Investigational Product	TTI-622 (SIRPα-IgG4 Fc)/PF-07901801
Protocol Number	TTI-622-02/C4971002
IND Number	157225
Phase of Clinical Development	I/II
Protocol Title	A Phase I/II Study of TTI-622 in Combination with Pegylated Liposomal Doxorubicin in Patients with Platinum-Resistant Ovarian Cancer
Version and Date	Version 2.0, 07 December 2022

1 PROTOCOL APPROVAL

Protocol Number	C4971002 (TTI-622-02)
Version and Date	Version 2.0, 07 December 2022
Protocol Title	A Phase I/II Study of TTI-622 in Combination with Pegylated Liposomal Doxorubicin in Patients with Platinum-Resistant Ovarian Cancer

2 SYNOPSIS

Protocol Number	C4971002 (TTI-622-02)
Version and Date	2.0, 07 December 2022
Phase of Clinical Development	Phase I/II
Protocol Title	A Phase I/II Study of TTI-622 in Combination with Pegylated Liposomal Doxorubicin in Patients with Platinum-Resistant Ovarian Cancer
Investigational Product	TTI-622 (SIRPα-IgG4 Fc)/PF-07901801
IND Number	157225
Study Population	Participants aged 18 years or older with platinum-resistant recurrent ovarian cancer who have not received more than four prior lines of treatment for platinum-resistant disease
General Investigative Plan	This study will investigate a new therapeutic regimen for participants with platinum-resistant recurrent epithelial ovarian cancer (EOC), defined as disease progression ≤6 months after the most recent platinum-based treatment regimen or patients who were no longer able to receive or declined treatment with platinum-based chemotherapy, and who have not received more than four regimens for platinum-resistant disease. The safety and MTD, if reached, and RP2D of PF-07901801 (TTI-622) administered by intravenous infusion on Day 1 and Day 15 of 28-day cycles in combination with fixed-dose pegylated liposomal doxorubicin (PLD) (40 mg/m^2 on Day 1 of 28-day cycles) will be established in the Phase 1 dose escalation portion of the study and the clinical activity of the MTD and RP2D will then be evaluated in an expansion cohort in the same participant population.
Investigative Sites	Up to 10 centers in the US
Planned Number of Subjects	Up to approximately 50 participants, including up to 18 DLT-evaluable in the Phase 1 dose escalation portion of the study and up to 30 treated in the Phase 2 expansion portion.
Background and Rationale	Ovarian cancer is the second most common gynecologic malignancy in developed countries and the third most common gynecologic malignancy in developing countries. The majority (95%) of ovarian malignancies are epithelial in nature.[1,2,3] High-grade serous carcinoma, the most common histologic subtype, generally includes fallopian tube and peritoneal serous carcinoma, based upon similarities in histology and clinical behavior. Epithelial cancers of ovarian, fallopian tube, and peritoneal origin exhibit similar clinical characteristics, behavior, and in many cases, share basic biology. As such, these are often considered collectively and defined as epithelial ovarian cancer (EOC) in clinical trials and clinical practice.

Despite initial therapy (usually consisting of surgical cytoreduction and platinum-taxane combination therapy), the majority of patients with advanced-stage ovarian cancer will relapse and require additional treatment. Patients with platinum-sensitive recurrent EOC, defined as recurrence at least 6 months after completion of prior-platinum-based treatment, are more likely to respond to retreatment with a chemotherapy regimen that contains a platinum. In addition, several trials suggest that patients with platinum-sensitive disease achieve better response rates and PFS using maintenance treatment. This may consist of bevacizumab or the PARP inhibitors olaparib, niraparib and rucaparib (all of which have been approved by FDA, although only bevacizumab has shown an overall survival benefit).

Patients with platinum-resistant recurrent EOC, defined as disease progression ≤ 6 months after the most recent platinum-based treatment regimen (versus platinum-refractory disease, defined as progression while on therapy or within three months of completing their primary first-line platinum-based treatment), present with disease that is generally not curable and treatments should aim to maximize quality of life while attempting to control disease. Thus, this setting is an urgent unmet medical need and current treatment options typically consist of single-agent chemotherapy, including weekly paclitaxel or PLD. In the AURELIA study, patients who received chemotherapy, including PLD at 40 mg/m^2, experienced a median PFS of less than 4 months and approximately 8% ORR.[4,5] Some patients are candidates for combination therapy with bevacizumab, which consistently results in better outcomes compared to chemotherapy alone, but this regimen is limited to those who did not receive bevacizumab in the platinum-sensitive setting and who have not had recent (prior 6 months) bowel obstruction and do not have malignant bowel involvement. The addition of bevacizumab to PLD chemotherapy in the AURELIA study raised the ORR to only 14% and the mPFS to 5 months.[4,5] highlighting the need for more effective treatments – treatments that offer disease control without increased toxicity – for this patient population.

PF-07901801 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. CCI [redacted]

	CCI [redacted] Many solid tumors, including ovary, brain, breast, colon, gastric, kidney, soft tissue sarcomas, liver, lung, melanoma, pancreatic, and prostate tumors have also been found to express high levels of CD47.[6-10] In many of these cases, high expression of CCI [redacted] CD47 protein is highly expressed in ovarian cancer and is correlated with poor clinical characteristics and prognosis.[11,12] Decreasing CD47 levels in ovarian cancer cell lines resulted in promotion of macrophage phagocytosis and tumor growth *in vivo*.[12] CCI [redacted] [3] Trillium's CD47-targeted molecules significantly inhibit the growth of ovarian cancer in xenograft models. It is hypothesized that blockade of CD47-mediated immune evasion and concomitant activation of phagocytosis with PF-07901801 will be clinically beneficial in participants with ovarian cancer in which CD47 is generally highly expressed. The favorable safety profile of PF-07901801 observed in an ongoing clinical trial (NCT03530683) suggests that combining PF-07901801 with other therapies might offer an effective treatment option for participants without the addition of prohibitive toxicity. Thus, the primary goal of this clinical trial is to evaluate the safety and activity of PF-07901801 administered in combination with the standard of care PLD regimen in participants with platinum-resistant EOC.
Study Design	This is a multi-center, open-label study designed to evaluate PF-07901801 administered in combination with PLD in participants with platinum-resistant recurrent EOC, including ovarian, peritoneal and fallopian tube malignancy. The study will consist of a 28-day screening period, a treatment period in which

	participants will receive PF-07901801 in combination with PLD in 28-day cycles until documentation of objective disease progression or development of unacceptable toxicity, and a long-term follow-up period to assess overall survival. Key inclusion criteria are ECOG performance status 0-1, platinum-resistant recurrent EOC, defined as disease progression ≤6 months after the most recent platinum-based-treatment regimen(or no longer able to receive platinum-based chemotherapy), no more than four prior regimens for platinum-resistant disease, measurable disease by RECIST v1.1, absence of bowel obstruction history, and adequate cardiac and end organ function. Participants with exposure to PLD, while platinum-resistant or in the treatment regimen immediately prior to enrollment in this study, will not be eligible for treatment under this protocol; however, earlier exposure to PLD, including while platinum-sensitive, or for an indication other than recurrent platinum-resistant EOC, eg, breast cancer, will be allowed for participants in the Phase 1 dose escalation portion of the study. In the Phase 2, dose expansion portion of the study, depending on clinical benefit during Phase 1, earlier exposure to PLD, including while platinum-sensitive, may be allowed if agreed upon by the investigators and Pfizer. Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin. In the Phase 1 dose escalation portion of the study, the primary objective is assessment DLTs, safety and tolerability of escalating dose levels of PF-07901801 in combination with PLD at the standard dose of 40 mg/m^2. Up to approximately 18 participants are planned to be enrolled in this portion of the study to evaluate three dose levels of PF-07901801 12 mg/kg (Dose Level 1), 24 mg/kg (Dose Level 2) and 48 mg/kg (Dose Level 3). In Cycle 1 for dose levels 1 and 2, PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 in combination with PLD on Day 1 of 28-day cycle. Beginning with Cycle 2 at dose levels 1 and 2, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow PF-07901801 levels to more quickly reach steady state. For dose level 3, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. Loading doses (Day 8 and Day 22) may be considered for Cycle 1 at the 48 mg/kg dose level if found to be safe and offer clinical

	benefit for participants. If Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg. One dose level combination will be selected for further evaluation in the Phase 2 expansion portion of the study. The primary objective of the Phase 2 expansion portion of the study is investigation of clinical activity of the PLD and PF-07901801 combination; clinical activity will be assessed using the overall response by RECIST v1.1 as the primary efficacy endpoint. Secondary objectives include further evaluation of the safety of the combination and assessment of other indicators of disease control, including progression-free survival, overall survival, duration of response, and disease control (CR, PR, or SD ≥12 weeks) as defined by RECIST v1.1 criteria. Exploratory objectives include, evaluation of CA-125 levels, characterization of PF-07901801 and PLD pharmacokinetics when co-administered, evaluation of development of antibodies directed against PF-07901801; exploration of possible relationships between PF-07901801 exposure and clinical outcome, safety and pharmacodynamics observations, and to understand the relationship between the therapeutic intervention(s) being studied and the biology of the participant's disease. Exploratory endpoints include but are not limited to PK and immunogenicity of PF-07901801, PK of PLD, CA-125 levels, measurements of biomarkers/pharmacodynamics, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study, as well as the single and multiple dose pharmacokinetics of PF-07901801. PLD will be administered at 40 mg/m^2 on Day 1 of each 28-day cycle. Medications to treat infusion-related reactions and CPR equipment must be available for immediate use prior to initiation of PLD infusion. The dose-limiting toxicity (DLT) evaluation period will consist of the 28-day Cycle 1 or until participants experience a DLT in Cycle 1. Participants will be considered DLT evaluable if they received PLD on Day 1 and at least two infusions of PF-07901801 (TTI-622) in the 28-day Cycle 1. A participant who withdraws from the study during Cycle 1 in the absence DLT evaluable (ie, not receiving PLD and at least two doses of PF-07901801) will be replaced. If a dose-limiting toxicity as defined in Section 5.4 is

	encountered in one participant in the initial three participants in a dose cohort, three additional participants will be enrolled in accordance with the standard 3+3 study design. The maximum tolerated dose (MTD) for this study will be defined as the highest PF-07901801 dose level at which <33% of participants within a dose cohort experience dose-limiting toxicity when administered in combination with PLD at 40 mg/m^2. While three pre-defined PF-07901801 dose levels are anticipated, intermediate dose levels may be studied to more closely characterize the safety profile of PF-07901801 in combination with PLD. After three to six participants in a dose cohort, complete the 28-day dose-limiting toxicity assessment period, the incidence of dose-limiting toxicity, treatment-related safety observations and other available data, such as pharmacokinetic data, will be reviewed by the medical monitor, sponsor and investigators. If no participant in a three-participant cohort or no more than one participant in a six-participant dose cohort experiences treatment-related dose-limiting toxicity, the dose level will be deemed safe and dose escalation may proceed unless there are other unsuspected but concerning safety observations that suggest either an expansion of the current dose level or implementation of an intermediate dose level. Objective disease assessments will be performed every 8 (±1) weeks through week 48, or until participant has been on study for one year, and every 12 (±2) weeks thereafter. Participants who withdraw from the study without objective evidence of disease progression will be followed until documentation of disease progression or initiation of another treatment. All participants will be followed in the Long-Term Follow-Up period for survival.
Assessment of Dose-Limiting Toxicity	Dose escalation and cohort expansion decisions will be based on the incidence of dose-limiting toxicity assessed in the 28-day Cycle 1. A participant will be evaluable for dose-limiting toxicity if the participant experiences a DLT during Cycle 1 or did not experience a DLT and received PLD on Day 1 andat least two infusions of PF-07901801 in the 28-day Cycle 1 and completed 28-day cycle safety evaluation period. A participant who withdraws from the study during Cycle 1 in the absence of DLT evaluable (ie, not receiving PLD and at least two doses of PF-07901801) will be replaced. Dose-limiting toxicity is defined as any of the following treatment-emergent adverse events that occurs during Cycle 1 and are judged by the Investigator as related to PF-07901801 or the combination of PF-07901801 and PLD. Adverse events that are in

	the opinion of the Investigator attributable exclusively to intravenous infusion of PLD or any PLD prophylaxis medication will not be considered a dose-limiting toxicity. CCI [redacted]

	CCI [redacted]
Duration of Treatment and Subject Participation	Participants may continue treatment until progression or development of unacceptable toxicity. Participants who receive at least four cycles of PLD in combination with PF-07901801 and experience adverse events associated with PLD that require discontinuation of PLD treatment may continue treatment with PF-07901801 monotherapy. With a 28-day screening period and an estimated 12 months of treatment, it is anticipated that participants may participate in the active portion of the study for up to approximately one year.
Inclusion Criteria	**General** 1. Written informed consent obtained prior to performing any study-specific procedure, including screening procedures 2. Females ≥18 years of age 3. ECOG Performance Status 0 or 1 **Disease Characteristics** 4. Histologically-confirmed epithelial ovarian cancer (EOC), fallopian tube carcinoma (FTC) or primary peritoneal carcinomas (PPC). Eligible histological subtypes are: • Adenocarcinoma NOS • Clear cell adenocarcinoma • Endometrioid adenocarcinoma • Malignant Brenner's tumor • Mixed epithelial carcinoma • Mucinous adenocarcinoma • Serous adenocarcinoma • Transitional cell carcinoma • Undifferentiated carcinoma 5. Platinum-resistant recurrent disease, defined as disease progression ≤6 months after the most recent of platinum-based treatment regimen (date calculated from the last administered dose of platinum) or the participant is no longer able to receive or declined treatment with platinum-based chemotherapy o Includes standard of care therapies, including platinum-based therapies, PARP inhibitors (poly ADP ribose polymerase) or bevacizumab in the platinum-

	sensitive setting or intolerability to such therapies or participant refusal 6. Measurable disease per RECIST v1.1; target lesions must not be chosen from a previously-irradiated field unless there has been radiographically and/or pathologically documented tumor progression in that lesion prior to enrollment **Organ Function** Adequate organ and hematologic function as defined below: 7. Serum AST and ALT ≤ 3 x upper limit of normal (ULN); ≤5 x ULN in the presence of liver metastasis 8. Serum bilirubin (total) ≤ 1.5 x ULN (≤ 2 x ULN if hyperbilirubinemia is due to Gilbert's syndrome) 9. Serum creatinine ≤1.5 x ULN OR creatinine clearance/estimated glomerular filtration rate (eGFR) ≥40 mL/min/1.73 m^2 if serum creatinine is >1.5 x ULN 10. Hemoglobin ≥9 g/dL; packed red blood cell transfusions are not allowed in the two weeks preceding screening evaluation 11. ANC ≥1.5 × 10^9/L 12. Platelet count ≥ 100 × 10^9/L 13. Left ventricular ejection fraction (LVEF) determined by echocardiogram or multigated acquisition scan >50% at screening
	Previous Therapy 14. Unlimited lines of therapies in the platinum-sensitive setting are allowed. Once a participant becomes platinum-resistant no more than 4 prior treatment regimens for platinum-resistant disease are allowed. • If bevacizumab was not used as a treatment option during the platinum-sensitive setting, then bevacizumab in combination with paclitaxel must be considered as the first-line platinum-resistant treatment option except in the case of intolerability to such therapies or participant refusal. 15. Participants with exposure to PLD while platinum-resistant or in the treatment regimen immediately prior to enrollment in this study, will not be eligible for treatment under this protocol; however, earlier exposure to PLD, including while platinum-sensitive, or for an indication other than recurrent platinum-resistant EOC, eg breast

	cancer, will be allowed for participants in the Phase 1 dose escalation portion of the study. In the Phase 2, dose expansion portion of the study, depending on clinical benefit during Phase 1, earlier exposure to PLD, including while platinum-sensitive, may be allowed if agreed upon by the investigators and Pfizer. Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin 16. All adverse events from prior treatment must be NCI CTCAE v5 Grade ≤1, except alopecia and stable neuropathy, which must have resolved to Grade ≤ 2 or baseline **Contraception** 17. Female participants of childbearing potential (CBP) who participate in the study should be counseled on the need to practice adequate birth control and on the importance of avoiding pregnancy during study participation. Please refer to Section 6.6 and Appendix C for detailed reproductive criteria. 18. Female participants of childbearing potential must have a serum pregnancy test at screening. Following screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL. A negative pregnancy test result at screening and at baseline is required before the first study drug administration.
Exclusion Criteria	1. Platinum-refractory disease, defined as progression on or within 3 months of completing primary first-line platinum-based treatment 2. Malignant mixed Mullerian tumors 3. Ovarian tumors with low malignant potential (i.e., borderline tumors), low grade serous ovarian cancer **Cardiovascular System** 4. History of acute coronary syndromes, including myocardial infarction, coronary artery bypass graft, unstable angina, coronary angioplasty or stenting within 24 weeks prior to first administration of study drug

	5. History of or current Class II, III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system or symptomatic or poorly controlled cardiac arrhythmia 6. Uncontrolled or poorly-controlled hypertension (defined as systolic blood pressure >160 mm Hg and/or diastolic >100 mg Hg) for more than four weeks despite optimal medical management 7. Peripheral vascular disease > Grade 3 (i.e., symptomatic and interfering with activities of daily living requiring repair or revision) **General and Infectious Disease** 8. Investigator site staff directly involved in the conduct of the study and their family members, site staff otherwise supervised by the investigator, and sponsor and sponsor delegate employees directly involved in the conduct of the study and their family members 9. Any comorbidity or concomitant medication or other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation that in the opinion of the investigator and/or sponsor medical monitor renders the participant unsuitable for participation in the trial or unlikely to fully comply with study procedures, restrictions and/or requirements that are considered relevant for evaluation of the efficacy or safety of the trial drug 10. Uncontrolled intercurrent illness, including active or chronic uncontrolled bacterial, fungal, or viral infection, including (but not limited to) HBV, HCV, and known HIV or AIDS related illness requiring systemic therapy or oral or systemic antibiotics within 14 days prior to study start. Participants with HIV with an undetectable viral load and a CD4 count ≥400 μL are eligible 11. History of non-viral hepatitis or cirrhosis, alcohol abuse or active tuberculosis 12. Administration of live attenuated vaccines within 28 days prior to start of treatment or anticipated need for vaccination with live attenuated vaccine during the study

	13. COVID-19/SARS-CoV-2: While SARS-CoV-2 testing is not mandated for entry into this study, testing should follow local clinical practice standards. If a participant has a positive test result for SARS-CoV-2 infection, is known to have asymptomatic infection or is suspected of having SARSCoV2, the participant is excluded until a negative antigen test and resolution of symptoms if applicable 14. Major surgery within 28 days of scheduled Cycle 1 Day 1 dosing or minor surgery within seven days prior to initiation of study treatment or elective or planned major surgery to be performed during the course of the clinical trial **CNS Disease Considerations** 15. History or evidence of known CNS metastases or carcinomatous meningitis; participants with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging for at least four weeks prior to the first dose of trial treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least seven days prior to study treatment; this exception does not include carcinomatous meningitis which is excluded regardless of clinical stability **Coagulation Considerations** 16. Significant bleeding disorders, vasculitis or a significant bleeding episode within three months prior to study entry. Ongoing prophylactic anticoagulation therapy at a stable dose for prevention of VTE (Venous Thromboembolism) are allowed. Note: Participants on therapeutic anticoagulation must not be started on study before therapy is completed and prophylactic anticoagulation is established. **Immune System** 17. History of severe hypersensitivity reactions to antibodies 18. Chronic systemic steroid therapy (> 10 mg daily prednisone or equivalent) or any other form of immunosuppressive therapy within seven days prior to the first dose of study treatment; topical, inhaled, nasal and ophthalmic steroids are not prohibited. Intermittent prophylaxis per site institutional policy is not prohibited as long as it does not exceed chronic daily use of >10 mg prednisone or equivalent eg prophylactic

	use of steroids for Palmar Plantar Erythrodysesthesia (PPE) toxicity with PLD is allowed. 19. History of autoimmune disease that has required systemic treatment with disease-modifying agents, corticosteroids, or immunosuppressive drugs unless in the opinion of the investigator the participant is in a complete and durable remission; physiologic replacement therapies, such as thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, is allowed 20. Prior organ transplantation including allogeneic or autologous stem cell transplantation **Oncology** 21. Concurrent or previous other malignancy within two years of study entry with the exception of cured basal or squamous cell skin cancer, superficial bladder cancer, carcinoma *in situ* of the cervix, other non-invasive or indolent malignancy, or surgically-excised malignancy that is considered cured 22. Concurrent enrollment in another therapeutic clinical study 23. Prior treatment with anti-CD47 or anti-SIRPα therapy

