity of the lowest planned dose of PF-07901800, 0.2 mg/kg, gleaned from other ongoing clinical trials, it is anticipated that this dose will serve as the PF-07901800 dose level for Cohort A. Thus, expansion Cohort A will open to enrollment once that dose level is judged to be safe in the dose escalation portion of the study; if a dose escalation cohort and expansion Cohort A are open to enrollment at the same time, priority for enrollment will be given to the dose escalation cohort and enrollment into expansion Cohort A will be limited to those patients who present to the study after enrollment to an escalation cohort is closed and meet all the eligibility criteria for the expansion portion of the study (including documentation of the leiomyosarcoma indication).

When both expansion cohorts are open to enrollment, assignment of eligible patients will be made on an alternating basis, with cohort assignment made by the CRO overseeing the study on behalf of the sponsor independent of investigator input and based strictly on chronology of verification of eligibility of patients as they complete screening assessments.

4.5 Assessment Schedule

The study participation for a patient might include the Screening Visit (Day -28 to -1); Cycle 1 (21-days cycle), Day 1 and Day 8; Cycle 2 to 6 (21-days cycles), Day 1 and Day 8 (± 1 day); Subsequent Cycles (28-days cycles), Day 1 and Day 15 (± 3 days); 7 (± 3 days) after last administration of study treatment; Safety Follow-up Period (30 + 5 days after last administration of study treatment or before initiation of subsequent anti-cancer therapy, whichever occurs soonest); and Long-Term Follow-Up, assessed every 12 ± 2 weeks.

The protocol provides additional details in Section 11.

5. Interventions

5.1 Study Procedures

Written informed consent must be granted by each patient prior to the initiation of any study procedure or assessment, including assessment of histology.

The study will consist of a 28-day screening period, a treatment period in which patients will receive doxorubicin in combination with PF-07901800 in 21-day cycles for a maximum of six cycles, followed by continued treatment with PF-07901800 as monotherapy in 28-day cycles until documentation of objective disease progression or development of unacceptable toxicity, and a long-term follow-up period for assessment of overall survival.

Serial blood samples will be obtained at baseline, during and after treatment for assessment of PF-07901800 pharmacokinetic and pharmacodynamic endpoints, as well as CCI [redacted]. End-of-Treatment (under protocol V1 only), Safety Follow-up and Long-Term Follow-Up Assessments will be performed.

Tissue biopsies will be collected during the screening period and after Cycle 2 for patients enrolled in the expansion cohorts; optional biopsies at the time of response and progression will be offered to patients.

The protocol v2.0 provides additional details on the activities and timing in Section 10, table 24 through 27.

6. General Analytical Considerations

6.1 Study Summaries and Tabulations

The definition of “treatment group” will be tabulated as follows:

- Dose escalation cohorts (Phase 1)
  - Dose 1 (0.2 mg/kg)
  - Dose 2 (0.7 mg/kg)
  - Dose 3 (2.0 mg/kg)
- Expansion cohorts (Phase 2)
  - Cohort A (0.2 mg/kg)
  - Cohort B (1.0 mg/kg)
  - Cohort C (2.0 mg/kg)
- Pooled cohorts by dose level
  - Lower dose (0.2 mg/kg)

- Higher dose (2.0 mg/kg)

- Overall
  - Phase 1 total
  - Phase 2 total
  - Phases 1 + 2 total (for non-efficacy summaries only)

Data will be summarized by treatment group as above, as applicable.

6.2 Data Sources

All reported study data will be recorded on the electronic case report forms (eCRF) using Medidata Rave. During the data collection process, automated quality assurance programs will be used to identify missing data, out-of-range data, and other data inconsistencies. Lab data (chemistry and hematology) will come from local labs through the EDC.

6.3 Definition of Baseline

Baseline is defined as the last measurement taken prior to the first infusion of study medication (Cycle 1 Day 1).

The average of the pre-infusion results will be considered as the baseline value for vital signs taken at different timepoints on the same pre-infusion day.

6.4 Definition of on-treatment period

Safety endpoints will be summarized based on the on-treatment period, unless otherwise specified.

On-treatment period is defined as the time from the first dose of study treatment through minimum (30 days + last dose of study treatment, start day of new anti-cancer therapy captured on the “Survival Status” CRF).

6.5 Missing Data

Due to the study design, data will be reported as collected and no imputation methods of missing values will be performed, except for partial dates. Below it is addressed how missing information will be handled for partial dates and incomplete disease assessments.

When no imaging/measurement is done at all at a particular time point, the patient is not evaluable (NE) at that time point. If only a subset of lesion measurements are made at an assessment, usually the case is also considered NE at that time point, unless a convincing argument can be made that the contribution of the individual missing lesion(s) would not

change the assigned time point response, which is most likely to occur in the case of PD (e.g., if only 2 of 3 baseline target lesions are assessed and result in a > 20% increase in the sum, then the patient would be assessed as a PD regardless of the missing lesion).

Partial dates are allowed on the eCRF for prior disease therapy start and stop dates, adverse event (AE) onset and end dates, concomitant medication start and stop dates, and concomitant procedure, procedure dates. An entry for the year is required in the eCRF system for each of these dates. Only the month and day may be entered as unknown. Dates from these forms will be reported in listings as collected. Every effort will be made to query missing dates.

For records with missing AE onset date, the following procedure will be employed for use in determining whether the AE is treatment emergent:

- AE onset dates with missing day and non-missing month will be assumed to occur on the first day of the non-missing month, except for AEs occurring in the month and year of first dosing, in which case the date will be imputed using the date of first dosing.
- AE onset dates with missing day and month will be assumed to occur on the first day of the non-missing year (*i.e.*, January 1), except for AEs occurring in the year of first dosing, in which case the date will be imputed using the date of the first dosing.
- AEs that are not ongoing and have an end date with missing day and non-missing month, they will be assumed to occur on the last day of the month, except when the end of study date or date of death is prior to the last day of the month. The date will be imputed as end of study date, or death date, whichever happens the earliest.
- AEs that are not ongoing and have missing month in the end date, the imputed end date should be set to the last day of the year 31DECYYYY, except when the end of study date or date of death is prior to the last day of the year. The date will be imputed as end of study date, or death date, whichever happens the earliest.