Objectives	**Primary Objectives** • Evaluate DLTs, safety and tolerability of escalating dose levels of PF-07901801 when administered in combination with 40 mg/m^2 PLD in 28-day cycles and establish the MTD and RP2D combination regimen (Phase 1 portion of study) • Assess ~~a~~ preliminary evidence of anti-tumor activity of PF-07901801 in combination with 40 mg/m^2 PLD (Phase 2 portion of study) **Secondary Objectives** • Further assess the overall safety profile of PF07901801 administered in combination with 40 mg/m^2 PLDAssess additional efficacy outcomes **Exploratory Objectives** • Assess effect of treatment with PF-07901801 in combination with PLD on CA-125 levels • Characterize the PF-07901801 concentration in serum when administered in combination with PLD • Characterize the PLD concentration in plasma when administered in combination with PF-07901801 • Assess DDI potential between PF-07901801 and PLD • Evaluate development of antibodies directed against PF-07901801 • Explore possible relationships between PF-07901801 exposure and clinical outcome, safety and pharmacodynamics observations • Understand the relationship between the therapeutic intervention(s) being studied and the biology of the participant's disease.
Endpoints	**Primary** • DLTs during the DLT observation period (28 days following C1D1). Objective response (CR, PR) as defined by RECIST v1.1 criteria **Secondary** • Overall safety profile as assessed by the type, frequency, severity, timing and causal relationship of any adverse events, changes in vital signs, ECG, serum chemistry or other laboratory assessment, treatment delays or discontinuations • PFS, OS, disease control (DC [CR or PR or SD]), and DOR). **Exploratory**

	• Evaluate CA-125 levels in serial blood samples • Measurements of biomarkers/pharmacodynamics, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study. • Immunogenicity: Incidence and titers of ADA and neutralizing antibodies against PF-07901801 • PF-07901801 PK: Single and multiple dose C_{max}, CCI and clearance. PLD PK: Single and multiple dose C_{max} and C_{trough}.
Drug Product PF-07901801 (TTI-622)	CCI CCI and supplied at a concentration of 10 mg/mL in 20 mL single use Type I borosilicate glass vials with butyl rubber stoppers and aluminum seals. Each vial contains an extractable volume of 14 mL PF-07901801 Drug Product. For administration to the participan, PF-07901801 Drug Product is diluted with 0.9% sodium chloride for injection USP and administered by intravenous infusion. Please see the Investigational Product Manual (IPM) for preparation information. The dose of PF-07901801 will be based upon the dose level cohort to which the participant is assigned; the duration of infusion is dependent on dose level: dose levels less than or equal to 33 mg/kg infused over 60 min and doses greater than 33 mg/kg infused over 90 minutes and will have doses equal to or less than 2500 mg in 250 mL and doses 2501 mg or more in 500 mL or neat drug if the drug volume is over 500 mL . In Cycle 1 for dose levels 12 mg/kg and 24 mg/kg only, PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 of a 28-day cycle. Beginning with Cycle 2, PF-07901801 will be administered on Day 1 and Day 15 of 28-day cycles. The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow PF-07901801 levels to more quickly reach steady state. For dose level 48 mg/kg , PF-07901801 will be administered on Day 1 and Day 15 of 28-day cycle. Loading doses (Day 8 and Day 22) may be considered for Cycle 1 at the 48 mg/kg dose level if found to be safe and offer clinical benefit for participants. If

	Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg. On days when PF-07901801 and PLD are both administered, PLD will be administered prior to infusion of PF-07901801. On each day of PF-07901801 administration, a 60-minute observation period will follow PF-07901801 infusion and vital signs will be assessed at 30-minute intervals during this observation period; at the investigator's discretion, the duration of the observation period may be decreased after completion of Cycle 1 for a participant who has not experienced infusion-related reaction.
Reference Product Pegylated Liposomal Doxorubicin (PLD)	Pegylated liposomal doxorubicin will be administered per the approved package insert. The IP Manual should be referenced for additional information. The Single Reference Safety Document (SRSD) for PLD is the PLD (DOXIL®) US Product Insert (USPI).
Statistical Considerations	Based on a standard 3+3 design, up to approximately six DLT-evaluable participants may be enrolled in each dose level cohort during the Phase 1 dose escalation portion of the study; a minimum of nine and a maximum of 18 DLT-evaluable participants is anticipated. The Phase 2 expansion cohort is anticipated to provide a reasonable estimate of disease control, defined for this study as objective response rate among 25 treated participants, defined by RECIST v1.1 criteria, to support planning of future studies. The Phase 2 expansion cohort is planned to evaluate a PF-07901801 dose level derived from the dose escalation portion of the study in combination with a fixed dose of PLD. In this hypothesis-generating study, assuming an overall response rate of 10% with PLD monotherapy and an alternative of 30%, a power of 80% and one-sided Type 1 error set at 0.05, the combination will be considered worthy of further study if at least six responses are observed in the 25-participant cohort. Other evidence of clinical activity, such as duration of response, progression-free survival, and overall survival will be evaluated descriptively..
Dose Delays, Dose Modifications, Guidelines for Treatment	Participants who enter the study with symptoms or laboratory values equivalent to NCI CTCAE Grade 1 or Grade 2 should not

Discontinuation and Study Withdrawal	have dose reductions related to the persistence or mild worsening of those symptoms or laboratory values. Dose reductions may be warranted if worsening of symptoms or laboratory values is clinically significant in the opinion of the investigator and in the case of unacceptable treatment-related adverse events. Recognizing that it may be difficult to make attribution to one agent or the other in the combination regimen and in collaboration with the medical monitor, best efforts should be made to consider the underlying reason for the worsening of symptoms or development of a treatment-related adverse event so that dosing of the appropriate study drug can be modified. Except in the case of proteinuria, asymptomatic laboratory abnormalities should not result in dose interruptions, modifications, or discontinuation of study therapy unless determined by the investigator to be clinically significant or life-threatening. The investigator should withdraw a participant from all study-related treatment for any of the following reasons: • An unacceptable adverse event or safety observation, such as a persistent moderate toxicity that is intolerable to the participant, that is in the opinion of the investigator clearly attributed to PF-07901801 • An unacceptable adverse event or safety observation, such as a persistent moderate toxicity that is intolerable to the participant, that is in the opinion of the investigator clearly attributed to PLD and the participant has received fewer than four cycles of PLD. A participant who has completed four cycles of PLD treatment and experiences an adverse event that requires discontinuation of PLD may continue on study receiving PF-07901801 monotherapy. • Any event which would cause PF-07901801 or PLD to be modified by more than two dose reductions or to be held for more than 42 days from the last administered dose and is not attributable to a particular agent of the combination regimen; exception is made for participants who are receiving meaningful disease control and the investigator feels, with medical monitor concurrence, that continued treatment is in the best interest of the participant • Any treatment-related adverse event that is deemed life-threatening, regardless of grade; exception is made for participants in whom the life-threatening adverse event is attributed to PLD and the participant has received at least four cycles of PLD treatment and the investigator feels,

	with medical monitor concurrence, that continuation with PF-07901801 monotherapy would be reasonable. • Documentation of objective (radiographic) disease progression; for participants with asymptomatic progression and in the absence of unacceptable toxicity, the participant should continue treatment and a confirmation scan should be conducted at least four weeks later to document objective progression prior to removing participant from study treatment. A participant should not be removed from study on the basis of change in CA-125 level in the absence of objective or asymptomatic progression. • Unacceptable toxicity which in the opinion of the investigator cannot be attributed to a specific study agent • An intercurrent illness or change in the participant's condition that renders the participant unsuitable for further treatment in the opinion of the investigator; exception may be made for participants in whom the intercurrent illness or change in condition is thought to render the participant ineligible for continued treatment with PLD and the participant has received at least four cycles of PLD and the investigator feels, with medical monitor concurrence, that continuation with PF-07901801 monotherapy would be reasonable and the participant meets criteria for PF-07901801 re-treatment • Significant noncompliance with study protocol • Withdrawal of consent for participation in the treatment portion of the study (participant may participate in Long-Term Follow-Up assessment of survival and disease status [if withdrawn prior to documentation of objective disease progression] if consent for Long-Term Follow-Up assessment is not withdrawn) • Termination of the study by the sponsor

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ABBREVIATIONS

ADA	anti-drug antibodies
ADCC	antibody-dependent cellular cytotoxicity
ADP	adenosine diphosphate
AE	adverse event
ALL	acute lymphoblastic leukemia
ALT	alanine aminotransferase
AML	acute myeloid leukemia
ANC	absolute neutrophil count
ASCO	American Society of Clinical Oncology
AST	aspartate aminotransferase
AUC	area under the curve
CCI	
BSA	bovine serum albumin
BUN	blood urea nitrogen
CBP	childbearing potential
CDC	complement-dependent cytotoxicity
CK	creatine kinase
CKD	chronic kidney disease
CL	clearance rate of drug
CLL	chronic lymphocytic leukemia
C_{max}	maximum blood concentration
COVID-19	coronavirus disease 2019
CNS	central nervous system
CR	complete response
CRO	contract research organization
CRF	case report form
CSR	Clinical Study Report
CT	computed tomography; clinical trial
CTCAE	Common Terminology Criteria for Adverse Events
CTCL	cutaneous T-cell lymphoma

CTIS	Clinical Trials Information System
$C_{through}$	lowest concentration prior to next administration of drug
CV	coefficient of variation
CYP	cytochrome P450
D	day
DC	disease control
DCR	disease control rate
DDI	drug-drug interaction
DLBCL	diffuse large B-cell lymphoma
DILI	drug induced liver injury
DL-1 or Dose Level-1	dose Level minus 1
DL-2 or Dose Level-2	dose Level minus 2
DLT	dose-limiting toxicity
DOR	duration of response
EC_{50}	effective half-maximal concentration
EC	ethics committee
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRCL	estimated creatinine clearance
eCRF	electronic case report form
EDB	exposure during breastfeeding
EDC	electronic data capture
EDP	exposure during pregnancy
eGFR	estimated glomerular filtration rate
ELISpot	enzyme-linked immune absorbent spot
EOC	epithelial ovarian cancer
EOI	end of infusion
EOT	end of treatment
EPI	epidemiology collaboration
EU	European Union

EudraCT	European Union Drug Regulating Authorities Clinical Trials (European Clinical Trials Database)
FDA	Food and Drug Administration
FFPE	fresh-fixed paraffin embedded
FSH	follicle-stimulating hormone
FTC	fallopian tube carcinoma
G-CSF	granulocyte colony-stimulating factor
GCP	Good Clinical Practice
GGT	gamma glutamyl transferase
GLP	Good Laboratory Practice
GM-CSF	granulocyte-macrophage colony-stimulating factor
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HFS	hand-foot syndrome
HIV	human immunodeficiency virus
HIPAA	Health Information Portability and Accountability Act
HL	Hodgkin lymphoma
HRT	hormone replacement therapy
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IgG1	immunoglobulin G1
IgG4	immunoglobulin G4
INR	International Normalized Ratio
IP	investigational product
IPM	Investigational Product Manual
IRB	Institutional Review Board
IRR	infusion-related reaction
IV	intravenous(ly)
LDH	lactate dehydrogenase
LFT	liver function test
LVEF	left ventricular ejection fraction

MDS	myelodysplastic syndromes
MedDRA	Medical Dictionary for Regulatory Activities
MHC	major histocompatibility complex
MRI	magnetic resonance imaging
MTD	maximum tolerated dose
MUGA	multigated acquisition
NAb	neutralizing antibodies
NBF	neutral-buffered formalin
NCI	National Cancer Institute
NCCN	National Comprehensive Cancer Network
ND	not determined
NE	not evaluable
NGS	next-generation sequencing
NHL	non-Hodgkin lymphoma
NOS	not otherwise specified
NSAID	nonsteroidal anti-inflammatory drug
ORR	overall response rate
OS	overall survival
PARP	poly ADP ribose polymerase
P-gp	P-glycoprotein
PD	pharmacodynamics; progressive disease
PD-1	programmed death-1
PD-L1	programmed death ligand-1
PET	positron emission tomography
PFS	progression-free survival
PK	pharmacokinetics
PLD	pegylated liposomal doxorubicin
PPC	primary peritoneal carcinomas
PPE	palmar plantar erythrodysesthesia
PPRIF	Pregnant Partner Release of Information Form
PR	partial response
PS	performance status
PSSA	Pfizer SAE Submission Assistant

PT	prothrombin time
PTT	partial thromboplastin time
PTCL	peripheral T-cell lymphoma
RBC	red blood cell
RECIST	Response Evaluation Criteria in Solid Tumours
RP2D	recommended Phase 2 dose
SAE	serious adverse event
SAP	Statistical Analysis Plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SCr	serum creatinine
Scys	serum cystatin C
SD	stable disease
SFU	safety follow up
SIRPα	signal regulatory protein alpha
SoA	schedule of activities
SOP	standard operating procedure
SRSD	Single Reference Safety Document
SUSAR	suspected unexpected serious adverse reaction
$t_{½}$	terminal half-life
TAM	tumor-associated macrophage
T bili	total bilirubin
TCR	T-cell receptor
TCRVβ	variable beta chain of the T-cell receptor
TEAE	treatment-emergent adverse event
T_{max}	time to C_{max}
TK	toxicokinetic
ULN	upper limit of normal
US	United States
USP	United States Pharmacopeia
USPI	United State Prescribing Information
VTE	venous thromboembolism
WBC	white blood cell
WOCBP	women of childbearing potential

3 INTRODUCTION

3.1 CD47 and Signal Regulatory Protein Alpha (SIRPα)

CD47 is a transmembrane glycoprotein normally expressed on all hematopoietic cells and additionally on epithelial and mesenchymal cells in many tissues.[14,15] CD47 binds several integrin proteins and the extracellular matrix protein thrombospondin-1 and is involved in a wide variety of physiologic processes including platelet and neutrophil activation, T-cell function, regulation of vascular signaling by nitric oxide, inhibition of dendritic cell activity, and inhibition of monocyte activation.[16-21]

Hematologic malignancies have been shown to have high expression of CD47, including non-Hodgkin lymphoma (NHL), acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), multiple myeloma, acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS).[22-28] Solid tumors have also been found to display high CD47 expression, including brain, breast, colon, gastric, kidney, soft tissue sarcomas including leiomyosarcoma, osteosarcoma liver, lung, melanoma, ovarian, pancreatic, and prostate tumors.[6-10] In many of these cases, high expression of CD47 is associated with poor prognosis.

3.2 Regulation of Macrophage Phagocytic Activity

Macrophage-mediated phagocytosis is regulated by both activating ("eat") and inhibitory ("do not eat") signals. Of the latter, the best characterized inhibitory signal is CD47, which suppresses phagocytosis by binding SIRPα on the surface of macrophages.[30] Upon binding to CD47, immunoreceptor tyrosine-based inhibitor motifs in the cytoplasmic tail of SIRPα become phosphorylated, resulting in recruitment and activation of downstream phosphatases, including SHP-1 and SHP-2, ultimately leading to inhibition of phagocytosis. The inhibition is thought to be mediated through deactivation of the contractile cytoskeletal activity involved in pulling the target cell into a macrophage for ingestion.[31] Interestingly, this strategy of immune evasion is used by both differentiated cancer cells and cancer stem cells.[32]

As noted above, elevated expression of CD47 has been correlated with poor clinical outcome. For example, overall survival was significantly lower for diffuse large B-cell lymphoma (DLBCL) or mantle cell lymphoma patients who had elevated CD47 expression.[23] CD47 expression was independently prognostic of DLBCL disease progression per multivariate analyses incorporating key prognostic factors. Similarly, patients with CLL that expressed high levels of CD47 experienced a significantly worse event-free survival compared with those

whose tumor expressed lower expression levels.[23] Similar trends have been reported in other hematologic malignancies[22,24,26] and in solid tumors.[8,10,33,34] Indeed, evidence exists that increased CD47 expression may be involved in the transition from low-risk to high-risk MDS and possible transformation to AML.[27] These findings are consistent with tumor cells exploiting the suppressive CD47-SIRPα axis to evade macrophage-mediated destruction. Blocking CD47 has emerged as a therapeutic strategy and several anti-CD47 developmental programs are underway to explore this approach.

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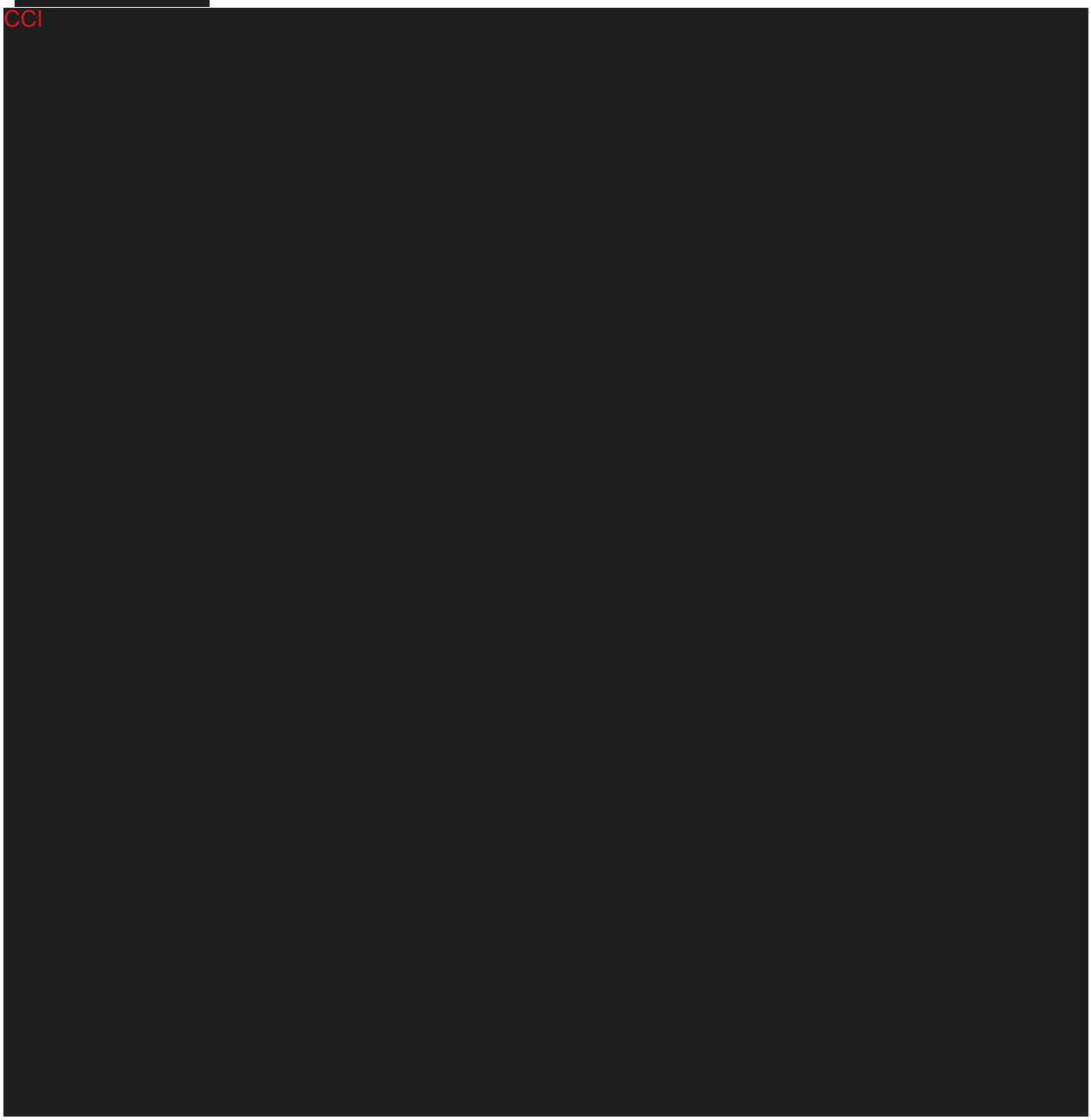

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3.4 Rationale for Patient Population and Study Design

Ovarian cancer is the second most common gynecologic malignancy in developed countries and the third most common gynecologic malignancy in developing countries. The majority (95%) of ovarian malignancies are epithelial in nature.[1,2,3]

High-grade serous carcinoma, the most common histologic subtype, generally includes fallopian tube and peritoneal serous carcinoma, based upon similarities in histology and clinical behavior. Epithelial cancers of ovarian, fallopian tube, and peritoneal origin exhibit similar clinical characteristics, behavior, and in many cases, share basic biology. As such, these are often considered collectively and define epithelial ovarian cancer (EOC) in clinical trials and clinical practice.