For records with a missing medication start and/or stop date, the following procedure will be employed for use in determining whether the medication is prior or concomitant:

- Medication start dates with a missing day and non-missing month will be assumed to occur on the first day of the non-missing month, except for medications occurring in the month of first dosing, in which case the date will be the date of first dosing.

- Medication start dates with missing day and month will be assumed to occur on the first day of the non-missing year (i.e., January 1), except for medications occurring in the year of first dosing, in which case the date will be the date of first dosing.
- Medications that are not ongoing and have a medication stop date with a missing day and non-missing month will be assumed to occur on the last day of the non-missing month.
- Medications that are not ongoing and have a medication stop date with missing day and month will be assumed to occur on the last day of the non-missing year (i.e., December 31).

For records with a missing procedure date, the following procedure will be employed for use in determining whether the procedure is prior or concomitant:

- Procedure dates with a missing day and non-missing month will be assumed to occur on the first day of the non-missing month, except for procedures occurring in the month of first dosing, in which case the date will be the date of first dosing.
- Procedure dates with missing day and month will be assumed to occur on the first day of the non-missing year (i.e., January 1), except for procedures occurring in the year of first dosing, in which case the date will be the date of first dosing.

For records with a missing disease progression date from prior therapy, the following procedure will be employed for use in analyzing time to event endpoints:

- If the disease progression date is completely missing OR only the year is available, set as missing.
- If both year and month of disease progression date from are available and only day is missing, the date of disease progression will be imputed by the last day of the month.

For records with a partial death date, the following procedure will be employed for use in deriving time to event variables.

- The death date will be imputed by the earliest possible date that is not contradicting with any other available data in the database.

6.6 Timing of Analyses

This is an open-label study, so analyses may be performed as the study progresses, such as efficacy and safety analysis for publication purposes. No formal interim analysis will be performed.

Details of analysis will follow each section described in this SAP and may include the following components:

- Disposition
- Protocol deviations
- Baseline characteristics: demographics, medical history, cancer history, concomitant medications and concomitant procedures
- Key components from efficacy analysis
- Key components from safety analysis

6.7 Analysis Populations

6.7.1 Full Analysis Set (FAS)

The FAS will include patients who were enrolled, allocated to treatment, and received at least one non-zero dose of study treatment.

This analysis population will be used for baseline summaries and the analysis of efficacy endpoints.

Patients will be classified according to the study treatment actually received. For patients who received a wrong study dose, they would be recoded in protocol deviation and dosing compliance; if the wrong dose occurred only once, the analysis will use the patients' initial planned dose as summary cohorts. If more than one wrong dose occurred, the analysis will use patients' actual dose as summary cohorts. If patients' doses were reduced, safety analysis will use the initial planned dose as summary cohorts. Patients receiving different dosing schedules will be presented in the listings only.

6.7.2 Safety Analysis Set (SAS)

The SAS is identical to the FAS, which will include patients who were enrolled, allocated to treatment, and received at least one non-zero dose of study treatment.

This analysis population will be used for the analysis of safety and exposure.

6.7.3 DLT-Evaluable Set (DES)

The DES is applicable to dose-escalation cohorts only. It will include patients who received the full dose of doxorubicin in Cycle 1 Day 1 and the planned doses of PF-07901800 on Day 1 and Day 8, and

have been followed for the entire 21-day DLT period (Cycle 1) or who have a DLT during Cycle 1.

6.8 Data Display Characteristics

Data displays produced for this study will include three types—summary tables, data listings, and figures. Unless stated otherwise, data listings will be produced for all recorded data. Additional data listings will be produced for outcome measures that involve extensive procedures to derive the analyzed outcomes. Summary tables and figures will be produced when specified in sections to follow. All analyses will be performed using SAS (Statistical Analysis Software).

Data listings will simply list the data recorded on the CRF or derived for each subject. As needed, they can be ordered by dose cohort, site, subject number, and time of assessment, and additional levels of ordering hierarchy may reflect subsets of assessments within subject. Subject-level identifiers appear on the first line of data, and identifiers for subgroups within subject appear only on the first line of each subgroup value.

Tables will display summary statistics calculated for each dose cohorts per study phase (escalation/expansion), unless described otherwise in the following sections. For most summary tables, the dose group will be presented in column and the summary statistics of interest will be presented in rows. About tables labelling, the text “Number (%) of Subjects” will be incorporated in the title, either the primary title or as a separate subtitle, and no further labeling (e.g., “n (%)”) will appear in the body of the table.

The summary statistics displayed will be a function of the type of data associated with the summarized assessment. Unless stated otherwise in relevant sections to follow, continuous data will be summarized with the number of non-missing values, mean, standard deviation, minimum, median, and maximum. Categorical data will be summarized with the number of non-missing values and the numbers of values equal to each of the possible values. Percentages of subjects with each of the possible values will be calculated from the number of subjects in the corresponding analysis population, unless stated otherwise, and those percentages will be presented with one decimal (XX.X%). Some continuous variables may also be grouped into categorical levels and evaluated in frequency tables.