Despite initial therapy (usually consisting of surgical cytoreduction and platinum-taxane combination therapy), the majority of patients with advanced-stage ovarian cancer will relapse and require additional treatment. Patients with platinum-sensitive recurrent EOC, defined as recurrence at least 6 months after completion of prior-platinum-based treatment, are more likely to respond to retreatment with a chemotherapy regimen that contains a platinum. In addition, several trials suggest that patients with platinum-sensitive disease achieve better response rates and progression-free survival with maintenance treatment, which may consist of

bevacizumab, olaparib or niraparib, although only bevacizumab has shown an overall survival benefit.

Patients with platinum-resistant recurrent EOC, defined as disease progression ≤6 months after the most recent-platinum-based treatment regimen (versus platinum-refractory disease, defined as progression while on therapy or within three months of completing their primary first-line platinum-based treatment), present with disease that is generally not curable and treatments should aim to maximize quality of life while attempting to control disease. Thus, this setting is an urgent unmet medical need and current treatment options typically consist of single-agent chemotherapy, including weekly paclitaxel or pegylated liposomal doxorubicin (PLD). In the AURELIA study, patients who received PLD at 40 mg/m^2 experienced a median PFS of 4 months and 8% ORR.[4,5] Some patients are candidates for combination therapy with bevacizumab, which consistently results in better outcomes compared to chemotherapy alone, but this regimen is limited to those who did not receive bevacizumab in the platinum-sensitive setting and who have not had recent (prior 6 months) bowel obstruction and do not have malignant bowel involvement. The addition of bevacizumab to PLD in the AURELIA study raised the ORR to only 14% and the mPFS to 5 months, highlighting the need for more effective treatments – treatments that offer disease control without increased toxicity – for this patient population.[4,5]

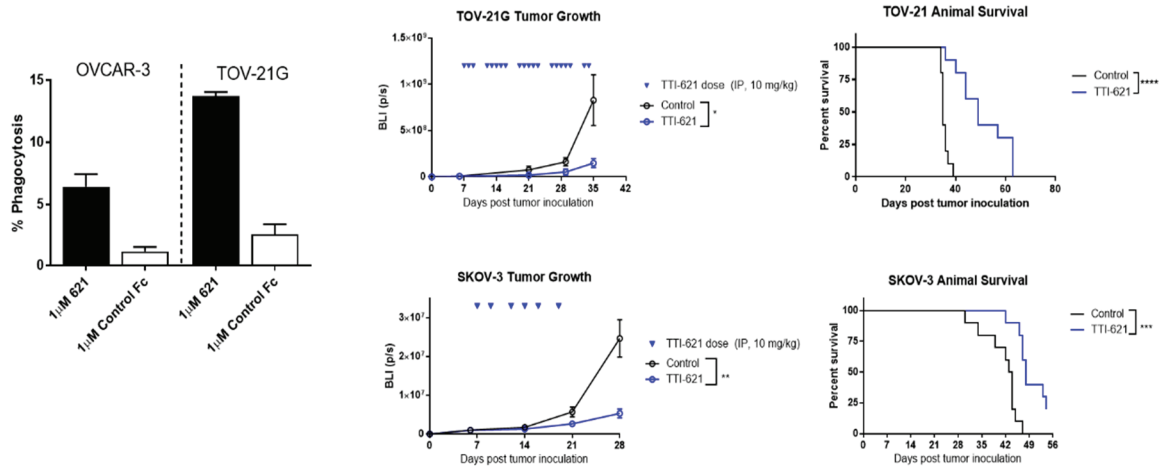
PF-07901801 is a recombinant soluble fusion protein designed to block the cell-surface protein CD47, which is found on the surface of many normal cell types and at high levels on many malignant tumor cells. CCI [redacted]

Many solid tumors, including ovary, brain, breast, colon, gastric, kidney, soft tissue sarcoma, liver, lung, melanoma, pancreatic, and prostate tumors have also been found to express high levels of CD47.[6-10] In many of these cases, high expression of CCI [redacted]. CD47 protein is highly expressed in ovarian cancer and is correlated with poor clinical characteristics and prognosis.[11,12] Decreasing CD47 levels in an ovarian cancer cell lines resulted in promotion of macrophage phagocytosis and tumor growth *in vivo*.[12] CCI [redacted].[13]

Trillium's CD47-targeted molecule TTI-621 significantly inhibits the growth of ovarian cancer cells in xenograft models, enhances phagocytosis and improves survival, as shown in Figure 3 and Figure 4. TTI-621 is very similar to PF-07901801, with the only difference being

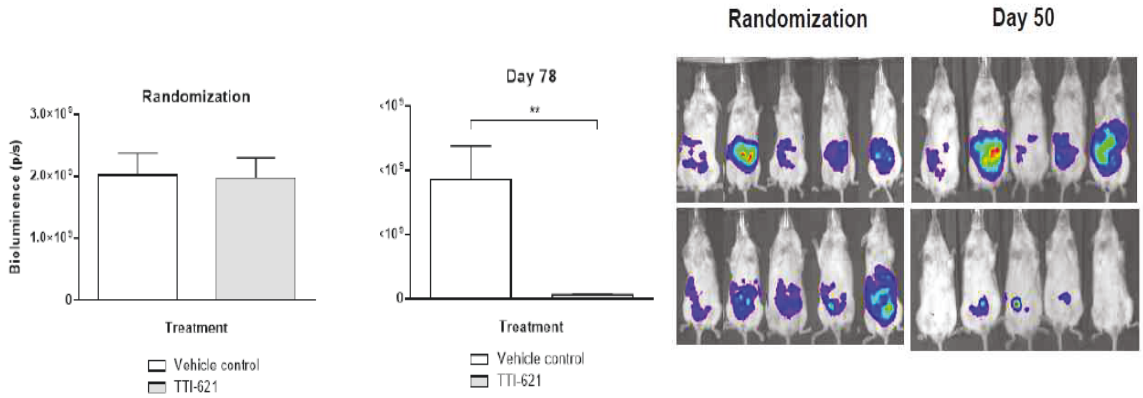
replacement of the IgG4 domain in PF-07901801 with an IgG1 domain to generate TTI-621, and thus serves to demonstrate the intended effect of CD47-mediated targeting in cancer.

Figure 3. The Effect of TTI-621 Monotherapy on Phagocytosis in Ovarian Cancer Cell Lines



The effect of TTI-621 monotherapy on phagocytosis in ovarian cancer cell lines and tumor growth and survival in TOV-21G and SKOV-3 xenograft models of ovarian cancer *In vitro* phagocytosis of OVCAR-3 and TOV-21G cell lines was evaluated in the presence of 1 μM TTI-621 or control Fc (left panel). To evaluate tumor growth and animal survival, NOD/SCID mice were implanted intraperitoneally with TOV-21G or SKOV-3 cells and treated with TTI-621 at 10mg/kg, as indicated by the inverted triangles in the middle panels. Tumor growth curves, measured by BLI, are shown in the middle panels; survival curves are shown on the right panels.

Figure 4. The Effect of TTI-621 Monotherapy on Ovarian Cancer Growth in Xenograft Models



The effect of TTI-621 monotherapy on ovarian cancer growth in xenograft models: NOD/SCID mice received intraperitoneal implants of luciferase-expressing OVCAR-3 cells. On Day 27 after implant, animals were randomized to TTI-621 or vehicle control administered intraperitoneally at 10 mg/kg three times per week for two weeks. Tumor burden was assessed by bioluminescence on Day 27 (left panel) and again on Day 78, approximately one month after cessation of treatment (middle panel). In the right panel, representative bioluminescence images at Day 27 and Day 50 are shown (upper panels: vehicle control; lower panels: TTI-621).

The combination of CD47-blockade and doxorubicin, the active component of liposomal doxorubicin, has been shown to enhance anti-tumor activity in multiple solid tumor models, including ovarian, breast and hepatocellular carcinoma.[13, 35-36] In an invasive breast cancer model, anti-CD47 antibody therapy enhanced the effect of doxorubicin by reducing tumor growth and metastatic spread to the lungs.[35] This anti-tumor effect was associated with increased macrophage-mediated killing of breast cancer cells. Moreover, CD47 blockade was found to protect against doxorubicin-induced cytotoxicity by enhancing cardiac tissue viability and function in mice. This cytoprotective effect was attributed to an increase in autophagic flux. In another study, CD47 blockade enhanced macrophage-mediated phagocytosis of hepatocellular carcinoma cell lines in the presence of doxorubicin *in vitro*.[36]

Together, these studies suggest that combining PF-07901801 with doxorubicin-based chemotherapy may be more effective than doxorubicin-based chemotherapy alone in tumor types that have high CD47 expression and have high numbers of macrophages, such as ovarian cancer.

An ongoing clinical trial of PF-07901801 in participants with advanced hematologic malignancies, including lymphoma, leukemia and multiple myeloma (Protocol TTI-622-01, NCT03530683) has demonstrated the safety of weekly infusions of PF-07901801. As of the cut-off date of 12 April 2021, 43 participants with advanced relapsed/refractory lymphoma have received PF-07901801 at doses ranging from 0.05 mg/kg to 18.0 mg/kg. A single DLT, reversible asymptomatic Grade 4 platelet count decrease was observed and managed without any clinical sequelae. No treatment-related serious adverse events have been reported. The favorable safety profile of PF-07901801 suggests that combining PF-07901801 with other therapies might offer an effective treatment option for patients without the addition of prohibitive toxicity. Thus, the primary goal of this clinical trial is to evaluate the safety and activity of PF-07901801 administered in combination with the standard of care PLD regimen in participants with platinum-resistant recurrent EOC. The safety and activity of escalating doses of PF-07901801 administered in combination with PLD administered at 40 mg/m^2 on Day 1 of 28-day cycles will be evaluated in the first part of this study and a maximum tolerated dose or recommended Phase 2 regimen will be identified; an expansion cohort will then be enrolled to evaluate the safety and activity of the maximum tolerated dose or recommended Phase 2 regimen with the goal of establishing a basis for subsequent clinical evaluations.

3.5 Investigational Medicinal Product PF-07901801

3.5.1 Nonclinical Experience with PF-07901801

3.5.1.1 Nonclinical Pharmacology of PF-07901801

TTI-622/PF-07901801 was evaluated in a series of studies that have collectively demonstrated the following:

- PF-07901801 bound to human hematopoietic tumor cell lines and primary tumor samples with an effective half-maximal (EC50) concentration of 140–924 nM (average: 361 ± 294 nM or 27.8 ± 22.7 µg/mL). Comparable binding of PF-07901801 was observed on normal human blood cells with the exception of RBCs, to which only minimal binding was observed

- PF-07901801 cross-reacted with cynomolgus monkey CD47 and bound strongly to monkey RBCs

- PF-07901801 induced macrophage-mediated phagocytosis of a range of hematologic and solid tumor cell lines and primary participant samples with an average EC_{50} value of 8 nM (0.6 μg/mL)

- Although phagocytosis of some normal cells such as platelets was observed, competition studies suggest that PF-07901801 triggers macrophages to selectively phagocytose tumor cells over normal cells

- PF-07901801 exhibited anti-leukemic activity in an AML xenograft model and was highly effective in reducing tumor burden and prolonging survival in a DLBCL xenograft tumor model and in a head and neck cancer xenograft model when combined with the anti-EGFR antibody cetuximab. PF-07901801 potentiated the efficacy of daratumumab by reducing the tumor volume and increasing survival in Burkitt lymphoma and multiple myeloma xenograft models

- PF-07901801 did not induce ADCC or CDC against tumor cells

- PF-07901801 did not trigger biologically relevant inhibition or activation of platelet aggregation at concentrations of up to 300 μg/mL in human whole blood or platelet rich plasma

Additional information and details of these studies may be found in the Investigator's Brochure.

3.5.1.2 Nonclinical Pharmacokinetics of PF-07901801

Four toxicokinetic (TK) studies were performed to characterize the TK properties of PF-07901801 in the cynomolgus monkey. The studies included two 4-week studies, a 4-week repeat-dose dose range finding study, and a 4-week repeat-dose GLP study. Across the studies, male and female cynomolgus monkeys received once weekly, twice weekly, or biweekly intravenous administrations of PF-07901801 at dose levels of 1, 3, 5, 8 or 12.5 mg/kg/dose.

Overall, the results of the TK studies indicated that when not affected by anti-drug antibodies, PF-07901801 exposure generally increased in a dose-proportional or greater than dose-proportional manner across dose levels ranging from 1 to 8 mg/kg/dose. Comparison between first and last dose indicated PF-07901801 accumulation up to 1.6-fold, indicating that exposure was maintained throughout the studies despite the development of anti-drug antibodies in the majority of animals.

Additional information may be found in the Investigator's Brochure.

3.5.1.3 Nonclinical Toxicology of PF-07901801

The safety of PF-07901801 was evaluated in four non-human primate repeat-dose toxicology studies in the cynomolgus monkey (*Macaca fascicularis*) in which CD47 has 98% sequence

homology with human CD47; in addition, PF-07901801 cross-reacts with CD47 and binds to red blood cells from this species. Three non-GLP dose range finding studies supported a GLP repeat-dose toxicity study. Across all four studies a total of 69 animals were dosed with PF-07901801 across a range of concentrations.

The GLP study in male and female cynomolgus monkeys was designed as a five-week study with either a once or twice weekly intravenous infusion of PF-07901801 at dose levels of 0 (vehicle control) or 1, 3, 5, or 8 mg/kg (8 mg/kg dose weekly administration only). Two animals/sex from the 0 (vehicle control), 5 mg/kg weekly, 8 mg/kg weekly and 5 mg/kg twice weekly dose groups were maintained for a four-week recovery period to assess the reversibility, persistence, and delayed occurrence of any effects.

Parameters evaluated included mortality, clinical signs, body weight; ophthalmoscopic, neurological, and electrocardiographic examinations; blood pressure and respiratory rate measurements; clinical pathology (hematology, coagulation, clinical chemistry, and urinalysis); anatomic pathology; toxicokinetics and immunogenicity. To further evaluate adverse effects of PF-07901801 and provide insight into the mechanism of toxicity, circulating immune complexes, complement activation, cytokine release, and immunohistochemistry assessments were also conducted.

Of the 54 animals dosed with PF-07901801 in this study, three were sacrificed at unscheduled intervals due to moribund condition or were found dead, including two males administered 3 mg/kg PF-07901801 once weekly. One of these animals was sacrificed *in extremis* on Day 15 after the completion of the third dose and the other animal was found dead on Day 15, 30 minutes following completion of the third dose. The third animal that died was from the 5 mg/kg twice weekly group; the animal expired during infusion of the seventh dose on Day 22. Clinical observations for the male that died *in extremis* included decreased activity, shallow breathing, hunched posture and red discharge/vomitus. The cause of death was pulmonary hemorrhage in the lungs. No clinical observations were noted for the other two animals at the time of death, nor were there any histopathological findings and the cause of death was undetermined. All three animals tested positive for anti-drug antibodies and had increased levels of IgG, IgM, and/or C3 compared to control animal; therefore, immune complex-mediated reactions may have been associated with the deaths.

Two males administered PF-07901801 at 5 mg/kg twice weekly were placed on a dosing holiday on Day 18 due to decreased red cell mass. Dosing was resumed on Day 22; however, the 5 mg/kg twice weekly dose level was considered to have exceeded the HNSTD (highest non-severely toxic dose). Findings in the other surviving animals were consistent with PF-07901801 related effects on RBCs and included mild-to-moderate decreases in red cell mass with increases in spherocytes and evidence of a regenerative erythroid response indicated by increases in reticulocytes. Mild decreases in platelet counts were also noted in males at 8 mg/kg (once weekly) and 3 mg/kg (twice weekly).

There was also a notable increase in complement components C4a and C3a in all PF07901801 -treated males and in females treated at doses ≥3 mg/kg; no dose response relationship was evident. Evidence of a mild-to-moderate inflammatory stimulus was observed in both sexes at

all dose levels, as indicated by decreases in albumin, albumin to globulin ratios, and increases in fibrinogen, globulin, ferritin, C-reactive protein, and pro- inflammatory cytokines.

Overall, there were no microscopic correlates for any of the clinical pathology changes and all changes generally resolved by the recovery necropsy.

At the end of the dosing period, the majority of surviving animals tested positive for anti-drug antibodies (27/30 animals receiving weekly dosing and 16/21 animals receiving twice weekly doses); the presence of anti-drug antibodies correlated with a decrease in systemic exposure. In the recovery animals, two males and two females at 5 and 8 mg/kg (once weekly) tested positive for anti-drug antibodies on Day 58. In animals administered PF-07901801 twice weekly, two of the four recovery animals at 5 mg/kg screened positive for anti-drug antibodies, 1 each on Day 54 and 58.

In the toxicokinetic portion of the study, systemic exposure (C_{max} and AUC_{0-25} and/or AUC_{all}) increased in a greater than dose proportional manner. Systemic exposure (AUC_{0-25}) was variable and generally appeared to decrease following repeat administration. These variable results may indicate a potential impact from the immune response.

Based on the magnitude and reversibility of changes associated with PF-07901801, the HNSTD for the pivotal GLP toxicity study was determined to be 8 mg/kg (once weekly) or 3 mg/kg (twice weekly).

Additional information for each toxicology study is found in the Investigator's Brochure.

3.5.2 Clinical Experience with PF-07901801

3.5.2.1 Study C4971001

PF-07901801 is being evaluated in an ongoing Phase 1 two-part, multicenter, open-label, dose escalation and expansion study in participants with advanced hematologic malignancies, including lymphoma, leukemia and multiple myeloma. In the Phase 1a dose escalation portion of the study, participants with advanced relapsed/refractory lymphoma are enrolled in sequential dose cohorts to receive PF-07901801 monotherapy by intravenous infusion over one hour once weekly to characterize the safety, tolerability and pharmacokinetics of PF-07901801 and to determine the maximum tolerated dose (MTD) and Phase 1b starting dose for this schedule. In the Phase 1b portion of the study, participants with advanced refractory hematologic malignancies will be treated with PF-07901801 in combination with selected approved anti-cancer agents in several cohorts to further define safety and to characterize efficacy.

The study is ongoing and the data presented here are based on a data cut-off of 12 April 2021.

3.5.2.1.1 Enrollment and Demographic Summary

Enrollment into the Phase 1a portion of the study is presented in Table 1; no participants have been enrolled into the Phase 1b portion of the study as of the data cut-off date.

As this was a first-in human study and PF-07901801 is a recombinant molecule, the possibility of infusion-related reaction was not unexpected. Therefore, a conservative dosing schema in which a two-week safety run-in with a lower dose prior full dosing was incorporated as noted in the table. In the complete absence of infusion-related reactions or dose-limiting toxicities in Cohorts 1-5, the safety run-in was deemed unnecessary and was eliminated beginning with Cohort 6.

Table 1. PF-07901801 Dose Levels and Enrollment by Cohort

1	0.1 mg/kg	0.05 mg/kg	**4**
2	0.3 mg/kg	0.2 mg/kg	**3**
3	0.8 mg/kg	0.4 mg/kg	**4**
4	2.0 mg/kg	1.0 mg/kg	**4**
5	4.0 mg/kg	2.0 mg/kg	**4**
6	8.0 mg/kg	n/a	**8**
7	12.0 mg/kg	n/a	**5**
8	18.0 mg/kg	n/a	**11**

The majority of participants were white (29, 67%) and 9 (21%) identified as black or African American. The majority were female (24, 56%). The median age was 67 years (range, 24 to 86 years). The majority of participants had a diagnosis of Non-Hodgkin Lymphoma (37, 86%), with 19 (51%) of the participants with NHL having the DLBCL form. One patient was determined after enrollment to have Erdheim-Chester disease and was allowed to remain on study. The remaining 5 participants (12%) had a diagnosis of Hodgkin Lymphoma.

3.5.2.1.2 Safety

3.5.2.1.2.1 Treatment-Emergent Adverse Events

Overall, 37 participants (86%) experienced at least one treatment-emergent adverse event. Adverse events reported in at least 10% of participants are summarized in Table 2.

Table 2. Adverse Events of Any Grade Regardless of Causality in ≥10% of Participants

Adverse Event	Number of Participants (Percent)
Any	37 (86%)
Thrombocytopenia	13 (30%)
Constipation	8 (19%)
Nausea	8 (19%)
Pyrexia	7 (16%)
Fatigue	6 (14%)
Neutropenia	6 (14%)
Diarrhoea	5 (12%)

3.5.2.1.2.2 Treatment-Emergent Adverse Event Related to Treatment with PF-07901801

Overall, 20 participants (47%) experienced at least one treatment-emergent adverse event that was assessed by the investigator as related to treatment with PF-07901801. Adverse events assessed as related to treatment and reported in at least 5% of participants are summarized in Table 3.

Table 3. Adverse Events of Any Grade Related to Treatment with PF-07901801 in ≥5% of Participants

Adverse Event	Number of Participants (Percent)
Any	20 (47%)
Thrombocytopenia	9 (21%)
Neutropenia	5 (12%)
Anemia	4 (9%)
Fatigue	4 (9%)
Nausea	3 (7%)
Abdominal pain	2 (5%)
ALT increased	2 (5%)
Blood alkaline phosphatase increased	2 (5%)
Chills	2 (5%)
Pyrexia	2 (5%)

3.5.2.1.2.3 Adverse Events Grade 3 or Grade 4 Regardless of Causality

Overall, 16 participants (37%) experienced at least one adverse event Grade 3 or Grade 4. Grade 3 or Grade 4 adverse events reported in at least 5% of participants are summarized in Table 4.

Table 4. Grade 3 or Grade 4 Adverse Events Regardless of Causality in ≥5% of Participants

Adverse Event	Number of Participants (Percent)
Any	16 (37%)
Neutropenia	5 (12%)
Thrombocytopenia	5 (12%)
Pneumonia	2 (5%)

3.5.2.1.2.4 Adverse Events Grade 3 or Grade 4 Related to Treatment with PF-07901801

Overall, 6 participants (14%) experienced at least one Grade 3 or Grade 4 adverse event that was assessed by the investigator as related to treatment with PF-07901801. All Grade 3 or Grade 4 adverse events assessed as related to treatment are summarized in Table 5.

Table 5. Grade 3 or Grade 4 Adverse Events Related to Treatment with PF-07901801

Adverse Event	Number of Participants (Percent)
Any	6 (14%)
Neutropenia	4 (9%)
Thrombocytopenia	2 (5%)
Anemia	1 (2%)

3.5.2.1.2.5 Serious Adverse Events Regardless of Causality

Overall, 9 participants (21%) experienced at least one serious adverse event. Serious adverse events reported in at least 5% of participants are summarized in Table 6.

Table 6. Serious Adverse Events Regardless of Causality in ≥5% of Participants

Adverse Event	Number of Participants (Percent)
Any	9 (21%)
Pyrexia	4 (9%)
Pneumonia	2 (5%)

3.5.2.1.3 Serious Adverse Events Related to Treatment with PF-07901801

No participant treated with PF-07901801 has experienced a serious adverse event assessed by the investigator as related to treatment with PF-07901801.

3.5.2.1.4 Adverse Events of any Grade Resulting in Death

One participant enrolled in Study TTI-622-01/C4971001 experienced adverse events unrelated to treatment with PF-07901801 that led to death. The participant, diagnosed with relapsed/refractory angioimmunoblastic T cell lymphoma, was enrolled into Cohort 4 (PF-07901801 weekly at 2.0 mg/kg) and received a total of 10 infusions of PF-07901801 between Day 1 and Day 92. The participant came off study on Day 99 due to an unrelated periorbital infection, was hospitalized for this and subsequently developed multiple organ dysfunction syndrome and acute respiratory distress syndrome, and expired 23 days after discontinuing from the study. The investigator assessed these adverse events as *unrelated* to treatment with PF-07901801 and assessed them as related to the disease under study.

No other participant enrolled in the study has experienced either of these adverse events.

3.5.2.1.5 Dose-Limiting Toxicity

The dose level of 8.0 mg/kg was associated with a reversible dose-limiting toxicity of Grade 4 platelet count decreased in one participant, which was asymptomatic, reversible and managed without any clinical sequelae. This cohort was expanded and no other participant experienced this or any other dose-limiting toxicity.

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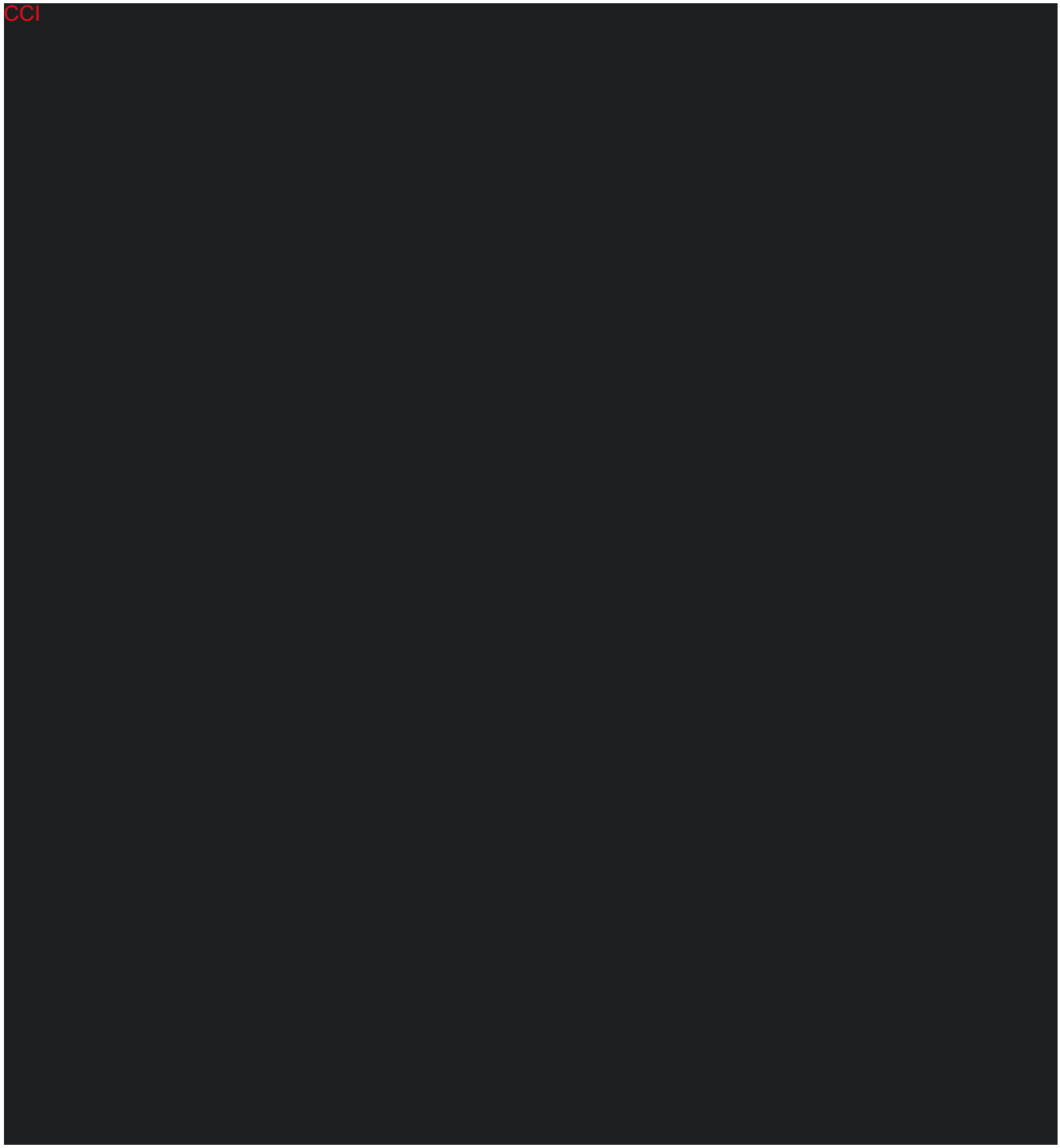

3.5.2.3 Clinical Activity

PF-07901801 has demonstrated single agent clinical activity in some of the 43 participants with advanced relapsed/refractory lymphoma enrolled in TTI-622-01/C4971001. To date, a 33% ORR has been observed in 27 response-evaluable participants enrolled across doses ranging from 0.8 – 18 mg/kg. There appears to be a fast onset of response, with PR or CR noted by Week 8 of treatment in this patient population.

Among responding participants there were two complete responses and one near-CR:

- One participant with DLBCL and four prior lines of therapy treated with PF-07901801 at 0.8 mg/kg experienced PR at Week 8 and CR at Week 36. At more than 22 months since initiation of treatment, the participant remains on study in CR without disease progression under a modified treatment regimen of a single infusion per month.

- One participant with CTCL with large cell transformation and six prior lines of therapy treated with PF-07901801 at 18 mg/kg experienced a CR at Week 8; the participant continues on study under a reduced schedule of one infusion every 21 days.

- A third participant, with DLBCL and three prior regimens treated with PF-07901801 at 4 mg/kg, had a 100% reduction in target lesions at Week 8 but was declared PR due to minimal residual signal on PET imaging. The participant continued on study and developed disease progression at Week 24.

Clinical activity with PF-07901801 as of the data cut-off of 12 April 2021 is summarized in Table 9.

Table 9. Clinical Activity with PF-07901801 Monotherapy at Doses Ranging from 0.8 – 18 mg/kg in Study TTI-622-01

Indication	Response-Evaluable Participant Population (N)	CR	PR	ORR
DLBCL	11	1 (9%)	2 (18%)	3 (27%)
PTCL	6	0 (0%)	2 (33%)	2 (33%)
CTCL	4	1 (25%)	2 (50%)	3 (75%)
FL	3	0 (0%)	1 (33%)	1 (33%)
HL	3	0 (0%)	0 (0%)	0 (0%)
Total	27	2 (7%)	7 (26%)	9 (33%)

3.6 Investigational Medical Product Pegylated Liposomal Doxorubicin (PLD)

Pegylated liposomal doxorubicin (doxorubicin hydrochloride liposome injection) is an anthracycline topoisomerase inhibitor indicated for ovarian cancer after failure of platinum-based chemotherapy and in other indications. PLD is one of a class of drug formulations that is delivered in liposome vesicles, in which the doxorubicin molecules are encapsulated in a bilayer sphere of lipids, which are then surrounded by a dense layer of polyethylene glycol (PEG), hence the name pegylated liposomal doxorubicin. The size of the liposomes, approximately 100 nm, prevents them from entering tissues with tight capillary junctions, such as the heart and gastrointestinal tract, leading to an improved safety profile when compared to the parent compound doxorubicin. The parent compound doxorubicin is a widely-used component of multi-agent adjuvant chemotherapy for many oncologic indications.

Refer to the current Full Prescribing Information for information on the safety and clinical activity of pegylated liposomal doxorubicin.

3.7 Rationale for Planned Regimens of Investigational Medical Products

3.7.1 PF-07901801

In the Phase 1 dose escalation portion of the study, increasing doses of PF-07901801 will be evaluated in combination with fixed-dose PLD in a standard 3+3 dose escalation scheme. Three dose levels will be evaluated starting with 12.0 mg/kg (Dose Level 1) administered by intravenous infusion over one hour. In Cycle 1 for dose levels 1 and 2, PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 in combination with PLD on Day 1 of 28-day cycle. Beginning with Cycle 2 at dose levels 1 and 2, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow PF-07901801 levels to more quickly reach steady state. For dose level 3, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles.

Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin.

The planned dose levels are presented in Table 10.

Table 10. PF-07901801 Dose Levels Planned for Evaluation in Combination with Doxorubicin

Dose Level	PF-07901801 Dose
1	12mg/kg
2	24 mg/kg
3	48 mg/kg

If Dose Level 1, 12 mg/kg, is found to be intolerable, a lower dose level may be evaluated. If Dose Levels 2 or 3 are not tolerated, intermediate dose levels may be evaluated.

As described in Section 3.5.2, PF-07901801 dose levels up to 18 mg/kg administered weekly were found to be safe and well-tolerated in Study TTI-622-01/C4971001, the two-part, multicenter, open-label, Phase 1a/1b dose escalation and expansion study of PF07901801 in participants with advanced hematologic malignancies, including lymphoma, leukemia and multiple myeloma. The study in participants with ovarian cancer plans to administer PF-07901801 weekly only during the first cycle for dose levels 1 and 2, and then decrease to every 14 days for the duration of participant participation. Dose level 3 will be biweekly regimen from the start.

3.7.2 Pegylated Liposomal Doxorubicin

Doxorubicin is considered a standard of care in the intended patient population and will be used in accordance with the approved PLD package insert.

3.8 Benefit-Risk Assessment

PLD is known to have clinical benefit in patients with platinum-resistant ovarian cancer and other single agent chemotherapeutic agents, including paclitaxel, may be used in the same setting of patients who have progressed on and are not resistant to platinum-based chemotherapy and who have received bevacizumab (or were intolerant of or not able to receive it) in an earlier setting and are not eligible for it in the platinum-resistant setting. However, with a response rate of less than 20%, a PFS of less than six months and median overall survival on the order of one year[5,37-41] with any of the single agent chemotherapy regimens, there is a significant need for improvement. It is hypothesized that blockade of CD47-mediated immune evasion and concomitant activation of phagocytosis with PF-07901801 will be clinically beneficial in patients with ovarian cancer in which CD47 is expressed and macrophage scores are increased. In addition, preclinical data demonstrating synergy between doxorubicin, the parent molecule of PLD, and anti-CD47 antibodies, further suggesting that administration of PF-07901801 will enhance the disease control provided by the doxorubicin chemotherapy component of PLD in patients with platinum-resistant ovarian cancer.

3.8.1 Expected Risks of PF-07901801

In clinical trial TTI-622-01/C4971001, a multicenter, open-label, Phase 1a/1b study in participants with advanced hematologic malignancies, including lymphoma, leukemia and multiple myeloma, and reflecting a data cut-off of 12 April 2021, PF-07901801 has been administered at doses up to 18 mg/kg by weekly intravenous infusion. PF-07901801 has been safe and well-tolerated. The most frequent treatment-related adverse events of any grade occurring in more than 5% of participants were thrombocytopenia, neutropenia, anemia, fatigue and nausea.

Grade ≥3 treatment-related adverse events were neutropenia, occurring in 4 participants (9%), thrombocytopenia, occurring in 2 participants (5%) and anemia (1 participant, 2%). Reflecting these observations, the safety monitoring schedule of this protocol includes routine hematology assessment.

3.8.2 Expected Benefits of PF-07901801

In the Phase 1 dose escalation component of Study TTI-622-01/C4971001 in which PF-07901801 is administered weekly, PF-07901801 has demonstrated single agent clinical activity in some of the 43 participants with advanced relapsed/refractory lymphoma. To date, a 33% ORR has been observed among response-evaluable participants enrolled across doses ranging from 0.8 – 18 mg/kg, including two CRs. A third participant had complete resolution of target lesions but was designated only PR on the basis of a residual PET imaging signal. There appears to be a fast onset of response, with responses noted by Week 8 of treatment in this participant population despite participant s having received numerous prior treatment regimens, as many as 10 prior regimens in a patient with DLBCL who achieved PR at Week 8 and continues on treatment without progression.

Thus, it is anticipated that PF-07901801 may offer disease control to patients with ovarian cancer who will have received prior treatment in the platinum-sensitive setting. Additionally, preclinical data suggesting synergy with a range of CD47-targeting molecules and doxorubicin

offers hope that the combination will provide a safe and effective treatment option for patients with platinum-resistant recurrent epithelial ovarian cancer.

More detailed information about the known and expected risks and adverse events of PF-07901801 may be found in the PF-07901801 Investigator Brochure, which is the SRSD for this study.

4 STUDY OBJECTIVES AND ENDPOINTS

4.1 Primary Objectives

- Evaluate DLTs, safety and tolerability of escalating dose levels of PF-07901801 when administered in combination with 40 mg/m^2 PLD in 28-day cycles and establish the MTD and RP2D combination regimen (Phase 1 portion of study)

- Assess preliminary evidence of anti-tumor activity of PF-07901801 in combination with 40 mg/m^2 PLD (Phase 2 portion of study)

4.2 Primary Endpoints

- DLTs during the DLT observation period (28 days following C1D1)Objective response (CR, PR) as defined by RECIST v1.1 criteria

4.3 Secondary Objectives

- Further assess the overall safety profile of PF-07901801 administered in combination with 40 mg/m^2 PLD

- Assess additional efficacy outcomes

4.4 Secondary Endpoints

- Overall safety profile as assessed by the type, frequency, severity, timing and causal relationship of any adverse events, changes in vital signs, ECG, serum chemistry or other laboratory assessment, treatment delays or discontinuations

- PFS, OS, disease control (DC [CR or PR or SD]), and DOR

4.5 Exploratory Objectives

- Assess effect of treatment with PF-07901801 in combination with PLD on CA-125 levels

- Characterize the PF-07901801 concentration in serum when administered in combination with PLD

- Characterize the PLD concentration in plasma when administered in combination with PF-07901801

- Assess DDI potential between PF-07901801 and PLD

- Evaluate development of antibodies directed against PF-07901801
- Explore possible relationships between PF-07901801 exposure and clinical outcome, safety and pharmacodynamics observations.
- Understand the relationship between the therapeutic intervention(s) being studied and the biology of the participant's disease.

4.6 Exploratory Endpoints

- Evaluate CA-125 levels in serial blood samples
- Measurements of biomarkers/pharmacodynamics, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study.
- Immunogenicity: Incidence and titers of ADA and neutralizing antibodies against PF-07901801
- PF-07901801 PK: Single and multiple Dose C_{max}, CCI [redacted], and clearance.
- PLD PK: Single and multiple dose C_{max} and C_{trough}.

5 INVESTIGATIONAL PLAN

5.1 Overall Study Design

Pegylated liposomal doxorubicin (PLD) is a standard treatment option for patients with platinum-resistant recurrent epithelial ovarian cancer who are not candidates for chemotherapy in combination with bevacizumab. However, despite being considered a standard treatment option, the clinical benefit of chemotherapy for this patient population is small. The goal of this clinical trial is to improve upon the activity of PLD in a safe manner to provide a more effective therapeutic option for this group of patients.

TTI-622-02/C4971002 is a multi-center, open-label study designed to evaluate PF-07901801 administered in combination with PLD in participants with platinum-resistant recurrent epithelial ovarian cancer, including ovarian, peritoneal and fallopian tube malignancy, and for whom PLD is a reasonable treatment option. The first portion of the study will evaluate the safety of increasing dose levels of PF-07901801 in combination with PLD at 40 mg/m^2 in participants with platinum-resistant EOC, including ovarian, peritoneal and fallopian tube malignancy, and establish a combination regimen for further evaluation in a dose expansion cohort. The study will consist of a 28-day screening period, a treatment period in which participants will receive PF-07901801 in combination with PLD in 28-day cycles until documentation of objective disease progression or development of unacceptable toxicity, and a long-term follow-up period to assess overall survival.