Dates in the clinical database are classified into the categories of procedure dates, log dates, milestone dates, outcome dates, and special dates:

- Procedure Dates (TARGET DATE): Dates on which given protocol-specified procedure are performed. They include the dates of laboratory testing, physical examinations, disease assessments, etc. They should be present whenever data for a protocol-specified procedure is present and should only be missing when a procedure is marked as NOT DONE in the database. Procedure dates will not be imputed.
- Log Dates: Dates recorded in CRF data logs. Specifically, they are the start and end dates for adverse events and concomitant medications/procedures. They should not be missing unless an event or medication is marked as ongoing in the database. Otherwise, incomplete log dates will be imputed according to the rules in Section 6.3 above. However, in listings, log dates will be shown as recorded without imputation.
- Milestone Dates: Dates of protocol milestones such as study drug start date, study drug termination date, study closure date, etc. They should not be missing if the milestone occurs for a subject. They will not be imputed.
- Outcome Dates: Dates corresponding to study endpoints such as survival, progression, etc. In most cases, they are derived either from a milestone (e.g., the survival date is derived from the death date), or a procedure date (e.g., the progression date is derived from the date of the tumor scan that was used to determine progression). They may be subject to endpoint-specific censoring rules if the outcome did not occur but are not otherwise subject to imputation.
- Special Dates: Dates that cannot be classified in any of the above categories and they include the date of birth. They may be subject to variable-specific censoring and imputation rules.

Calculations using dates (e.g., subject's age or relative day after the first dose of study medication) will adhere to the following conventions:

- Trial Day 1 of Cycle 1 is defined as the day on which the dose of Doxorubicin and PF-07901800 is administered after screening. Study days after trial day 1 will be calculated as the difference between the date of interest and the first date of dosing of study medication plus 1 day. The generalized calculation algorithm for relative day: STUDY DAY = [(TARGET DATE – DSTART) + 1 where DSTART = the start day of study drug].
- For dates of interest before the first date of dosing of study medication, the study day will be calculated as: STUDY DAY = TARGET DATE – DSTART. Negative study days are reflective of

observations obtained prior to first study drug administration. Note: Partial date for the first study drug is not imputed in general. All effort should be tried to avoid incomplete study drug start date.

- Age (years) at informed consent will be calculated as: (Date of informed consent – date of birth + 1) / 365.25, and then truncated to an integer. In case of partial birth date: impute missing day as 15th of the month; impute missing month as July (month 7); set missing age in case of missing year.
- Duration will be calculated by the difference of start and stop date + 1. AE duration (days) = AE end date – AE start date +1
- Study drug exposure duration (weeks) is detailed in section 9.1. Exposure.
- Time since disease diagnosis (months) will be calculated as (Informed Consent Date – Diagnosis Date + 1) / 30.4167.
- The time to event will be calculated as date of event minus reference date + 1. The specific censoring rules on time to event endpoints will follow Section 8 (for efficacy and PRO) and Section 9 (for ECOG performance status).
- The following conversion factors will be used to convert days to months or years:
  - 1 month = 30.4375 days
  - 1 week = 7 days
  - 1 year = 365.25 days

6.8.1 Multiple Assessments for the Same Assessment Time Point

In the case of multiple observations (e.g., scheduled vs. unscheduled) at a specific visit, the first non-missing measurement will be used for analysis, unless multiple study assessments are expected (e.g., pre-dose vs. post-dose). When multiple study assessments are expected, the first non-missing measurement for the visit and assessment time point will be used for analysis.

7. Subject Accountability

7.1 Subject Characteristics

Subject characteristics will be summarized by treatment group based on the FAS, which consist of all subjects who received at least one non-zero dose of study treatment.

Demography. Data collected about the following subject characteristics at the screening visit will be summarized:

- Age (in years). Age will be calculated as the number of years elapsed between birth date and the date of the screening visit.

- Age strata:
  - < 40
  - 40 - < 65 years
  - 65 - <75 years
  - 75 - <85 years
  - ≥ 85 years
- Sex
- Race. If more than one race selected, summarize race as multiple.
- Ethnicity
- Height (cm)
- Weight (kg)
- Body Surface Area (BSA) (m^2) = ([height (cm) × weight (kg)] / 3600)$^{0.5}$

Medical History. Medical Histories will be summarized as the numbers and percentages of subjects with histories significant for each of the medical-history elements recorded on the MH CRF form. Coding will be performed using Medical Dictionary for Regulatory Activities (MedDRA), latest version. System Organ Class (SOC) and Preferred Term (PT) will be summarized by number and percentage of patients having at least one occurrence of a disease. All Medical history information, including diagnosis and start/end date will be listed for the FAS.

Disease Characteristics. Disease characteristics will be summarized as the numbers and percentages of subjects with significant medical-history elements recorded on the Disease History CRF form, and target tumor sites at baseline from disease assessment CRFs. Disease History information, including histology information, stages, progressive disease date of most recent progression, and target tumor site will be listed.

Prior anti-cancer therapies. The prior anti-cancer therapies are collected under the 'Prior Treatment for Disease Under Study' and 'Prior Surgeries for Current Diagnosis' eCRF pages.

The number and percentage of participants in each of the following anti-cancer therapy categories will be tabulated:

- Participants with at least one prior anti-cancer drug therapy
- Participants with at least one prior anti-cancer surgery

Prior anti-cancer drug therapy will be summarized as follows based on the number and percentage of participants with the following:

- One prior anti-cancer drug therapy
- Two prior anti-cancer drug therapy regimens

- Best response for each regimen: CR, PR, SD, PD, Unknown, Not applicable.

Prior treatment regimens can include Docetaxel, Gemcitabine, or/and other. If the starting date for Docetaxel and Gemcitabine and other anti-cancer drugs is the same or occurred within 14 days, these two treatments are considered as part of the same regimen.

Concomitant Medication. Concomitant medication is defined as any medication with a start date prior to the date of the first dose of study treatment and continuing after the first dose of study treatment or with a start date between the dates of the first and last dose of study treatment. Any medication with a start date after the date of the last dose of study treatment will not be considered a concomitant medication. Any medication with a stop date prior to the first dose of study treatment is defined as a prior treatment.