Key inclusion criteria are ECOG performance status 0-1, platinum-resistant recurrent epithelial ovarian cancer, defined as disease progression ≤6 months after the most recent platinum-based

treatment regimen or participants who were no longer able to receive or declined treatment with platinum-based chemotherapy, no more than four prior treatment regimens for platinum-resistant disease, measurable disease by RECIST v1.1, absence of bowel obstruction history, and adequate cardiac and end organ function. Participants with exposure to PLD while platinum-resistant or in the treatment regimen immediately prior to enrollment in this study, will not be eligible for treatment under this protocol; however, earlier exposure to PLD, including while platinum-sensitive, or for an indication other than recurrent platinum-resistant EOC, eg, breast cancer, will be allowed for participants in the Phase 1 dose escalation portion of the study. In the Phase 2, dose expansion portion of the study, depending on clinical benefit during Phase 1, earlier exposure to PLD, including while platinum-sensitive, may be allowed if agreed upon by the investigators and Pfizer. Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin.

In the Phase 1 dose escalation portion of the study, the primary objectives are assessment of DLTs, safety and tolerability of escalating dose levels of PF-07901801 in combination with PLD at the standard dose of 40 mg/m^2 and establish the MTD and RP2D. Up to approximately 18 participants are planned to be enrolled in this portion of the study to evaluate three dose levels of PF-07901801: 12 mg/kg (Dose Level 1), 24 mg/kg (Dose Level 2) and 48 mg/kg (Dose Level 3). In Cycle 1 for dose levels 1 and 2, PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 in combination with PLD on Day 1 of 28-day cycle. Beginning with Cycle 2 at dose levels 1 and 2, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow PF-07901801 levels to more quickly reach steady state. For dose level 3, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. Loading doses (Day 8 and Day 22) may be considered for Cycle 1 at the 48 mg/kg dose level if found to be safe and offer clinical benefit for participants. If Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg.

One dose level combination will be selected for further evaluation in the Phase 2 expansion portion of the study. The primary objective of the Phase 2 expansion portion of the study is investigation of clinical activity of the PLD and PF-07901801 combination; clinical activity will be assessed using the overall response by RECIST v1.1 as the primary efficacy endpoint.

Secondary objectives include further evaluation of the safety of the combination and assessment of other indications of disease control, including progression-free survival, overall survival, duration of response, and disease control (CR, PR, or SD ≥ 12 weeks) as defined by RECIST v1.1 criteria.

Exploratory objectives include, evaluation of CA-125 levels, characterization of PF-07901801 and PLD pharmacokinetics when co-administered, evaluation of development of antibodies directed against PF-07901801; exploration of possible relationships between PF-07901801 exposure and clinical outcome, safety and pharmacodynamics observations, and to understand the relationship between the therapeutic intervention(s) being studied and the biology of the

participant's disease. Exploratory endpoints include but are not limited to PK and immunogenicity of PF-07901801, PK of PLD, CA-125 levels, measurements of biomarkers/pharmacodynamics, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study, as well as the single and multiple dose pharmacokinetics of PF-07901801.

PLD will be administered at 40 mg/m^2 on Day 1 of each 28-day cycle.

PF-07901801 will be administered by intravenous infusion; the duration of infusion is dependent on dose level with dose levels less than or equal to 33 mg/kg infused over 60 min and doses greater than 33 mg/kg infused over 90 minutes and will have doses equal to or less than 2500 mg in 250 mL and doses 2501 mg or more in 500 mL or neat drug if the drug volume is over 500 mL. Medications to treat infusion-related reactions and CPR equipment must be available for immediate use prior to initiation of PLD infusion.

The dose-limiting toxicity evaluation period will consist of the 28-day Cycle 1 or until participants experience a DLT in Cycle 1. Participants will be considered DLT evaluable if they receive PLD on Day 1 and at least two infusions of PF-07901801 in the 28-day Cycle 1. A participant who withdraws from the study during Cycle 1 in the absence of DLT evaluable (ie, not receiving PLD and at least two doses of PF-07901801) will be replaced If a dose-limiting toxicity as defined in Section 5.4 is encountered in one participant in the initial three participants in a dose cohort, three additional participants will be enrolled in accordance with the standard 3+3 study design. The maximum tolerated dose (MTD) for this study will be defined as the highest PF-07901801 dose level at which <33% of participants within a dose cohort experience dose-limiting toxicity when administered in combination with PLD at 40 mg/m^2. While three pre-defined PF-07901801 dose levels are anticipated, intermediate dose levels may be studied to more closely characterize the safety profile of PF-07901801 in combination with PLD.

After three to six participants in a dose cohort complete the 28-day dose-limiting toxicity assessment period, the incidence of dose-limiting toxicity, treatment-related safety observations and other available data, such as pharmacokinetic data, will be reviewed by the medical monitor, sponsor and investigators. If no participant in a three-participant cohort or no more than one participant in a six-participant dose cohort experiences treatment-related dose-limiting toxicity, the dose level will be deemed safe and dose escalation may proceed unless there are other unsuspected but concerning safety observations that suggest either an expansion of the current dose level or implementation of an intermediate dose level.

Objective disease assessments will be performed after every 8 (±1) weeks through week 48, or until participant has been on study for one year, and every 12 (±2) weeks thereafter. Participants who withdraw from the study without objective evidence of disease progression will be followed until documentation of disease progression or initiation of another treatment. All participants will be followed in the Long-Term Follow-Up period for survival.

5.2 Doses and Schedule of Administration of Investigational Agents

PLD will be administered on Day 1 of 28-day cycles.

In Cycle 1 for dose levels 1 (12 mg/kg) and 2 (24 mg/kg), PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 of a 28-day cycle. Beginning with Cycle 2, PF-07901801 will be administered on Day 1 and Day 15 only of each 28-day cycle.

For dose level 3 (48 mg/kg) PF-07901801 will be administered on Day 1 and 15 of a 28-day cycle starting from Cycle 1. Loading doses (Day 8 and Day 22) may be considered for Cycle 1 at the 48 mg/kg dose level if found to be safe and offer clinical benefit for participants. If Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg.

The following rules apply during dose escalation:

- Starting dose at dose level 1 is 12 mg/kg.
- At least 3 participants will be enrolled at each dose level. When all participants at a dose level complete DLT assessments, the study will escalate to the next dose level and another 3 participants will be recruited in this order until MTD/RP2D.
- If agreed upon by the investigators and Pfizer (eg, based on safety, incidence of DTL, PK and dose-exposure data from prior and current cohorts) that increasing the dose further may not yield additional benefit, the dose may stay at the current dose level, be de-escalated to any dose, or no future escalation may be made, even if the dose escalation rule indicates to escalate.
- The need for dose escalation to a specific dose beyond 48 mg/kg or de-escalation to an intermediate dose level will be evaluated jointly by investigators and Pfizer based on cumulative clinical safety, PK, and preliminary efficacy data.

Table 11. Participants Dose-Grouping, Dose Escalation Plan

Cohort #/Dose Level	Dose of PF-07901801 (Intravenous)	Dose of PLD (Intravenous)
1	12 mg/kg	40 mg/m^2
2	24 mg/kg	40 mg/m^2
3	48 mg/kg	40 mg/m^2

• Participants will be considered DLT evaluable if they receive PLD on Day 1 and at least two infusions of PF-07901801 in the 28-day Cycle 1

• A participant who withdraws from the study during Cycle 1 in the absence of DLT evaluable (ie, not receiving PLD and at least two doses of PF-07901801) will be replaced

- Participants who complete the DLT assessment window will be allowed to continue treatment until disease progression, intolerable toxicity, withdrawal of consent, lost to follow-up, end of study, or death, whichever comes first.
- Participants with an early observation of disease progression, but without deterioration in clinical conditions or unacceptable toxicitywill be allowed to continue treatment until disease progression is verified by repeated disease assessment at least 4-weeks later.

A participant who completes at least four cycles of treatment with PF-07901801 in combination with PLD and requires discontinuation of PLD due to PLD-related toxicity and who is receiving disease control may continue on study receiving PF-07901801 monotherapy beginning with the next cycle provided the participant has not experienced disease progression and PF-07901801 re-treatment guidelines as described in Section 9.1.2 are met. The investigator may consult with the medical monitor on a participant -by-participant basis in the event that early evidence of doxorubicin-related toxicity arises.

On Day 1 of each cycle, PLD will precede administration of PF-07901801. An observation period between completion of PLD infusion and initiation of PF-07901801 infusion is not mandated.

5.2.1 PLD

Pegylated liposomal doxorubicin will be administered intravenously at a dose of 40 mg/m^2 on Day 1 of each 28-day cycle. Doses up to 90 mg must be diluted in 250 mL of 5% Dextrose Injection, USP for administration to the participant; doses exceeding 90 mg will be diluted in 500 mL of 5% Dextrose Injection, USP for administration to the participant. The initial infusion rate should be 1 mg/min to minimize the risk of infusion reactions. If no infusion-related adverse reactions are observed, the rate of infusion can be increased to complete administration of the drug over one hour in accordance with institutional guidelines.

The dose of PLD should be calculated at the beginning of each cycle.

5.2.2 PF-07901801

PF-07901801 will be administered by intravenous infusion on Day 1, Day 8, Day 15 and Day 22 of the 28-day Cycle 1and on Day 1 and Day 15 of subsequent 28-day cycles (i.e., Cycle 2 onward) for dose levels 1 and 2. For dose level 3, PF-07901801 will be administered by intravenous infusion on Day 1 and 15 of a 28-day cycle starting from Cycle 1.

The dose of PF-07901801 will be based upon the dose level cohort to which the participant is assigned; the duration of infusion is dependent on dose level: dose levels less than or equal to 33 mg/kg infused over 60 min and doses greater than 33 mg/kg infused over 90 minutes and will have doses equal to or less than 2500 mg in 250 mL and doses 2501 mg or more in 500 mL or neat drug if the drug volume is over 500 mL. At the investigator's discretion, the duration of infusion can be lengthened but not abbreviated. Preparation instructions can be found in the IPM.

In any cycle in which PLD and PF-07901801 are administered on the same day, PLD treatment will precede administration of PF-07901801. A delay before initiation of PF-07901801 (TTI-622) is not mandated.

For the purposes of safety decisions that guide cohort expansion and considerations of PF-07901801 dose adjustment, the safety period will consist of the 28-day Cycle 1.

A participant who completes at least four cycles of PF-07901801 in combination with PLD and experiences PLD-mediated toxicity that requires its discontinuation may revert to PF-07901801 monotherapy with the next cycle provided the participant has not experienced

disease progression and PF-07901801 re-treatment guidelines as described in Section 9.1.2 are met.

Preparation of the PF-07901801 dose is based on body weight in kg and should be calculated at the beginning of each cycle and may be used throughout the cycle unless a participant experiences a >10% variation in weight within a cycle.

As described previously and presented again in Table 12 below, three dose levels of PF-07901801 are planned to be evaluated in combination with fixed-dose PLD in a 3+3 study design in the dose escalation portion of the study. After review of emerging safety and other data from these dose levels, alternate PF-07901801 dose levels may be evaluated to more fully understand safety or pharmacodynamics of PF-07901801 in combination with PLD, to more fully identify dose-limiting toxicities, to more clearly define the maximum tolerated dose, and/or to optimize selection of the most appropriate dose(s) for evaluation in the expansion cohorts.

Table 12. PF-07901801 Dose Levels Planned for Evaluation in Combination with PLD

Dose Level	PF-07901801 Dose
1	12 mg/kg
2	24 mg/kg
3	48 mg/kg

If Dose Level 1, 12 mg/kg, is found to be intolerable, a lower dose level may be evaluated. If Dose Levels 2 or 3 are not tolerated, intermediate dose levels may be evaluated.

5.3 Criteria for Treatment Discontinuation

Participants may withdraw voluntarily from participation in the study or from study treatment at any time and for any reason. A participant ’s participation in the study may terminate at his/her/their request or on the basis of the investigator’s clinical judgment. The reason for participant withdrawal will be documented in the source data and noted on the electronic case report form (eCRF).

At a minimum, all participants who discontinue study treatment, including those who refuse to return for a final visit, will be contacted for safety evaluations at the 30-Day Safety Follow-Up Visit.

If such withdrawal occurs, or if the participant fails to return for visits, the investigator must determine the primary reason for a participant’s withdrawal from the study and record the information on the eCRF. If the reason for withdrawal is an adverse event, monitoring should continue until the outcome is evident. The specific event or test result(s) must be recorded in the eCRF. At the discretion of the sponsor, participants may also be removed from the study.

It should be clearly documented in the source data whether participants withdrew consent for participation in the study, including study treatment and participation in the long-term follow-up phase or if participants withdrew from study treatment but will continue further participation in the long-term follow-up portion of the study.

Treatment may be continued until one of the following criteria applies:

- An unacceptable adverse event or safety observation, such as a persistent moderate toxicity that is intolerable to the participant, that is in the opinion of the investigator clearly attributed to PF-07901801.

- An unacceptable adverse event or safety observation, such as a persistent moderate toxicity that is intolerable to the participant, that is in the opinion of the investigator clearly attributed to PLD and the participant has received fewer than four cycles of PLD. A participant who has completed four cycles of PLD treatment and experiences an adverse event that requires discontinuation of PLD may continue on study receiving PF-07901801 monotherapy after discussion with the sponsor medical monitor.

- Any event which would cause PF-07901801 or PLD to be modified by more than two dose reductions or to be held for more than 42 days from the last administered dose and is not attributable to a particular agent of the combination regimen; exception is made for participants who are receiving meaningful disease control and the investigator feels, with sponsor medical monitor concurrence, that continued treatment is in the best interest of the participant.

- Any treatment-related adverse event that is deemed life-threatening, regardless of grade. For Grade 4 adverse events, discontinuation of PF-07901801 should be considered. If it is in the participant's best interest to continue PF-07901801 per investigator assessment, withhold dose until resolved to ≤Grade 1 or baseline, then reduce by 1 dose level. If the participant is receiving disease control and the investigator judges that continued treatment may be in the participants best interest, PF-07901801 treatment may be resumed when the adverse event resolves to a level that meets re-treatment criteria. In consultation with the sponsor medical monitor, the dose level may be resumed; exception is made for participants in whom the life-threatening adverse event is attributed to PLD and the participant has received at least four cycles of PLD treatment and the investigator feels, with sponsor medical monitor concurrence, that continuation with PF-07901801 monotherapy would be reasonable.

- Documentation of objective (radiographic) disease progression; for participants with asymptomatic progression and in the absence of unacceptable toxicity, the participant should continue treatment and a confirmation scan should be conducted at least four weeks later to document objective progression prior to removing participant from study treatment. A participant should not be removed from study on the basis of change in CA-125 level in the absence of objective or asymptomatic progression.

    - The mechanism of immunotherapy is mechanistically distinct from other types of therapy. The patterns of response and progression to immunotherapeutic agents, such as TTI-622, often differ temporally, qualitatively and quantitatively from those observed with cytotoxic and targeted agents. The goal of immunotherapy is to overcome immunosuppression induced by a tumor and its microenvironment, thereby allowing the immune system to develop or activate an immune response that

targets and kills cancer cells. Some patients have experienced pseudo-progression or immune-mediated inflammation, in which areas of disease showed an initial surge followed by shrinkage that led to development of immune-related disease response criteria that supports continued treatment beyond progression in patients whose clinical conditions have not worsened and who have not experienced severe toxicities. Recognizing that immunotherapy represents a paradigm shift in oncology treatment, patients with an early observation of disease progression but without deterioration in clinical conditions or unacceptable toxicity and who consent should continue treatment until disease progression is verified by a repeated disease assessment at least four weeks later.

- Unacceptable toxicity which in the opinion of the investigator cannot be attributed to a specific study agent.
- An intercurrent illness or change in the participant's condition that renders the participant unsuitable for further treatment in the opinion of the investigator; exception may be made for participants in whom the intercurrent illness or change in condition is thought to render the participant ineligible for continued treatment with PLD and the participant has received at least four cycles of PLD and the investigator feels, with medical monitor concurrence, that continuation with PF-07901801 monotherapy would be reasonable and the participant meets criteria for PF-07901801 re-treatment
- Significant noncompliance with study protocol.
- Withdrawal of consent for participation in the treatment portion of the study (participant may participate in Long-Term Follow-Up assessment of survival and disease status [if withdrawn prior to documentation of objective disease progression] if consent for Long-Term Follow-Up assessment is not withdrawn).
- Participant is lost to follow-up.
- Termination of the study by the sponsor.

At the investigator's discretion and in agreement with the sponsor, treatment after objective disease progression may continue for a participant who is clinically stable and receiving meaningful disease control and the investigator feels it is in the participant's best interest to continue treatment. The reason for continuing treatment must be thoroughly discussed, agreed with the sponsor medical monitor, and clearly documented in the study files.

5.4 Dose-Limiting Toxicity Criteria for the Dose Escalation Portion of the Study

Dose-limiting toxicity is defined as any of the following treatment-emergent adverse events that occurs during the 28-day Cycle 1 and are judged by the investigator as related to PF-07901801 or the combination of PF-07901801 and PLD. Adverse events that are in the opinion of the investigator attributable exclusively to intravenous infusion of PLD or any PLD prophylaxis medication will not be considered a dose-limiting toxicity.

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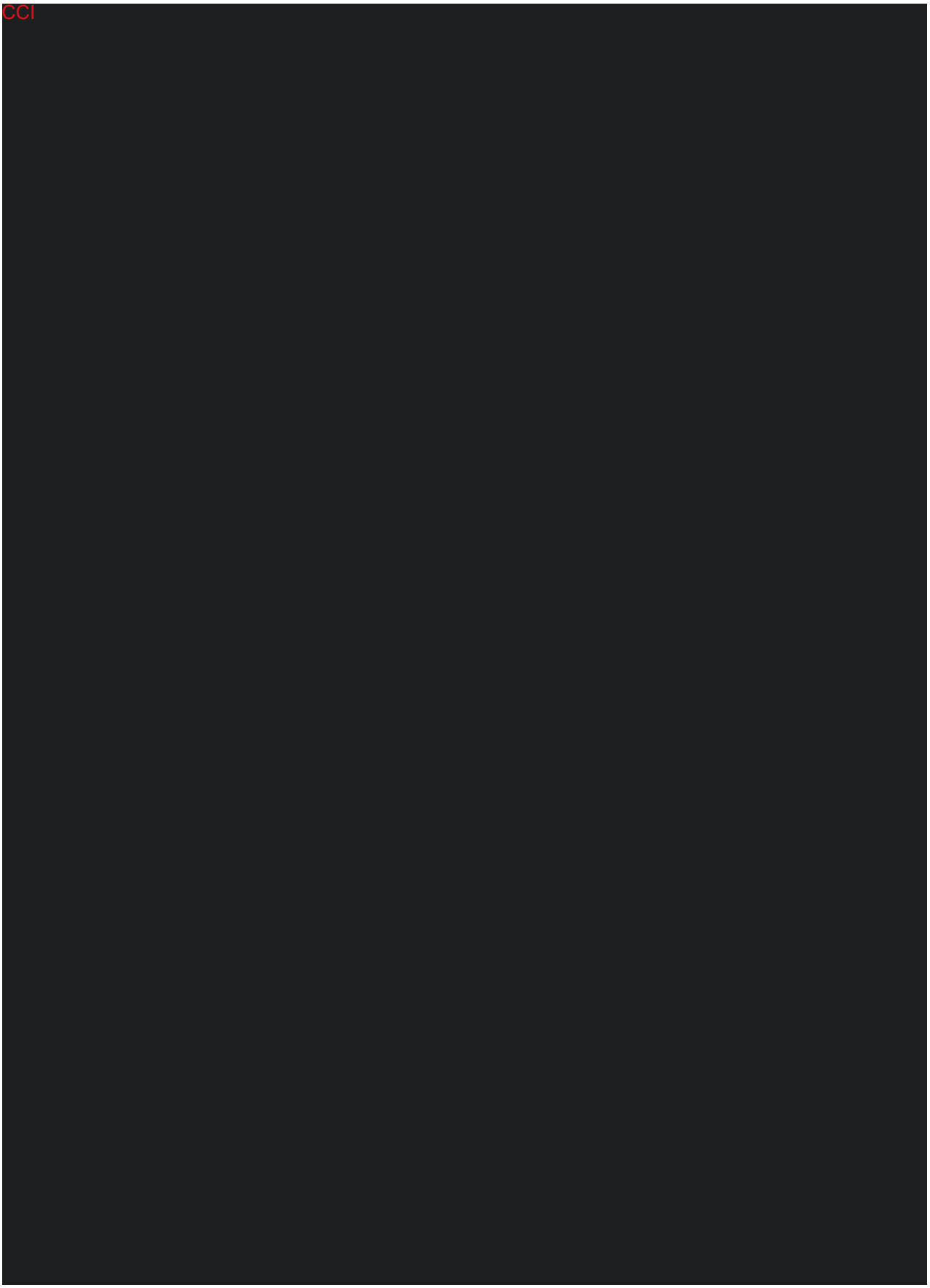

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6 STUDY POPULATION

6.1 Number of Participants

Up to approximately 50 participants are anticipated to participate in the study, with up to 18 DLT-evaluable in the Phase 1 dose escalation portion of the study and up to 30 treated in the Phase 2 dose expansion portion.

6.2 Inclusion Criteria

Participant must meet all the following criteria to be enrolled in the study:

General

1. Written informed consent obtained prior to performing any study-specific procedure, including screening procedures

2. Females ≥ 18 years of age

3. ECOG Performance Status 0 or 1

Disease Characteristics

4. Histologically-confirmed epithelial ovarian cancer (EOC), fallopian tube carcinoma (FTC) or primary peritoneal carcinomas (PPC).

   Eligible histological subtypes are:

   - Adenocarcinoma NOS
   - Clear cell adenocarcinoma
   - Endometrioid adenocarcinoma
   - Malignant Brenner's tumor
   - Mixed epithelial carcinoma
   - Mucinous adenocarcinoma
   - Serous adenocarcinoma
   - Transitional cell carcinoma
   - Undifferentiated carcinoma

5. Platinum-resistant recurrent disease, defined as disease progression ≤6 months after the most recent platinum-based treatment regimen (date calculated from the last administered dose of platinum) or the participant is no longer able to receive or declined treatment with platinum-based chemotherapy

   - Includes standard of care therapies, including platinum-based therapies, PARP inhibitors (Poly ADP Ribose Polymerase) or bevacizumab in the

platinum-sensitive setting or intolerability to such therapies or participant refusal

6. Measurable disease per RECIST v1.1; target lesions must not be chosen from a previously-irradiated field unless there has been radiographically and/or pathologically documented tumor progression in that lesion prior to enrollment.

Organ Function

Adequate organ and hematologic function as defined below:

7. Serum AST and ALT ≤3 x upper limit of normal (ULN); ≤5 x ULN in the presence of liver metastasis

8. Serum bilirubin (total) ≤1.5 x ULN (≤2 x ULN if hyperbilirubinemia is due to Gilbert's syndrome)

9. Serum creatinine ≤1.5 x ULN OR creatinine clearance/estimated glomerular filtration rate (eGFR) ≥40 mL/min/1.73 m^2 if serum creatinine is >1.5 x ULN

10. Hemoglobin ≥9 g/dL; packed red blood cell transfusions are not allowed in the two weeks preceding screening evaluation

11. ANC ≥1.5 × 10^9/L

12. Platelet count ≥100 × 10^9/L

13. Left ventricular ejection fraction (LVEF) determined by echocardiogram or multigated acquisition scan >50% at screening

Previous Therapy

14. Unlimited lines of therapies in the platinum-sensitive setting are allowed. Once a participant becomes platinum-resistant no more than four prior treatment regimens for platinum-resistant disease are allowed

    - If bevacizumab was not used as a treatment option during the platinum-sensitive setting, then bevacizumab in combination with paclitaxel must be considered as the first-line platinum-resistant treatment option except in the case of intolerability to such therapies or participant refusal.

15. Participants with exposure to PLD while platinum-resistant or in the treatment regimen immediately prior to enrollment in this study, will not be eligible for treatment under this protocol; however, earlier exposure to PLD, including while platinum-sensitive, or for an indication other than recurrent platinum-resistant EOC, eg, breast cancer, will be allowed for participants in the Phase 1 dose escalation portion of the study. In the Phase 2, dose expansion portion of the study, depending on clinical benefit during Phase 1, earlier exposure to PLD, including while platinum-sensitive, may be allowed if agreed upon by the investigators and Pfizer.

Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin

16. All adverse events from prior treatment must be NCI CTCAE v5 Grade ≤ 1, except alopecia and stable neuropathy, which must have resolved to Grade ≤ 2 or baseline

Contraception

17. Female participants of childbearing potential (CBP) who participate in the study should be counseled on the need to practice adequate birth control and on the importance of avoiding pregnancy during study participation. Please refer to Section 6.6 and Appendix C for detailed reproductive criteria

18. Female participants of childbearing potential must have a serum pregnancy test at screening. Following screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL. A negative pregnancy test result at screening and at baseline is required before the first study drug administration

6.3 Exclusion Criteria

1. Platinum-refractory disease, defined as progression on or within 3 months of completing primary first-line platinum-based treatment

2. Malignant mixed Mullerian tumors

3. Ovarian tumors with low malignant potential (i.e., borderline tumors), low grade serous ovarian cancer

Cardiovascular System

4. History of acute coronary syndromes, including myocardial infarction, coronary artery bypass graft, unstable angina, coronary angioplasty or stenting within 24 weeks prior to first administration of study drug

5. History of or current Class II, III or IV heart failure as defined by the New York Heart Association (NYHA) functional classification system or symptomatic or poorly controlled cardiac arrhythmia

6. Uncontrolled or poorly-controlled hypertension (defined as systolic blood pressure >160 mm Hg and/or diastolic > 100 mg Hg) for more than four weeks despite optimal medical management

7. Peripheral vascular disease > Grade 3 (i.e., symptomatic and interfering with activities of daily living requiring repair or revision)

General and Infectious Disease

8. Investigator site staff directly involved in the conduct of the study and their family members, site staff otherwise supervised by the investigator, and sponsor and sponsor delegate employees directly involved in the conduct of the study and their family members

9. Any comorbidity or concomitant medication or other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation that in the opinion of the investigator and/or sponsor medical monitor renders the participant unsuitable for participation in the trial or unlikely to fully comply with study procedures, restrictions and/or requirements that are considered relevant for evaluation of the efficacy or safety of the trial drug

10. Uncontrolled intercurrent illness, including active or chronic uncontrolled bacterial, fungal, or viral infection, including (but not limited to) HBV, HCV, and known HIV or AIDS related illness requiring systemic therapy or oral or systemic antibiotics within 14 days prior to study start. Participants with HIV with an undetectable viral load and a CD4 count ≥400 μL are eligible

11. History of non-viral hepatitis or cirrhosis, alcohol abuse or active tuberculosis

12. Administration of live attenuated vaccines within 28 days prior to start of treatment or anticipated need for vaccination with live attenuated vaccine during the study

13. COVID-19/SARS-CoV-2: While SARS-CoV-2 testing is not mandated for entry into this study, testing should follow local clinical practice standards. If a participant has a positive test result for SARS-CoV-2 infection, is known to have asymptomatic infection or is suspected of having SARS-CoV-2, the participant is excluded until a negative antigen test and resolution of symptoms if applicable

14. Major surgery within 28 days of scheduled Cycle 1 Day 1 dosing or minor surgery within seven days prior to initiation of study treatment or elective or planned major surgery to be performed during the course of the clinical trial

CNS Disease Considerations

15. History or evidence of known CNS metastases or carcinomatous meningitis; participants with previously treated brain metastases may participate provided they are stable (without evidence of progression by imaging for at least four weeks prior to the first dose of trial treatment and any neurologic symptoms have returned to baseline), have no evidence of new or enlarging brain metastases, and are not using steroids for at least seven days prior to study treatment; this exception does not include carcinomatous meningitis which is excluded regardless of clinical stability

Coagulation Considerations

16. Significant bleeding disorders, vasculitis or a significant bleeding episode within three months prior to study entry. Ongoing prophylactic anticoagulation therapy at a stable dose for prevention of VTE (Venous Thromboembolism) are allowed. Note:

Participant on therapeutic anticoagulation must not be started on study before therapy is completed and prophylactic anticoagulation is established.

Immune System

17. History of severe hypersensitivity reactions to antibodies

18. Chronic systemic steroid therapy (>10 mg daily prednisone or equivalent) or any other form of immunosuppressive therapy within seven days prior to the first dose of study treatment; topical, inhaled, nasal and ophthalmic steroids are not prohibited; Intermittent prophylaxis per site institutional policy is not prohibited as long as it does not exceed chronic daily use of >10 mg prednisone or equivalent e.g. prophylactic use of steroids for Palmar Plantar Erythrodysesthesia (PPE) toxicity with PLD is allowed.

19. History of autoimmune disease that has required systemic treatment with disease-modifying agents, corticosteroids, or immunosuppressive drugs unless in the opinion of the investigator the participant is in a complete and durable remission; physiologic replacement therapies, such as thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, is allowed

20. Prior organ transplantation including allogeneic or autologous stem cell transplantation

Oncology

21. Concurrent or previous other malignancy within two years of study entry with the exception of cured basal or squamous cell skin cancer, superficial bladder cancer, carcinoma *in situ* of the cervix, other non-invasive or indolent malignancy, surgically-excised malignancy that is considered cured

22. Concurrent enrollment in another therapeutic clinical study

23. Prior treatment with anti-CD47 or anti-SIRPα therapy

6.4 Re-Screening

A participant who fails to qualify for the study based on laboratory tests may be considered for rescreening at the discretion of the investigator and after consultation with the sponsor medical monitor if it is considered that the participant status has changed and the participant may now qualify for the study. Screening is limited to 2 attempts (initial screening and 1 rescreening attempt).

6.5 Waivers of Inclusion/Exclusion Criteria

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

6.6 Participants of Reproductive Potential

The investigator or their designee, in consultation with the participant, will confirm that the participant is using an appropriate method of contraception for the individual participant and their partner(s) from the permitted list of contraception methods (see Appendix C) and will confirm that the participant has been instructed in its consistent and correct use. At time points indicated in the SoA (Table 28), the investigator or designee will inform the participant of the need to use highly effective contraception consistently and correctly and document the conversation and the participant's affirmation in the participant's chart. Participants need to affirm their consistent and correct use of the selected methods of contraception (refer to Appendix C), considering that their risk for pregnancy may have changed since the last visit.

In addition, the investigator or designee will instruct the participant to call immediately if the selected contraception method is discontinued and document the requirement to use an alternate protocol-specified method, including if the participant will no longer use abstinence as the selected contraception method, or if pregnancy is known or suspected in the participant or partner.

Pregnancy testing will be conducted prior to administration of IP and throughout study participation on every woman of childbearing potential. A woman who is found to be pregnant at the screening visit will be excluded from the study and considered to be a screen failure.

A serum pregnancy test is required at screening. Following screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL. Pregnancy tests will be performed in WOCBP at the times listed in the Schedule of Assessments (Table 28). Following a negative pregnancy test result at screening, appropriate contraception must be commenced and a second negative pregnancy test result will be required at the baseline visit prior to the participant receiving the study treatment. Pregnancy tests will also be done whenever one menstrual cycle is missed during the active treatment period (or when potential pregnancy is otherwise suspected) and at the end of the study. Pregnancy tests may also be repeated if requested by IRBs/ECs or if required by local regulations. If a urine test cannot be confirmed as negative (e.g., an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded if the serum pregnancy result is positive.

Participants will be instructed to notify the investigator if pregnancy is discovered either during or within 45 days after the last dose of PF-07901801 or during and six months after the last dose of PLD in combination treatment (as per the full prescribing information in the USPI for PLD [DOXIL®]), which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). The investigator must report information to Pfizer Safety through Pfizer SAE Submission Assistant (PSSA) using the CT SAE Report Form and EDP Supplemental Form.

7 ENROLLMENT PROCEDURE AND METHOD OF ASSIGNING SUBJECTS TO TREATMENT GROUPS

7.1 Enrollment Procedure

At the time a prospective patient signs the informed consent form, a unique patient number will be assigned and the appropriate portion of a Registration/Enrollment form will be completed and sent to the sponsor or designee. Patients will be screened for eligibility according to the criteria outlined in Section 6. Once a patient is deemed eligible, the completed Registration/Enrollment form will be sent to the investigator or designee, at which time the PF-07901801 dose level and cohort will be assigned.

7.2 Method of Assigning Subjects to Treatment Groups

The dose escalation portion of the study carries a traditional 3+3 design to evaluate three dose levels of PF-07901801 in combination with fixed-dose PLD (40 mg/m^2). Standard guidelines for enrollment for the 3+3 design will be followed, with requirement that three participants complete the 28-day safety assessment period before the next dose cohort is open to enrollment and expansion to six participants in the case of a treatment-related dose-limiting toxicity.

Only a single PF-07901801 dose level in combination with fixed-dose PLD (40 mg/m^2) is planned for evaluation in the dose expansion portion of the study. During the dose expansion portion of the study, eligible participants will be enrolled into this cohort in chronological order of eligibility verification as they complete screening assessments.

8 DESCRIPTION OF STUDY TREATMENT

8.1 PF-07901801

CCI

8.1.1 How Supplied

Sterile formulated PF-07901801 Drug Product is supplied at a concentration of 10 mg/mL in single-use 20 mL Type I borosilicate glass vials with butyl rubber stoppers and aluminum seals. The extractable volume is 14 mL PF-07901801 Drug Product.

8.1.2 Storage Conditions

PF-07901801 Drug Product storage conditions and allowances at clinical sites based on evolving stability data is provided in the Pharmacy Manual.

8.2 Pegylated Liposomal Doxorubicin

The active ingredient in doxoribucin hydrochloride liposome injection is doxorubicin hydrochloride that is encapsulated in liposomes for intravenous use. Doxorubicin hydrochloride liposome injection is a sterile, translucent, red liposomal dispersion. Each single-dose vial of doxorubicin hydrochloride liposome injection contains 20 mg (20 mg/10 mL in a 10 mL vial) or 50 mg (50 mg/25 mL in a 30 mL vial) doxorubicin hydrochloride at a concentration of 2 mg/mL (equivalent to 1.87 mg/mL of doxorubicin) and at a pH of 6.5. Unopened vials should be refrigerated at 2°C to 8°C (36°F to 46°F); do not freeze.

8.3 Preparation and Administration of Study Treatments

All administration of study treatments should be performed in a setting with emergency medical facilities and staff who are trained to monitor for and respond to medical emergencies.

8.3.1 PF-07901801

The required number of vials of PF-07901801 Drug Product, determined based on the dose level and participant's body weight, will be prepared.

See the IP Manual for instructions on how to store and prepare the study intervention for administration. Study intervention should be prepared and dispensed by an appropriately qualified and experienced member of the study staff (eg, physician, nurse, physician's assistant, nurse practitioner, pharmacy assistant/technician, or pharmacist) as allowed by local, state, and institutional guidance. A second staff member will verify the dispensing.

8.3.2 Pegylated Liposomal Doxorubicin

8.4 Pegylated liposomal doxorubicin will be administered per the approved package insert. The IP Manual should be referenced for additional information.Blinding of Treatment

This is an open-label study; study treatments will not be blinded.

8.5 Treatment Compliance

The study treatments will be administered by personnel at the study site to ensure compliance.

8.6 Study Drug Accountability

Study personnel will maintain accurate records of study drug shipments, receipt and dispensing. The site is responsible for the return or destruction of PF-07901801 as required.

8.7 Concomitant Medications

Participants are allowed to continue medications that they are taking at baseline. Participants may also receive concomitant medications that are medically indicated for the treatment of symptoms and intercurrent illnesses. Medications to treat concomitant diseases, e.g., diabetes, hypertension, chronic obstructive pulmonary disease, are allowed. Prophylaxis for infusion-related reactions is not mandated but the investigator at his/her/their discretion may provide prophylaxis medications to prevent development of infusion-related reactions prior to infusions of PF-07901801 or PLD; the participant may receive therapy for symptom control and/or to mitigate side effects of the study medication as clinically indicated, as well as best supportive care as per institutional guidelines. This may include, e.g., anti-emetics, anti-diarrheals, anti-cholinergics, anti-spasmodics, anti-pyretics, anti-histamines, analgesics, antibiotics and other medications such as analgesics, electrolyte replacement, hydration, and/or blood product transfusions intended to treat symptoms. Other prescribed medications for non-neoplastic conditions are allowed, as well as vitamins and nutritional supplements (at doses per the Recommended Dietary Allowance or supplementing a known deficiency). The investigator should instruct the participant not to take any additional medications (including over-the-counter products) during the study without prior consultation.

All concomitant medications, including dose and reason for administration, will be recorded in the eCRF.

8.7.1 Concomitant Corticosteroids

Chronic use of steroid above a daily equivalent dose of 10 mg prednisone is not permitted on study; Intermittent prophylaxis per site institutional policy is not prohibited as long as it does not exceed chronic daily use of >10 mg prednisone or equivalent e.g. prophylactic use of steroids for Palmar Plantar Erythrodysesthesia (PPE) toxicity with PLD is allowed

8.7.2 Concomitant Hematopoietic Growth Factors and Blood Products

Participants must have adequate hematological function with no transfusion or colony stimulating factor or erythropoiesis-stimulating agent for at least 2 weeks prior to Cycle 1 Day 1.

Primary prophylactic use of colony stimulating factors or erythropoiesis-stimulating agents or blood product transfusions are not permitted during the first 28 days of Phase 1 Cycle 1 (DLT evaluation period), unless indicated due to medical emergency.

Beginning with Cycle 2,myeloid growth factors are permitted for treatment-emergent Grade 3 or Grade 4 neutropenia. Likewise, erythropoiesis-stimulating or megakaryopoiesis-stimulating agents may be used for treatment-emergent anemia or thrombocytopenia, respectively and , prophylactic use of G-CSF according to institutional standards is permitted.

Transfusion thresholds for blood product support will be in accordance with institutional guidelines.

8.7.3 Concomitant Anti-Coagulants

Ongoing prophylactic anticoagulation therapy at a stable dose (low molecular weight heparin, heparin, warfarin or dabigatran) for prevention of Cancer-Associated Venous Thromboembolic Disease, per local institutional guidelines is permitted. Note: Participants on therapeutic anticoagulation must not be started on study before therapy is completed and prophylactic anticoagulation is established.

8.7.4 Prohibited Medications and Potential Drug-Drug Interactions

There are currently no drugs identified to have potential DDI concerns with PF-07901801.

Investigators should consult the USPI for PLD for information regarding medication that are prohibited for concomitant use.

The Pfizer study team is to be notified of any prohibited medications taken during the study. After consulting with the sponsor, the investigator will make a judgment on the ongoing participation of any participant with prohibited medication use during the study.

a. Participants must not receive live, attenuated vaccines (eg, FluMist®) within four weeks prior to first day of study treatment, at any time during the study, or through 90 days after the last dose of PF-07901801. Inactivated vaccines are allowed. Influenza vaccination should be given during influenza season only (approximately October to March).

b. Doxorubicin, the active component of PLD, is a major substrate of cytochrome P450 CYP3A4 and CYP2D6, and P-glycoprotein (P-gp). Clinically significant interactions have been reported with inhibitors of CYP3A4, CYP2D6, and/or P-gp (e.g., verapamil), resulting in increased concentration and clinical effect of doxorubicin. Inducers of CYP3A4 (e.g., phenobarbital, phenytoin, St. John's Wort) and P-gp inducers may decrease the concentration of doxorubicin. While the Prescribing Information for PLD does not carry these statements, the investigator may consider whether concurrent use of inhibitors and inducers of CYP3A4, CYP2D6 or P-gp is warranted or should be avoided when PLD is being administered or may wish to employ alternate medications when possible. The investigator should consult with the sponsor medical monitor when considering use of one of these agents.

c. Due to potential impact on metabolism of both PF-07901801 and PLD, THC/CBD and herbal products are prohibited while the participant is receiving treatment on study. The investigator may discuss this potential interaction with the sponsor medical monitor.

d. Chronic use of steroid above a daily equivalent dose of 10 mg prednisone is not permitted on study except in circumstances outlined in Section 8.7.1.