All concomitant medications and dietary supplements received within 28 days prior to the first dose of study treatment through 30 days after the last dose of study treatment will be recorded in the eCRFs, using generic drug names when possible. Concomitant medications will be coded using the WHO-DD current version and will be summarized by the 2nd ATC level and by preferred drug name of the coded medication. Patients are counted only once in each therapeutic class category. Concomitant medication will be summarized using the FAS and be tabulated for each dose level using frequencies and percentages. Percentages will be based on the number of patients in each dose level.

7.2 Disposition

The percentages below will be calculated based on the number of patients in the FAS.

End of Treatment (EOT): Subject's status (completed treatment [for doxorubicin only] or discontinued treatment), as well as the reasons for discontinuation of each study drug (Doxorubicin and PF-07901800 captured on separated forms) will be summarized.

End of Study (EOS): Subjects who discontinued or withdrew from the study, as well as the reasons, will be summarized.

All disposition data will be presented in a listing.

7.3 Protocol Deviations

A listing will identify subjects who were enrolled even though they did not meet one or more eligibility criteria (Data recorded in the EOS eCRF page), or any other situations that were not compliant with the protocol. This data will be classified as major or minor deviation by the clinical team, that will review periodically the protocol deviations and finalize the deviations prior to the database lock and efficacy analyses.

A summary table of major protocol deviations will be provided. A listing of protocol deviations related to COVID-19 will also be provided.

8. Efficacy Analyses

Efficacy analyses will use data from the FAS (for all efficacy endpoints) and will be descriptive in nature. Summary tables and figures will be presented by treatment group as described in Section 6.1, as applicable.

8.1 Efficacy Outcomes

For the primary endpoint, the clinical efficacy of PF-07901800 in combination with doxorubicin will be evaluated by tumor response as assessed by the investigators using RECIST v1.1, according to protocol appendix B (Eisenhauer, 2009).

The response categories of target lesions and its definitions are described below:

Complete Response (CR)	Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10 mm.
Partial Response (PR)	At least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD.
Stable Disease (SD)	Neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for PD, taking as reference the smallest sum LD since the treatment started.
Progressive Disease (PD)	At least a 20% increase in the sum of the LD of target lesions, 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 sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered PD.

Not Evaluable (NE)	No imaging/measurement is done at all at a particular time point. If only a subset of lesion measurements is made at an assessment, usually the case is also considered NE at that time point, unless a convincing argument can be made that the contribution of the individual missing lesion(s) would not change the assigned time point response, which is most likely to occur in the case of PD.

The response categories of non-target lesions and its definitions are described below:

Complete Response (CR)	Disappearance of all non-target lesions and normalization of tumor marker level.
Stable Disease/ Incomplete Response (Non-CR/Non-PD)	Persistence of one or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits.
Progressive Disease (PD)	Appearance of one or more new lesions and/or unequivocal progression of existing non-target lesions.

Best overall response (BOR) will be assessed based on reported overall lesion responses at different evaluation time points from the date of first study treatment until the first documentation of PD, according to the following rules. Only tumor assessments performed on or before the start date of any subsequent anti-cancer therapies (from the "Survival Status" eCRF) will be considered in the assessment of BOR. Clinical deterioration will not be considered as documentation of disease progression.

BOR based on confirmed responses (primary definition):

Best Overall Response (BOR) is defined as the best response recorded (CR, PR, SD, PD, NE per RECIST) from the start of the treatment until disease progression, taking as reference for PD the smallest measurements recorded since the treatment started. The patient's best response assignment will depend on the achievement of both measurement and confirmation criteria.

The tumor responses are required to be confirmed by radiographic tumor assessments. If an initial CR or PR is noted, confirmatory scans must be performed at least 4 weeks later. In the case of SD, follow-up measurements must have met the SD criteria at least once after study entry at a minimum interval of no less than 4 weeks.

- CR = at least two determinations of CR at least 4 weeks apart and before first documentation of PD.
- PR = at least two determinations of PR or better (PR followed by PR or PR followed by CR) at least 4 weeks apart and before first documentation of PD (and not qualifying for a CR).
- SD (applicable only to patients with measurable disease at baseline) = at least one SD assessment (or better) ≥ 4 weeks after the date of first study treatment and before first documentation of PD (and not qualifying for CR or PR).
- Non-CR/non-PD (applicable only to patients with non-measurable disease at baseline) = at least one non-CR/non-PD assessment (or better) ≥ 4 weeks after the date of first study treatment and before first documentation of PD (and not qualifying for CR or PR).
- PD = first documentation of PD ≤ 12 weeks after the date of first study treatment (and not qualifying for CR, PR, SD or non-CR/non-PD4
- NE: all other cases.

Objective Response (OR) is defined as confirmed BOR of CR or PR according to RECIST v1.1. OR rate (ORR) is the proportion of patients with OR in the analysis set.

BOR based on unconfirmed responses (secondary definition):

- Unconfirmed CR (uCR) = one objective status of CR before first documentation of PD.
- Unconfirmed PR (uPR) = one objective status of PR before first documentation of PD (and not qualifying for uCR).
- SD (applicable only to patients with measurable disease at baseline) = at least one SD assessment (or better) ≥ 4 weeks after the date of first study treatment and before first documentation of PD (and not qualifying for uCR or uPR).
- Non-uCR/non-PD (applicable only to patients with non-measurable disease at baseline) = at least one non-uCR/non-PD assessment (or better) ≥ 4 weeks after the date of first study treatment and before first

documentation of PD (and not qualifying for uCR or uPR).

- PD = first documentation of PD ≤ 12 weeks after the date of r first study treatment (and not qualifying for uCR, uPR, SD or non-CR/non-PD).
- NE: all other cases.

An objective status of uPR or SD cannot follow one of uCR. SD can follow uPR only in the rare case that tumor increases by less than 20% from the nadir, but enough that a previously documented 30% decrease from baseline no longer holds.

Unconfirmed Objective Response (uOR) is defined as unconfirmed BOR (uBOR) of uCR or uPR according to RECIST v1.1. Unconfirmed OR rate (uORR) is the proportion of patients with uOR in the analysis set.

8.2 Primary Efficacy Outcome Analysis

Baseline documentation of “target” and “non-target” lesions (lesion count and maximum lesion length) will be recorded in listings. The sum of diameters will be calculated for all target lesions at baseline and at each subsequent tumor assessment as a measure of tumor burden. The baseline lesion size value will be used as reference by which to characterize the lesion response.

Other lesions (or sites of disease) not selected as target lesions (measurable or non-measurable), including pathological lymph nodes, should be identified as non-target lesions and should also be recorded during screening. Measurements of these lesions are not recorded, but the presence or absence of each, including any progression, should be noted throughout the study. The appearance of new malignant lesions denotes disease progression.

Per RECIST criteria, target lesions considered ‘too small to measure’ will be assigned a default value of 5 mm and those identified as ‘not present’ will be assigned 0 mm for purposes of analysis.

All FAS patients will be included in the denominators for percentage, even if the patient had a NE response. The ORR and uORR will be summarized descriptively for RECIST assessment method, with a 95% confidence interval (CI) using Wilson’s score method.

Overall tumor response assessment data will be presented in listings.

8.3 Secondary Efficacy Analyses

Duration of response (DOR) will be calculated for patients who achieve a CR or PR, and is defined as the time from the date of first documented response (CR or PR) to the date of documented progression or death of any cause after achieving response. Patients who discontinue the study without disease progression or death or patients with an event after 2 or more missing/inadequate disease assessment or patients with an event after the start date of alternate anti-cancer therapy will be censored at their last response assessment date or last assessment prior to the start date of alternate anti-cancer therapy, whichever is earlier. The number of events and the number of censored patients will be summarized, and the median time to PD or death event (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method.

Disease Control Rate (DCR) is defined as the percentage of patients who have achieved CR, PR, or SD lasting at least 4 weeks. DCR at any time during the study will be summarized, as per the RECIST assessment method.

Progression Free Survival (PFS) is defined as the time from the first PF-07901800 infusion (Cycle 1 Day 1) to PD or death of any cause, whichever is first. Patients without disease progression or death or patients with an event after 2 or more missing/inadequate disease assessment or patients with an event after the start date of alternate anti-cancer therapy will be censored at their last response assessment date or last assessment prior to the start date of alternate anti-cancer therapy, whichever is earlier.

The number of events and the number of censored patients will be summarized. PFS rate at selected times, as well as the median time to event (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method. Kaplan-Meier plot of PFS will also be provided.

Overall Survival (OS) is defined as the time from the first PF-07901800 infusion (Cycle 1 Day 1) to death of any cause. Patients last known to be alive will be censored at their last known alive date. Kaplan-Meier methodology similar to the PFS analysis will be used to summarize the results.

Duration of Disease Control (DDC) is defined in patients who achieved a best overall response of SD or better, as the time from the first PF-07901800 infusion (Cycle 1 Day 1) to the date of documented progression or death of any cause, and will be calculated for patients who achieve a CR, PR or SD lasting at least 4 weeks. Patients without disease progression or death or patients with an event after 2 or more missing/inadequate disease assessment or patients with an event after the start date of alternate anti-cancer therapy will be censored at their last response assessment date or last assessment prior to the start date of alternate anti-cancer therapy, whichever is earlier. The number of events and the number of censored patients will be summarized, and the median time to PD or death event (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method.

Time to progression (TTP) is defined the same as PFS, except that death is not considered an event. Patients who die without PD or patients with PD after 2 or more missing/inadequate disease assessment or patients with PD after the start date of alternate anti-cancer therapy will be censored at their last disease assessment prior to the start date of alternate anti-cancer therapy, whichever is earlier. The number of events and the number of censored patients will be summarized. The median TTP (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method.

Time to new lesion is defined as the time from the first PF-07901800 infusion (Cycle 1 Day 1) to a new lesion appearance. Patients without new lesion or patients with new metastases after 2 or more missing/inadequate disease assessment or patients with new metastases after the start date of alternate anti-cancer therapy will be censored at their last response assessment date or last assessment prior to the start date of alternate anti-cancer therapy whichever is earlier. The number of events and the number of censored patients will be summarized. The median time to event (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method.

Waterfall plot for target lesion tumor response by individual will be presented, indicating best tumor response (maximum tumor reduction from baseline) at any time point for each subject. The plot will have one bar per subject sorted from worst to best response with color by dose administered. Tumor response will be calculated based on the type of cancer that the patient has, with the appropriate measure using RECIST.

Swimmer plots for tumor response will be generated with RECIST assessment. The plots will have one horizontal bar per subject firstly sorted by Best Response, and then sorted from earliest to latest time to start of response for CR and PR; within categories of SD, PD and NE, patients will be sorted by maximum observation duration. Symbols within the swimmer plot will indicate time to start and end of each new level of response (if the end of one response is the start of a new type of response by definition, only the start will be shown). The plots will also show the length of treatment duration a patient had.

8.3.1 Patient-Reported Outcomes

Patient-Reported Outcomes (PRO) analyses will use data from the FAS. PRO will be assessed at Cycle 1 Day 1, at all study treatment day 1 of each cycle, and at Safety Follow up visit, following the European Organisation for Research and Treatment of Cancer (EORTC) Quality-of-Life Questionnaire Core 30 (QLQ-C30) tool (Aaronson, 1993).