8.8 Treatment of Overdose

There are no known antidotes for overdoses of PF-07901801, PLD or doxorubicin, the active component of PLD. In the event of an overdose of PF-07901801 or PLD, discontinuation of

treatment may not have immediate therapeutic effect. In the event of a known or suspected overdose, the participant should be monitored with appropriate hematology and clinical chemistry and should receive supportive therapy, as necessary.

The PLD Full Prescribing Information reports that overdosage with doxorubicin hydrochloride causes increased risk of severe mucosities, leukopenia and thrombocytopenia. Treatment of a severely myelosuppressed participant require hospitalization, anti-microbials, platelet transfusions and symptomatic treatment of mucositis. Use of hematopoietic growth factor (G-CSF, GM-CSF) may be considered.

Doxorubicin hydrochloride liposome injection Prescribing Information carries a warning that myocardial damage, include left ventricular failure, can occur. Thus, dexrazoxane may be considered for cardioprotection in participants who have received an excess of doxorubicin. The Prescribing Information also carries a warning that serious, life-threatening, and fatal infusion-related reactions can occur but does not mandate prophylaxis for such reactions. At the discretion of the investigator and in accordance with institutional guidelines, the investigator may implement prophylaxis.

Decisions regarding dose interruptions or modifications for PF-07901801 and/or PLD in the case of a suspected overdose will be made by the investigator in consultation with the sponsor medical monitor based on the clinical evaluation of the participant.

Information regarding the quantity of the excess dose as well as the duration of the overdosing should be documented in the appropriate eCRF.

9 MONITORING AND MANAGEMENT OF EXPECTED OR POTENTIAL ADVERSE EVENTS

Participant safety will be monitored throughout the study and supportive measures consistent with optimal participant care according to institutional standards should be provided throughout the study. Emergency resuscitation equipment and medications should be readily available. Additional supportive measures should also be available and may include epinephrine, antihistamines, corticosteroids, IV fluids, vasopressors, oxygen, bronchodilators and acetaminophen.

Adverse events observed, mentioned or spontaneously reported by the participant will be documented. The investigator will be responsible for monitoring the safety of participants and for alerting the sponsor or its designee of any event that seems unusual, even events considered an unanticipated benefit to the participant. The investigator is responsible for appropriate medical care of participants during the study and for adverse events that are serious in nature, considered related or unrelated to the study intervention or that cause the participant to discontinue. Laboratory abnormalities and adverse events will be graded according to NCI CTCAE version 5.0.

In the following section, guidelines are presented for management of adverse events attributed to PF-07901801 (Section 9.1) or PLD (Section 9.2) and management of adverse events when attribution to neither agent is possible in the opinion of the investigator (Section 9.3).

9.1 Management of Adverse Events Associated with PF-07901801

Except in the case of proteinuria, asymptomatic laboratory abnormalities should not result in dose interruptions, modifications, or discontinuation of study therapy unless determined by the investigator to be clinically significant or life-threatening.

9.1.1 PF-07901801 Treatment Interruptions

Treatment with PF-07901801 may be interrupted for up to 56 days for toxicity assessed as related to treatment with PF-07901801; treatment may be interrupted for up to 28 days for reasons unrelated to toxicity if the participant is receiving disease control and after discussion with the sponsor medical monitor. Treatment may be re-instated after discussion with the medical monitor. In general, if an interruption of more than 56 days is required due to adverse events, PF-07901801 will be permanently discontinued; however, if in the judgment of the investigator, the participant is likely to derive disease control from PF-07901801 after a hold of more than 56 days, study drug may be re-started with the approval of the sponsor medical monitor. The infusion duration may be increased and/or other precautionary measures instituted after discussion with the sponsor medical monitor, but the PF-07901801 dose level does not require modification when administration is re-started. Longer interruptions may be acceptable on a participant -by- participant basis at the discretion of the investigator after discussion with the sponsor medical monitor.

9.1.2 PF-07901801 Re-Treatment Guidelines

The parameters described in Table 14 should be met for re-treatment with PF-07901801 on any study day.

Table 14. Requirements for Re-Treatment with PF-07901801

Parameter	Criterion
ANC	≥1.0 × 10^9/L
Platelet Count	≥75 × 10^9/L
Bilirubin	≤1.5 × ULN (≤2 x ULN if hyperbilirubinemia is due to Gilbert's syndrome)
AST, ALT	≤3 × ULN (<5 × ULN if liver metastases)
Treatment-Related Adverse Event	NCI CTCAE Grade <2 or baseline level (except for alopecia)

9.1.3 PF-07901801 Dose Modification Guidelines

Table 15 describes modifications for the dose levels intended to be evaluated in the dose escalation portion of the study.

Table 15. PF-07901801 Dose Modifications

Dose Level	Dose Level -1	Dose Level -2
48 mg/kg	32 mg/kg	24 mg/kg
24 mg/kg	18 mg/kg	12 mg/kg
12 mg/kg	8.0 mg/kg	4.0 mg/kg

While PF-07901801 has demonstrated clinical activity in Study TTI-622-01 at dose levels as low as 0.8 mg/kg, the agent has demonstrated a very promising safety profile suggesting that dose reductions may not be routinely required. Thus, the study does not prospectively envision

requirement for a dose level below 4.0 mg/kg but a lower dose level may be allowed after consultation with the sponsor medical monitor for a participant who is receiving disease control and remaining on treatment is, in the opinion of the investigator, a reasonable treatment option for the participant.

9.1.4 Hematologic Adverse Events Related to PF-07901801 Administration

Blood counts will be monitored regularly as outlined in the Schedule of Assessments, Table 28 in Section 10, with additional testing obtained according to standard clinical practice. Management of hematologic adverse events associated with PF-07901801 administration is summarized in Table 16, Management of Hematologic Adverse Events Associated with PF-07901801 Platelet transfusion is allowed to manage thrombocytopenia to prevent and minimize bleeding according to ASH and ASCO guidelines. Per these guidelines, the platelet count threshold for prophylactic platelet transfusion is <10,000 × 10^9/L. Investigators should consider the participant's medical history, concomitant medications and concurrent conditions to provide support for thrombocytopenia.

Table 16. Management of Hematologic Adverse Events Associated with -PF-07901801 Administration

Observation	Management Guidelines
Grade 3 thrombocytopenia Grade 4 thrombocytopenia lasting ≤72 hours	• Continue PF-07901801 at the same dose when the re-treatment criterion (≥75 x 10^9/L or baseline) is met
Grade 4 thrombocytopenia lasting >72 hours Platelets ≤ 10 × 10^9/L at any time	• Delay PF-07901801 dosing until the re-treatment criterion (≥75 x 10^9/L or baseline) is met • Transfuse platelet prophylactically against bleeding when platelets ≤10 × 10^9/L per ASCO practice guideline, then resume PF-07901801: o At the same dose if dose delay was ≤1 week o One dose level reduction if dose delay was >1 week o One dose level reduction if the event recurs
Grade ≥3 thrombocytopenia with clinical bleeding (more than easily-controlled epistaxis, mild gum bleeding or menses)	Delay PF-07901801 dosing until the re-treatment criterion (≥75 x 10^9/L or baseline) is met and then resume PF-07901801 at a reduced dose (1 dose level reduction)
Grade 4 neutropenia lasting >72 hours	• Delay PF-07901801 dosing until the re-treatment criterion (ANC >1.0 × 10^9/L) is met, then resume PF-07901801: o At the same dose if dose delay was ≤1 week o One dose level reduction if dose delay was >1 week o One dose level reduction if the event recurs

Table 16. Management of Hematologic Adverse Events Associated with -PF-07901801 Administration

Observation	Management Guidelines
Grade 3 febrile neutropenia lasting >72 hours Grade 3 neutropenia with clinical evidence of infection Grade 4 febrile neutropenia	Delay PF-07901801 dosing until the re-treatment criterion (ANC > 1.0×10^9/L) is met, then resume PF-07901801 at one dose level reduction
Grade 3 anemia	• Delay PF-07901801 dosing until resolution to Grade ≤ 1 or baseline, then resume PF-07901801 treatment: o At the same dose if dose delay was ≤ 1 week o One dose level reduction if dose delay was >1 week o One dose level reduction if the event recurs
Grade 4 anemia	• For Grade 4 events, discontinuation of PF-07901801 should be considered. If it is in the participant's best interest to continue PF-07901801 per investigator assessment, withhold dose until resolved to ≤Grade 1 or baseline, then reduce by 1 dose level

9.1.5 Non-Hematologic Adverse Events Related to PF-07901801 Administration

PF-07901801 (TTI-622) dose adjustments based on the occurrence of non-hematologic treatment-related adverse events are described in Table 17.

Table 17. Management of Non-Hematologic Adverse Events Associated with PF-07901801 Administration

Observation	Management Guidelines
Grade ≥3 events with the following exceptions: • Nausea and/or vomiting lasting <72 hours with supportive care • Fatigue lasting ≤72 hours • Laboratory abnormalities lasting <72 hours and judged by the investigator as not clinically significant	• For Grade 3 events, delay PF-07901801 dosing until the re-treatment criteria are met, then resume PF-07901801 at one dose level reduction • No dose reduction is required for the exceptions listed • For Grade 4 events, discontinuation of PF-07901801 should be considered unless the adverse event was transient and/or asymptomatic and/or not clinically significant. If the investigator judges that continued treatment may be in the participant 's best interest, PF-07901801 treatment can be resumed when the adverse event resolves to a level that meets re-treatment criteria. In consultation with the medical monitor, the dose level may be reduced.

9.1.6 Management of Other Adverse Events Related to PF-07901801 Administration

PF-07901801 dose adjustments based on the occurrence of other treatment-related adverse events are described in Table 18.

Table 18. Management of other Treatment-Related Adverse Events

Severity of Event	Management Guidelines
Grade 1	• Maintain PF-07901801 dose level • Provide treatment to control symptoms if applicable
Grade 2 (tolerable)	• Maintain PF-07901801 dose level • Provide treatment to control symptoms if applicable
Grade 2 (intolerable)	• Hold administration of PF-07901801 until the adverse event recovers to Grade ≤1 or to baseline level, then resume treatment with PF-07901801
Grade 3	• Hold administration of PF-07901801 until the adverse event recovers to Grade ≤1 or to baseline level, then resume treatment with PF-07901801
Grade 4	• Discontinue PF-07901801 unless participant is receiving disease control, adverse event recovers to baseline level and treating physician recommends continuation of treatment at a lower dose level or under a modified schedule

9.1.7 Grading and Management of Infusion-Related Reactions

Infusion-related reactions are not expected to be prevalent in this study. However, in the event that infusion-related reactions are observed, they will be graded as described in Table 19. Guidelines for management of infusion-related reactions are provided in Table 20.

Table 19. Definition of Infusion-Related Reaction by CTCAE Grade

CTCAE Grade	Definition
Grade 1 Infusion-Related Reaction	Mild transient reaction; infusion interruption not indicated; intervention not indicated
Grade 2 Infusion-Related Reaction	Therapy or infusion interruption indicated but responds promptly to symptomatic treatment (e.g., anti-histamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for ≤ 24 hours
Grade 3 Infusion-Related Reaction	Prolonged (i.e., not rapidly responsive to symptomatic medication, brief interruption of infusion, or both); recurrence of symptoms following initial improvement; hospitalization indicated for clinical sequelae
Grade 4 Infusion-Related Reaction	Life-threatening consequences; urgent intervention indicated

Note: An acute infusion reaction may occur with an agent that causes cytokine release (e.g., monoclonal antibodies or other biological agents). Signs and symptoms usually develop during or shortly after drug infusion and generally resolve completely within 24 hours of completion of infusion. Signs/symptoms may include: allergic reaction/hypersensitivity (including drug fever); arthralgia (joint pain); bronchospasm; cough; dizziness; dyspnea (shortness of breath); fatigue (asthenia, lethargy, malaise); headache; hypertension; hypotension; myalgia (muscle pain); nausea; pruritis/itching; rash/desquamation; rigors/chills; sweating (diaphoresis); tachycardia; tumor pain (onset or exacerbation of tumor pain due to treatment); urticaria (hives, welts, wheals); vomiting.

Table 20. Management of Infusion-Related Reactions Associated with PF-07901801 Administration

CTCAE Grade	Management Guidelines
Grade 1 Infusion-Related Reaction	• The infusion may be stopped or continued at a reduced (50%) infusion rate at the discretion of the investigator. • If symptoms resolve, the infusion can be re-started or increased, as tolerated, to the baseline rate. • The participant may receive appropriate further treatment for infusion-related reaction if clinically indicated per the site's standard practice for management of IRR.
Grade 2 Infusion-Related Reaction	• The infusion should be stopped. • The participant should receive appropriate further treatment with an anti-histamine and/or acetaminophen if clinically indicated per the site's standard practice for management of IRR. Further medications can be administered if necessary. • Once symptoms have resolved or reduced to Grade 1, the infusion can be continued at a reduced (50%) infusion rate. If after one hour the participant's symptoms do not return and vital signs are stable, the infusion rate may be increased every 30 minutes, as tolerated, to the baseline rate.
Grade 3 Infusion-Related Reaction	• The infusion should be stopped promptly. • The participant must receive appropriate treatment with an anti-histamine and/or acetaminophen and/or methylprednisolone or equivalent and, if necessary, further medications (i.e., epinephrine, bronchodilator). • Only after the complete resolution to Grade ≤1, and after having received appropriate prophylactic medication(s) as described above, the infusion may be resumed at an infusion rate of 25%. If after one hour the participant's symptoms do not return and vital signs are stable, the infusion rate may be increased to a maximum of 50%. • If after the resumption of infusion, symptoms return (irrespective of grade), the infusion must be stopped and the infusion tubing should be disconnected. • The duration of infusion may be prolonged in order to ameliorate IRR but PF-07901801 dose does not require reduction. • the sponsor medical monitor should be apprised of any ≥ G3 IRR that occurs during the study
Grade 4 Infusion-Related Reaction	• The infusion should be stopped promptly and the infusion tubing should be disconnected. • The participant should receive appropriate treatment with an anti-histamine and/or acetaminophen and/or methylprednisolone (or equivalent) and, if necessary, further medications (i.e., epinephrine, bronchodilator). • After discussion with the sponsor medical monitor, the participant must not receive further infusions of PF-07901801 if PF-07901801 is judged by the investigator to be the cause of the infusion-related reaction and the investigator feels that implementation of alternative or more aggressive prophylaxis would not be sufficient.

9.2 Management of Adverse Events Associated with PLD

General guidelines for dose modifications in response to observed adverse events is presented in this section. In consideration that PLD is being used as a standard of care anti-cancer therapy in the enrolled participant population and based on investigator and site experience with PLD in the enrolled participant population, alternate dose modifications may be implemented after discussion with the medical monitor. In general, the PLD dose should not be increased after a dose reduction for toxicity; on a participant -specific basis, the investigator may discuss a dose increase with the sponsor medical monitor.

9.2.1 PLD Treatment Interruptions

Treatment with PLD may be temporarily suspended for up to 56 days to allow for resolution of adverse events. Dose interruptions for reason(s) other than toxicity and re-treatment may be allowed in accordance with standard of care if the participant is receiving disease control and after discussion with the sponsor medical monitor. In general, if an interruption of more than 56 days is required due to adverse events, PLD will be permanently discontinued; however, if in the judgment of the investigator, the participant is likely to derive disease control from PLD after a hold of more than 56 days, study drug may be re-started with approval of the sponsor medical monitor. Longer interruptions may be acceptable on a participant-by-participant basis at the discretion of the investigator after discussion with the sponsor medical monitor.

9.2.2 PLD Re-Treatment Guidelines

The laboratory parameters described in Table 21 should be met for re-treatment with PLD (i.e., initiation of a new cycle).

Table 21. Requirements for Re-Treatment with PLD

Parameter	Criterion
ANC	$\geq 1.5 \times 10^9$/L
Platelet Count	$\geq 75 \times 10^9$/L
Bilirubin	≤1.5 × ULN (≤ 2 x ULN if hyperbilirubinemia is due to Gilbert's syndrome)
AST, ALT	≤3 × ULN (<5 × ULN if liver metastases)
Treatment-Related Adverse Event	NCI CTCAE Grade <2 or baseline level (except for alopecia)

9.2.3 PLD Dose Modification Guidelines

Table 22 describes PLD dose reduction levels in the case of PLD-related adverse events.

Table 22. PLD Dose Modifications

Dose Level	First Dose Reduction	Second Dose Reduction
40 mg/m^2	30 mg/m^2	22.5 mg/m^2

If more than two dose reductions are required for a participant, the investigator should consult with the sponsor medical monitor to determine the appropriate course of action for the participant.

In case a participant's bilirubin level is elevated >1.2 mg/dL due to impaired liver function, the dose of PLD should be reduced as follows: serum bilirubin 1.2 to 3.0 mg/dL - give ½ normal dose; serum bilirubin > 3 mg/dL - give ¼ normal dose.

9.2.4 Management of Infusion-Related Reactions Associated with PLD

Infusion-related reactions will be graded as described in Table 19. Management of infusion-related reactions associated with PLD administration are described in Table 23.

Table 23. Management of Infusion-Related Reactions Associated with PLD

CTCAE Grade	Management Guidelines
Grade 1 Grade 2 Grade 3	• Slow the infusion rate or stop the infusion • Provide appropriate further treatment for infusion-related reaction if clinically-indicated per the site's standard practice. • If symptoms resolve, the infusion can be re-started at a reduced infusion rate. • Consider premedications and reduced infusion rate for subsequent infusions.
Grade 4	• Stop the infusion • Aggressively manage symptoms per the site's standard practice for management of PLD-associated or any infusion-related reaction • Do not retreat with PLD

9.2.5 Management of Cardiomyopathy Associated with PLD

Doxorubicin hydrochloride, the active component of PLD, can cause myocardial damage, including acute left ventricular failure. The risk of cardiomyopathy is generally proportional to the cumulative exposure. Include prior use of other anthracycles or anthracenediones in calculations of cumulative dose. The risk of cardiomyopathy may be increased at lower cumulative doses in participants with prior mediastinal irradiation.

Because of the risk of cardiomyopathies with Doxorubicin it is important to assess left ventricular cardiac function prior to initiation of treatment. Participants will undergo baseline Left Ventricular Ejection Fraction (LVEF) determination by ECHO or MUGA scan to be performed at screening visit only. This evaluation may be repeated at any time during the study if clinically indicated.

9.2.6 Management of Hematologic Adverse Events Associated with PLD

Participants must have adequate hematological function with no transfusion or colony stimulating factor or erythropoiesis-stimulating agent for at least 2 weeks prior to Cycle 1 Day 1.

Primary prophylactic use of colony stimulating factors or erythropoiesis-stimulating agents or blood product transfusions are not permitted during the first 28 days of Phase 1 Cycle 1 (DLT evaluation period), unless indicated due to medical emergency.

Therapeutic and prophylactic use of G-CSFs is allowed per ASCO and NCCN guidelines. Management of hematologic adverse events associated with PLD administration is described in Table 24.

Table 24. Management of Hematologic Adverse Events Associated with PLD

CTCAE Grade	Management Guidelines
Grade 1 Neutropenia Grade 1 Thrombocytopenia	Resume treatment with no dose reduction
Grade 2 Neutropenia Grade 2 Thrombocytopenia	Hold administration of PLD until the adverse event recovers to Grade ≤1 or to baseline level, then resume treatment with no dose reduction
Grade 3 Neutropenia Grade 3 Thrombocytopenia	Hold administration of PLD until the adverse event recovers to Grade ≤1 or to baseline level, then resume treatment with no dose reduction
Grade 4 Neutropenia Grade 4 Thrombocytopenia	Hold administration of PLD until the adverse event recovers to Grade ≤1 or to baseline level, then resume treatment with first dose reduction

Management should be guided by the more severe toxicity if neutropenia and thrombocytopenia are both observed.

9.2.7 Management of Hand-Foot Syndrome Associated with PLD

Management of hand-foot syndrome (HFS) associated with PLD administration is described in Table 25.