Fifteen separate scales/items within 3 broad categories (9 multi-item scales and 6 single-item symptom measures) will be assessed (Fayers, 2001):

- Global health status / QoL (revised) (Items 29 and 30)
- Functional scales
  - Physical functioning (revised) (Items 1 to 5)
  - Role functioning (revised) (Items 6 and 7)
  - Emotional functioning (Items 21 to 24)
  - Cognitive functioning (Items 20 and 25)
  - Social functioning (Item 26 and 27)
- Symptom scales
  - Fatigue (Items 10, 12 and 18)
  - Nausea and vomiting (Items 14 and 15)
  - Pain (Items 9 and 19)
  - Dyspnea (Item 8)
  - Insomnia (Item 11)
  - Appetite loss (Item 13)
  - Constipation (Item 16)
  - Diarrhea (Item 17)
  - Financial difficulties (Item 28)

The EORTC QLQ-C30 will be scored according to its user guides (https://www.eortc.org/app/uploads/sites/2/2018/02/SCmanual.pdf) (Fayers, 2001).

Time to first worsening of PRO assessments is defined as the time from the first PF-07901800 infusion (Cycle 1 Day 1) to the first observation of at least a 10-point decrease from baseline in the standardized score (linear transformation) of Global Health Status/QoL (Osoba, 1998). Patients without a worsening event will be censored on the last date of PRO assessments or the date of first study treatment, whichever is the latter. The number of events and the number of censored patients will be summarized only for expansion cohorts. The median time to event (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method.

9. Safety Analyses

Summary of AEs and other safety parameters will be based on the SAS by treatment group as described in Section 6.1, except for the DLT, which will be based on DLT-Evaluable Set (DES) by treatment group.

9.1 Exposure

In the combination portion of the study, Cycle 1 through Cycle 6, doxorubicin will be administered at 75 mg/m2 on Day 1 of each 21-day cycle. A maximum of six cycles of doxorubicin (18 weeks of treatment) is permitted.

In Cycle 1 through Cycle 6, PF-07901800 will be administered by intravenous infusion over 120 minutes on Day 1 and Day 8 of each 21-day cycle. Beginning with Cycle 7, PF-07901800 will be administered as monotherapy on Day 1 and Day 15 of 28-day cycles until documentation of disease progression or unacceptable toxicity. Monotherapy will be considered starting on the first cycle without doxorubicin.

PF-07901800 dose levels planned for evaluation in combination with doxorubicin in the dose escalation portion of the study are as follow:

Dose Level	PF-07901800 Dose
1	0.2 mg/kg
2	0.7 mg/kg
3	2.0 mg/kg

During the dose expansion portion of the study, two dose levels of PF-07901800 are planned to be evaluated in combination with fixed-dose

doxorubicin. The low dose of PF-07901800 is anticipated to be 0.2 mg/kg and the high dose is anticipated to be the maximum of other PF-07901800 dose levels evaluated in the dose escalation portion of the study, prospectively planned to be 2.0 mg/kg, but alternate dose levels may require evaluation and a different dose may be taken forward based after discussion with treating physicians and the Sponsor.

Exposure to PF-07901800 and doxorubicin will be summarized with descriptive statistics for the number of non-zero doses received, duration of dosing (weeks), total cumulative dose (mg/kg for PF-07901800, mg/m^2 for doxorubicin).

Total cumulative dose is the sum of the actual doses of PF-07901800 or doxorubicin received.

Duration of dosing is defined as the time (in weeks) from first dose of study drug in cycle 1 to the last dose of study drug in the last cycle a patient had.

The calculation algorithm for duration of exposure (in days) for each drug will be:

- Doxorubicin:
    - Last Doxorubicin dose date – first Doxorubicin dose date + 21

- PF-07901800:
    - If the last dose is on Day 1 of Cycles 1-6: (Last PF-07901800 dose date – first PF-07901800 dose date + 7)
    - If the last dose is on Day 8 of Cycles 1-6, and any time after Cycle 6: (Last PF-07901800 dose date – first PF-07901800 dose date + 14)

The number of participants with infusion interruption, dose reduction, infusion held (i.e. dose omitted) from study drug administration CRFs and number of participants with cycle delayed from date of visit CRF will also be summarized descriptively for each study drug by treatment group.

In addition, the planned dosing date and the actual dosing date will be listed. Listings will be provided with the information from all the study drug administration eCRFs. Reasons for missed doses, and reasons for dose reduction, infusion interruption, and cycle delay of PF-07901800 and Doxorubicin will be listed.

9.2 Dose-Limiting Toxicity

Dose-limiting toxicity (DLT) is defined as a hematologic and/or non-hematologic treatment-emergent adverse event that occurs during the 21-day Cycle 1 and that are judged by the Investigator as related to PF-07901800 or the combination of PF-07901800 and doxorubicin, in those patients receiving the full dose of doxorubicin and the planned doses of PF-07901800 on Cycle 1 Day 1 and Day 8 and have been followed for the entire 21-day DLT period. Hematologic and Non-Hematologic AEs to be considered as DLT are listed in the study protocol. These DLT will be summarized, including number and percentage of patients, in the DES.

Adverse events that are in the opinion of the investigator attributable exclusively to intravenous infusion of doxorubicin or any doxorubicin prophylaxis medication will not be considered a dose-limiting toxicity. AEs and Serious AEs (SAE) will be determined to be dose-limiting if they occur in this timeframe and meet the described criteria. AEs or SAEs experienced after the end of Cycle 1 will not be reported as DLTs but will be documented. Patients who experience a DLT (other than grade 5) will remain on the study to complete the safety evaluations and follow-up until resolution or stabilization of the DLT.

9.3 Adverse Events

Adverse events (AEs) will be documented on the AE eCRF and monitored continuously throughout the study. Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), latest version, associating lower-level terms with PT and SOC by the primary hierarchy.

Treatment Emergent Adverse Events (TEAEs) are those events with onset date occurring during the on-treatment period. The tables will display counts and percentages of patients who reported at least one TEAE in each SOC represented in the AE data. Within each SOC, the tables will display the counts and percentages of patients reporting at least one TEAE, as designated by the PT.

The severity of adverse events will be graded using the NCI Common Toxicity Criteria for Adverse Events (CTCAE version 5.0). The intensity is assigned a grade of 1 through 5 using the following CTCAE guidelines: Grade 1 – Mild; Grade 2 – Moderate; Grade 3 – Severe; Grade 4 – Life-threatening; Grade 5 – Death.

The causality of AE are reported as either related to study drug or not related to study drug for each study drug. Related AEs are those related to any study drug (i.e., at least one of the study drugs).

If a patient has multiple occurrences of an adverse event, the strongest level of relationship to study drug(s) and the worst toxicity grade a patient experiences for a given AE will be used in these tables. No imputation will be performed for missing toxicity grade or causality data.

AEs that have missing onset dates will be considered as TEAE unless the stop date is known to be prior to the first administration of the study medication. If the AE onset date is partial, the date will be correlated as far as possible with the date of first dose of study medication. AE will be assumed to be TEAE, unless there is clear evidence (through comparison of partial dates) to suggest that the adverse event started prior to the first dose of study medication. Detailed imputation rules can be found in section 6.3. If patients died during the study and experienced AEs at the time of death, the AEs that lead to death will use death date as the AE end date; otherwise, AEs that do not lead to death will be reported as ongoing.

Adverse Events of Special Interest (AESI) include the following:

- Thrombocytopenia: Haematopoietic thrombocytopenia – SMQ Broad
- Anemia: Haematopoietic erythropenia – SMQ broad
- Hemorrhage: Haemorrhage terms (excl. laboratory terms) – SMQ narrow
- Infusion related reactions (PT of Infusion-related reaction as recorded on the Adverse Event CRF)

The following TEAE summary tables will be produced by treatment group as described in Section 6.1:

a. An overall summary of safety will summarize the numbers (and percentages) of patients with the following:
   - TEAEs (separately for combination period and monotherapy period, and overall), where combination period is defined as from the date of first study treatment to the date of last doxorubicin + 21 days
   - Grade ≥ 3 TEAEs (separately for combination period and monotherapy period, and overall)
   - Treatment-related TEAEs (separately for combination period and monotherapy period, and overall)
   - Treatment-related grade ≥ 3 TEAEs (separately for combination period and monotherapy period, and overall)
   - Serious TEAEs
   - Treatment-related Serious TEAEs
   - TEAEs leading to dose reduction (of PF-07901800 and doxorubicin, separately)
   - TEAEs leading to drug interruption (of PF-07901800 and doxorubicin, separately)

- TEAEs leading to permanently discontinued study drug (PF-07901800, doxorubicin, and both)
- Treatment related TEAEs leading to permanent discontinuation of PF-07901800
- Treatment-related TEAEs leading to permanent discontinuation of doxorubicin
- Treatment-related TEAEs leading to permanent discontinuation of both drugs
- TEAEs leading to death
- Treatment-related TEAEs leading to death
- At least one TEAE of special interest: Thrombocytopenia SMQ (broad)
- At least one TEAE of special interest: Anemia SMQ (broad)
- At least one TEAE of special interest: Hemorrhage SMQ (narrow)
- At least one TEAE of special interest: Infusion related reactions

b. Separate summaries of TEAEs by SOC and PT, as follows:
   - TEAEs by maximum severity (separately for combination period and monotherapy period, and overall)
   - Treatment-related TEAEs (separately for combination period and monotherapy period, and overall)
   - DLT
   - Serious TEAEs
   - Treatment-related Serious TEAEs
   - TEAEs leading to dose reduction (of PF-07901800 and doxorubicin separately)
   - TEAEs leading to drug interruptions (of PF-07901800 and doxorubicin separately)
   - TEAEs leading to permanent discontinuation (of PF-07901800 and doxorubicin separately, and both)
   - Treatment-related TEAEs leading to permanent discontinuation of (of PF-07901800 and doxorubicin separately, and both)
   - TEAEs leading to death
   - Treatment-related TEAEs leading to death

c. Separate summaries of TEAEs by PT, as follows:
   - Most common TEAEs (Any grade and Grade ≥ 3)
     Most common Treatment-related TEAEs (Any grade and Grade ≥ 3)

d. Summary of TEAEs (any grade and Grade ≥ 3) of special interest will be summarized by SMQ and PT, as appliable:

   - Thrombocytopenia (broad)
   - Anemia (broad)

- Hemorrhage (narrow)

e. Summary of infusion related reactions (any grade and Grade ≥ 3) by SOC and PT

The following AE listings will be produced, sorted by dose cohort, patient, and timing, with relevant information:

- All AEs
- All DLTs
- AEs leading to death
- COVID-19 related AEs

9.4 Deaths

The frequency (number and percentage) of subjects in the SAS who died and who died within 30 days after last dose of study treatment as well as the reason for death, will be tabulated:

- All deaths
- Deaths within 30 days after last dose of study treatment
- Reason for death

In addition, date and cause of death will be provided in individual participant data listing together with selected dosing information (study treatment received, date of first / last administration, dose) and will include the following information:

- AEs with fatal outcome (Listing of PTs of AEs with outcome=Fatal, as well as AEs of Grade 5)
- Flag for death within 30 days of last dose of study treatment.
- Flag for death related to COVID-19

9.5 Clinical Laboratory Results

Clinical laboratory tests (serum chemistry and hematology) will be performed at Screening and each cycle Day 1 and 8, unless otherwise specified, as indicated in Section 10 of the protocol. Baseline laboratory measurements do not need to be repeated if screening measurements were performed within 3 days prior to Cycle 1 Day 1. All laboratory data will be converted to standardized conventional units for reporting purposes.

Hematology and chemistry evaluations which cannot be graded per CTCAE criteria will be summarized as counts and percentages of patients

with shifts from baseline to worst on-treatment assessment (normal/low/high).

For hematology and chemistry evaluations which can be graded per CTCAE v5.0, the following summary table will be created:

- Shift summary of baseline CTCAE grade versus the worst on-treatment CTCAE grade (The highest CTCAE grade during the on-treatment period is considered as the worst grade [Grade 0, 1, 2, 3, or 4] for the summary)
- Shift summary from ≤ Grade 2 at baseline to ≥ Grade 3 postbaseline

An evaluation of Drug-Induced Serious Hepatotoxicity (eDISH) plot will also be created, with different symbols for different treatment groups, by graphically displaying:

- peak serum ALT(/ULN) vs peak total bilirubin (/ULN), including reference lines at ALT=3×ULN and total bilirubin =2×ULN.
- peak serum AST(/ULN) vs peak total bilirubin (/ULN), including reference lines at AST=3×ULN and total bilirubin =2×ULN .

9.6 Vital Signs

Vital signs (weight, systolic blood pressure, diastolic blood pressure) will be summarized with continuous descriptive statistics at Screening, on Cycle 1 Day 1 (assessed in 30-minute intervals), on all study treatment day 1 of each cycle, at EOT/Early Termination, and at Safety Follow up visit.

Vital Signs will be listed by patient and summarized by treatment and visit in the SAS.

9.7 ECOG

ECOG Performance Status will be assessed as described in the protocol Appendix A, at Screening, on Cycle 1 Day 1, on all study treatment day 1 of each cycle, at EOT/Early Termination, and at Safety Follow up visit.

Time to first worsening of ECOG performance status is defined as the time from the first PF-07901800 infusion (Cycle 1 Day 1) to the first date when a worsening from baseline (*i.e.*, increase) in the ECOG assessment level is recorded in two consecutive assessments. Patients without a worsening event will be censored on the last date of ECOG assessments or the date of first study treatment, whichever is the later.

The number of events and the number of censored patients will be summarized, and the median time to worsening event (reported in days), its 95% confidence interval, and the 25th and 75th percentiles on the time to event will be summarized using Brookmeyer-Crowley method.

9.8 Electrocardiograms

Supine position 12-lead ECGs will be performed at screening and reviewed locally at each visit.

Corrected QT, PR and QRS data will be collected on the ECG eCRF page. Data will be summarized using QTc.

The frequency (number and percentage) of participants with notable ECG values according to the following categories will be summarized:

- QTc increase from baseline >30 ms, >60 ms
- QTc > 450 ms, > 480 ms, > 500 ms
- PR ≥ 220 ms and increase from baseline ≥ 20 ms
- QRS ≥ 120 ms

Participants with notable ECG interval values and qualitative ECG abnormalities will be listed for each participant and time point and the corresponding notable values and abnormality findings will be included in the listings.

9.9 Transthoracic echocardiogram or Multigated Acquisition Scan

Patients must undergo a Transthoracic Echocardiogram (ECHO) or Multigated Acquisition (MUGA) Scan during the screening period, as well as in Cycle 5 day 1, Cycle 8 day 1 and in the Safety Follow-Up Visit, unless performed within previous 4 weeks. Left Ventricular Ejection Fraction (LEVF) and an overall interpretation (normal/abnormal) will be summarized by visit.

10. References

Aaronson NK, Ahmedzai S, Bergman B et al. The European Organisation for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. J Natl Cancer Inst. 1993;85:365-376.

Borden EC, Amato DA, Rosenbaum C et al. Randomized comparison of three adriamycin regimens for metastatic soft tissue sarcomas. J Clin Oncol 1987;5:840-50.

D'Ambrosio L, Touati N, Blay JY et al. Doxorubicin plus dacarbazine, doxorubicin plus ifosfamide, or doxorubicin alone as a first-line treatment for advanced leiomyosarcoma: A propensity score matching analysis from the European Organization for Research and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. Cancer 2020;126:2637-47.

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

Fayers PM, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A, on behalf of the EORTC Quality of Life Group. The EORTC QLQ-C30 Scoring Manual (3rd Edition). Published by: European Organisation for Research and Treatment of Cancer, Brussels 2001.

Italiano A, Toulmonde M, Cioffi A et al. Advanced well-differentiated /dedifferentiated liposarcomas: role of chemotherapy and survival. Ann Oncol 2012;23:1601-7.

Judson I, Radford JA, Harris M et al. Randomised phase II trial of pegylated liposomal doxorubicin (DOXIL/CAELYX) versus doxorubicin in the treatment of advanced or metastatic soft tissue sarcoma: a study by the EORTC Soft Tissue and Bone Sarcoma Group. Eur J Cancer 2001;37:870-7.

Osoba D, Rodrigues G, Myles J, Zee B, Pater J. Interpreting the significance of changes in health-related quality-of-life scores. J Clin Oncol. 1998 Jan;16(1):139-44.

Penel N, Italiano A, Ray-Coquard I et al. Metastatic angiosarcomas: doxorubicin-based regimens, weekly paclitaxel and metastasectomy significantly improve the outcome. Ann Oncol 2012;23:517-23.

Schoenfeld DA, Rosenbaum C, Horton J et al. A comparison of adriamycin versus vincristine and adriamycin, and cyclophosphamide versus vincristine,

actinomycin-D, and cyclophosphamide for advanced sarcoma. Cancer 1982;50:2757-62.

Somarouthu B, Lee SI, Urban T et al. Immune-related tumour response assessment criteria: a comprehensive review. Br J Radiol 2018;91:20170457.

11. CCI [redacted]

CCI [redacted]

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