Table 25. Management of Hand-Foot Syndrome Associated with PLD

CTCAE Grade	Management Guidelines
Grade 1: Mild erythema, swelling, or desquamation not interfering with daily activities	• If no previous Grade 3 or Grade 4 HFS: no dose adjustment If previous Grade 3 or Grade 4 HFS: delay dose up to two weeks, then decrease dose by 25%
Grade 2: Erythema, desquamation, or swelling interfering with but not precluding normal physical activities; small blisters or ulcerations less than 2 cm in diameter	• Delay dosing up to two weeks or until resolved to Grade 0 - 1 • Discontinue if no resolution after two weeks • If resolved to Grade 0 – 1 with two weeks and: • no previous Grade 3 or Grade 4 HFS: continue treatment at previous dose • previous Grade 3 or Grade 4 toxicity: decrease dose by 25%
Grade 3: Blistering, ulceration, or swelling interfering with walking or normal daily activities; cannot wear regular clothing	• Delay dosing up to two weeks or until resolved to Grade 0 – 1, then decrease dose by 25% Discontinue if no resolution after two weeks
Grade 4: Diffuse or local process causing infectious complications, or a bed-ridden state or hospitalization	• Delay dosing up to two weeks or until resolved to Grade 0 – 1, then decrease dose by 25% • Discontinue if no resolution after two weeks

9.2.8 Management of Stomatitis Associated with PLD

Management of stomatitis associated with PLD administration is described in Table 26.

Table 26. Management of Stomatitis Associated with PLD

CTCAE Grade	Management Guidelines
Grade 1: Painless ulcers, erythema, or mild soreness	• If no previous Grade 3 or Grade 4 toxicity: no dose adjustment • If previous Grade 3 or Grade 4 toxicity: delay dose up to two weeks, then decrease dose by 25%
Grade 2: Painful erythema, edema, or ulcers, but can eat	• Delay dosing up to two weeks or until resolved to Grade 0 - 1 • Discontinue if no resolution after two weeks • If resolved to Grade 0 – 1 with two weeks and: • no previous Grade 3 or Grade 4 stomatitis: continue treatment at previous dose • previous Grade 3 or Grade 4 toxicity: decrease dose by 25%
Grade 3: Painful erythema, edema, or ulcers, and cannot eat	• Delay dosing up to two weeks or until resolved to Grade 0 – 1, then decrease dose by 25% and return to original dose interval • Discontinue if no resolution after two weeks

Table 26. Management of Stomatitis Associated with PLD

CTCAE Grade	Management Guidelines
Grade 4: Requires parenteral or enteral support	• Delay dosing up to two weeks or until resolved to Grade 0 – 1, then decrease dose by 25% and return to original dose interval • Discontinue if no resolution after two weeks

9.2.9 Secondary Oral Neoplasms Related to PLD Administration

Secondary oral cancers, primarily squamous cell carcinoma, have been reported from post-marketing experience with patients with long-term (more than one year) exposure. Examine participants at regular intervals for the presence of oral ulceration or with any oral discomfort that may be indicative of secondary oral cancer.

9.2.10 Extravasation and Tissue Necrosis Related to PLD Administration

Infusion should be discontinued for burning or stinging sensation or other evidence indicating perivenous infiltration or extravasation. Manage confirmed or suspected extravasation as follows:

- Do not remove the needle until attempts are made to aspirate extravasated fluid
- Do not flush the line
- Avoid applying pressure to the site
- Apply ice to the site intermittently for 15 minutes four times each day for three days
- If the extravasation is in an extremity, elevate the extremity

9.3 Management of Adverse Events not Attributable to a Specific Study Treatment

Guidelines for managing adverse events when attribution to either TTI-622 or PLD is not possible in the opinion of the investigator are provided in Table 27. Discussion with the medical monitor is recommended to ensure homogeneity in adverse event management across all participants to the extent possible.

Table 27. General Guidelines for Management of Adverse Events when Attribution is not Possible in the Opinion of the Investigator

Observation	Management Guidelines
• **Hematologic Toxicity**[1] Grade ≥ 3 neutropenia (ANC < 1 x 10^9/L) • Grade ≥ 3 thrombocytopenia(platelets <50 x 10^9/L) • Grade ≥ 3 anemia • Hemoglobin < 8 g/dL **Non-Hematologic Toxicity**[1] Grade ≥ 3 events excluding: • Sub-optimally treated nausea, vomiting, diarrhea • Alopecia • Transient fatigue of a duration consistent with that associated with doxorubicin treatment (1-2 weeks) • Infusion-related reaction in the absence of described prophylaxis • Laboratory abnormalities that are asymptomatic and/or judged by the investigator as not clinically significant for the patient	First Appearance • Delay study treatment until recovery to Grade ≤ 1 or baseline with ANC >1.5 x 10^9/L and platelets ≥75x 10^9/L. If no recovery after a delay of >21 days, discontinue PF-07901801 and remove participant from study. First Re-Appearance • Delay study treatment until recovery to Grade ≤1 or baseline. If no recovery after a delay of >21 days, discontinuePF-07901801 and remove participant from study. • Reduce PF-07901801 dose level by one dose level. • No change in PLD dose level. Second Re-Appearance • Reduce PF-07901801 dose level by one additional dose level. • No change in PLD dose level. Third Re-Appearance • Reduce PLD dose level by one dose level. • No change from previous PF-07901801 dose level. Fourth Re-Appearance • Reduce PLD dose level by one additional dose level. • No change from previous PF-07901801 dose level.
Hematologic Toxicity • Grade 1 or Grade 2 • **Non-Hematologic Toxicity** Grade 1 or Grade 2	• No treatment delay • No change in dose level

1 Interventional or supportive care may be introduced (e.g., G-CSF for neutropenia)

10 STUDY ASSESSMENTS

The procedures and assessments that will be conducted during this study are described in this section and summarized in the Schedule of Assessments (Table 28). Detailed instructions regarding all laboratory procedures, including collection and handling of samples, will be included in the study Laboratory Manual provided by the sponsor.

The schedule for collection of blood samples for analysis of PF-07901801 concentrations is presented in the Schedule of Assessments (Table 29). The schedule for collection of blood samples for analysis of PLD concentrations is presented in Table 30. The schedule for collection of samples for anti-drug antibody analyses is presented in Table 31. The schedule for collection of samples for biomarker/pharmacodynamics analyses is presented in Table 32.

Written informed consent must be granted by each participant prior to the initiation of any study procedure or assessment.

Planned timepoints for all safety assessments are provided in the Schedule of Assessments (Table 28). Unscheduled safety measurements may be obtained at any time during the study to assess any perceived safety issues.

Table 28. Schedule of Assessment

ACTIVITY	Screening	Cycle 1 Day in Cycle				Cycle 2, Cycle 3 Day in Cycle (± 3 days)				Cycle 4 Day in Cycle (± 3 days)		Subsequent Cycles Day in Cycle (± 3 days)		End of Treatment Visit[z]	Safety Follow-Up Visit[aa]	Long-Term Follow-Up Period
	Day -28 to -1	1	8	15	22	1	8	15	22	1	15	1	15			
Informed Consent	X															
Demographics	X															
Inclusion and exclusion criteria	X															
Medical history	X															
Cancer history	X															
Physical exam, vital signs[a]	X	X				X				X		X		X	X	
Brief physical exam, vital signs[b]			X	X	X			X			X		X			
LVEF[c]	X															
ECOG PS	X	X				X				X		X			X	
Serum chemistry[d]	X	X[r]	X[r]	X[r]	X[r]	X[r]		X[r]		X[r]	X[r]	X[r]	X[r]		X	
Hematology[e]	X	X[r]	X[r]	X[r]	X[r]	X[r]	X[r*]	X[r]	X[r*]	X[r]	X[r]	X[r]	X[r]		X	
Coagulation[f]	X	X[r]														
ECG[g]	X	X[r]				X[r]				X[r]		X[u]			X	
Pregnancy test[h]	X	X				X				X		X			X	
Radiologic assessment of disease status[i]	X	X[i]													X	X
Administer PLD[j]		X				X				X		X				
Administer PF-07901801[k] (12 and 24 mg/kg dose levels only)		X[s]	X[s]	X[s]	X[s]	X		X		X	X	X	X			
Administer PF-07901801[k] (48 mg/kg dose level only)		X[s]		X[s]		X		X		X	X	X	X			
Adverse events		Ongoing														
Concomitant medications, procedures		Ongoing														
Blood collection for CA-125		X		X		X		X		X		X			X	
Blood collection for PLD[l]		X[ee]								X[ee]						

Table 28. Schedule of Assessment

ACTIVITY	Screening	Cycle 1 Day in Cycle				Cycle 2, Cycle 3 Day in Cycle (± 3 days)				Cycle 4 Day in Cycle (± 3 days)		Subsequent Cycles Day in Cycle (± 3 days)		End of Treatment Visit[z]	Safety Follow-Up Visit[aa]	Long-Term Follow-Up Period
	Day -28 to -1	1	8	15	22	1	8	15	22	1	15	1	15			
Blood collection for PF-07901801 concentration[ll, cc]		X[ff]	X[ff]	X[ff]	X[ff]	X[ff]		X[ff]		X[ff]	X[ff]	X[ff]	X[ff]	X	X	
Blood collection for Biomarker/PD[m]		X[dd]	X	X		X[dd]		X		X		X[w,x]				
Blood collection for ADAs and NAbs of PF-07901801[n]		X				X				X		X[v]		X	X[bb]	See note[bb]
Tissue collection for Biomarker/PD[o]	X[q]				X[t,y]											
Survival, initiation of new anti-cancer therapy[p]																X

a. Complete physical examination by body system, including vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight); height collected during screening only
b. Symptom-directed physical examination, with vital signs limited to temperature, blood pressure, pulse rate, respiratory rate
c. Assessed by transthoracic echocardiogram or MUGA at screening. Note:.Additional LVEF assessments may be performed as clinically indicated and in accordance with the PLD SRSD (Doxil® USPI).
d. Glucose, sodium, potassium, calcium, chloride, phosphate, bicarbonate, blood urea nitrogen or urea, creatinine, total protein, albumin, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, indirect bilirubin, uric acid, calcium, magnesium, lactate dehydrogenase (LDH)
e. Hemoglobin, hematocrit, platelets, white blood cells (WBC), neutrophils, lymphocytes, eosinophils, basophils, monocytes, WBC with automated 5-part differential, RBC, absolute reticulocytes, reticulocytes %, MCH, MCV, RDW
f. International normalized ratio (INR)/prothrombin time (PT), partial thromboplastin time (PTT). To be repeated more frequently) if clinically-indicated (e.g., INR/PT for participants on anti-coagulants)
g. 12-lead ECG with triplicate assessments obtained with participant in supine position and within 10 minutes total time; to be performed prior to Cycle 1, Cycle 3, Cycle 4 and Cycle 6; prior to every second cycle beginning with Cycle 7; and at the Safety Follow-Up Visit.
h. Pregnancy tests will be performed in WOCBP. A serum pregnancy test is required at screening. Following screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL. A pregnancy test must be performed and be negative prior to treatment with IP at baseline and at subsequent treatment visits. Participants will also be counseled on the use of appropriate contraceptive methods at these timepoints.
i. Assessed objectively by CT, MRI or PET/CT; the method used at baseline should be used for the duration of participant participation. Performed every 8 ± 1 week until Week 48 or participant has been on study for one year, and every 12 ± 2 weeks thereafter. CR or PR should be confirmed by repeat assessment at least four weeks after initial observation; treatment can continue during the interval between initial observation and confirmation. In the event that a participant is removed from the study in the absence of radiologic disease progression, a radiologic disease assessment should be performed at the Safety Follow-Up Visit if not performed within the previous four weeks and disease status should be assessed during Long-Term Follow-Up until radiologic demonstration of progression or initiation of new anti-cancer therapy, whichever occurs first

Table 28. Schedule of Assessment

ACTIVITY	Screening	Cycle 1 Day in Cycle				Cycle 2, Cycle 3 Day in Cycle (± 3 days)				Cycle 4 Day in Cycle (± 3 days)		Subsequent Cycles Day in Cycle (± 3 days)		End of Treatment Visit[z]	Safety Follow-Up Visit[aa]	Long-Term Follow-Up Period
	Day -28 to -1	1	8	15	22	1	8	15	22	1	15	1	15			

j. PLD should be administered through a free-flowing catheter at 40 mg/m^2 by intravenous infusion. The initial infusion rate should be 1 mg/min to minimize the risk of infusion reactions. If no infusion-related adverse reactions are observed, the rate of infusion can be increased to complete administration of the drug over one hour in accordance with institutional guidelines. Medications for treatment of infusion-related reaction and CPR equipment must be available before start of treatment; prophylaxis in accordance with institutional guidelines is acceptable

k. PF-07901801 is administered intravenously through a free-flowing catheter; the duration of infusion is dependent on dose level: dose levels less than or equal to 33 mg/kg infused over 60 min and doses greater than 33 mg/kg infused over 90 minutes and will have doses equal to or less than 2500 mg in 250 mL and doses 2501 mg or more in 500 mL or neat drug if the drug volume is over 500 mL. Prophylaxis for potential infusion-related reaction in accordance with institutional guidelines is acceptable. If Cycle 1 loading doses are implemented, all dosing and lab schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg

l. Detailed sample collection schedule provided in Table 30

ll Detailed sample collection schedule provided in Table 29

m. Detailed sample collection schedule provided in Table 32

n. Detailed sample collection schedule provided in Table 31

o. Detailed sample collection schedule provided in Table 32

p. Assessed every 12 ± 2 weeks; telephone contact is acceptable

q. Newly-acquired FFPE/NBF tumor tissue (tumor block preferred; if tumor block is not available, unstained slides are acceptable). Tumor tissue to be collected anytime after signing of informed consent and prior to treatment on Cycle 1 Day 1. Archival tissue from most recent biopsy is acceptable if fresh tissue specimen is not available at screening. The baseline tissue chosen should be the most recently collected specimen before the start of the study therapy and after the most recent systemic therapy. Detailed sample collection schedule provided in Table 32

r. Does not need to be performed if previous assessment was within 72 previous hours

s. Participants should be observed for one hour after infusion with vital signs assessment in 30-minute intervals for signs of infusion-related reaction in Cycle 1; the observation period may be removed at the investigator's discretion in participants who tolerate the infusion well and do not experience infusion-related reaction during Cycle 1.

t. Target date for FFPE/NBF tumor tissue collection date is Cycle 2 Day 1 but can be collected anytime within 7 days prior to and up to 14 days after Cycle 2 Day 1 (i.e. Tumor tissue should be collected within a 21-day window); other times may be acceptable after consultation with sponsor; tumor block preferred; if block is not available, unstained slides are acceptable. Detailed sample collection schedule provided in Table 32

u. Prior to initiation of every second cycle (Cycle 7, Cycle 9, Cycle 11, etc)

v. Cycle 5, Cycle 7, Cycle 9 and every second cycle thereafter (Cycle 11, Cycle 13, etc)

w. Cycle 5, Cycle 7, Cycle 9 and every second cycle thereafter (Cycle 11, Cycle 13, etc): blood collection for assessment of Peripheral Receptor Occupancy, Nanostring/RNA Sequencing, TCRVβ. Refer to Table 32 for details

x. Cycle 5, Cycle 9, Cycle 13 and every fourth cycle thereafter (Cycle 17, Cycle 21, etc): blood collection for assessment of Adaptive and Innate Immunity only. Refer to Table 32 for details

y. FFPE/NBF tumor biopsies may be collected at response, progression, at the time of any surgical intervention, end of treatment and at investigator's discretion; tumor block preferred; if block is not available, unstained slides are acceptable. Detailed sample collection schedule provided in Table 32

z. Seven ± three days after last administration of study treatment

aa. To be performed 30 + five days after last administration of study treatment or before initiation of subsequent anti-cancer therapy, whichever occurs first

Table 28. Schedule of Assessment

ACTIVITY	Screening	Cycle 1 Day in Cycle				Cycle 2, Cycle 3 Day in Cycle (± 3 days)				Cycle 4 Day in Cycle (± 3 days)		Subsequent Cycles Day in Cycle (± 3 days)		End of Treatment Visit[z]	Safety Follow-Up Visit[aa]	Long-Term Follow-Up Period
	Day -28 to -1	1	8	15	22	1	8	15	22	1	15	1	15			

bb. Participants with an unresolved AE at the Safety Follow-Up visit considered possibly related to ADA formation may be asked to return to the clinic for ADA blood sampling at approximately 3-month intervals (if feasible given the underlying disease) until the AE or its sequelae resolve or stabilize at a level acceptable to the investigator and sponsor up to a maximum of 12 months
cc. All post-dose sample collection times are relative to the start of the last infusion of PF-07901801
dd. These visits have multiple collection timepoints, see Table 32 for more details
ee. These visits have multiple collection timepoints, see Table 30 for more details
ff. These visits have multiple collection timepoints, see Table 29 for more details
* Only for 48mg/kg dose level. May be completed by a local lab

Table 29. Sample Collection Schedule for Analysis of PF-07901801 Concentration

Cycle	Day	Nominal Time	Allowable Time Window
1	1	pre-infusion (within 30 min)	
	1	EOI	+ 5 min
	1	T0 + 2 hr[a]	±15 min
	1	T0 + 4 hr[a]	±15 min
	8	pre-infusion (within 30 min)	
	8	EOI	+ 5 min
	15	pre-infusion (within 30 min)	
	15	EOI	+ 5 min
	22	pre-infusion (within 30 min)	
	22	EOI	+ 5 min
2	1	pre-infusion (within 30 min)	
	1	EOI	+ 5 min
	15	pre-infusion (within 30 min)	
	15	EOI	+ 5 min
	15	T0 + 2 hr[a]	±15 min
	15	T0 + 4 hr[a]	±15 min
3	1	pre-infusion (within 30 min)	
	1	EOI	+ 5 min
	15	pre-infusion (within 30 min)	
	15	EOI	+ 5 min
4	1	pre-infusion (within 30 min)	
	1	EOI	+ 5 min
	15	pre-infusion (within 30 min)	
	15	EOI	+ 5 min
	15	T0 + 2 hr[a]	±15 min
	15	T0 + 4 hr[a]	±15 min
5+ (Every other cycle)	1	pre-infusion (within 30 min)	
	1	EOI	+ 5 min
	15	pre-infusion (within 30 min)	
	15	EOI	+ 5 min
EOT		X	
SFU		X	

On Day 1 of each cycle, PLD infusion precedes PF-07901801 infusion. Samples should be collected from the arm contralateral to that used for infusion. If a port is used for infusion, the port should be thoroughly flushed before sample collection.
EOI=immediately after the end of infusion PF-07901801 (ie, post-flush); EOT=End of Treatment; SFU=Safety Follow-Up; T0=start time of last PF-07901801 infusion;

Table 29. Sample Collection Schedule for Analysis of PF-07901801 Concentration

Cycle	Day	Nominal Time	Allowable Time Window

Note: For treatment visits where PLD and PF-07901801 are both administered, collect pre-infusion sample before administration of either the combination product or PF-07901801
X: Anytime during the visit

Table 30. Sample Collection Schedule for Analysis of PLD Concentration

Cycle	Day	Nominal Time	Allowable Time Window
1	1	pre-infusion (within 30 min)[a]	
	1	EOI[b]	+ 2 min
4	1	pre-infusion (within 30 min)[a]	
	1	EOI[b]	+ 2 min

EOI=immediately after the end of infusion of PLD
a. Pre-dose sample of PLD before infusion/administration of ANY drug for treatment visits where PLD and PF-07901801 are both administered
b. Sample relative to last PLD infusion

Table 31. Sample Collection Schedule for Analysis of PF-07901801 Anti-Drug Antibodies

	Cycle 1				Cycle 2		Cycle 3		Cycle 4		Cycle 5[1]		End of Treatment Visit	Safety Follow-Up Visit[2]	Long-term Follow-Up Period[2]
	D1	D8	D15	D22	D1	D15	D1	D15	D1	D15	D1	D15			
PLD Administration	•				•		•		•		•				
PF-07901801 Administration (Dose levels 12 and 24 mg/kg)	•	•	•	•	•	•	•	•	•	•	•	•			
PF-07901801 Administration (Dose level 48 mg/kg)[3]	•		•		•	•	•	•	•	•	•	•			
Collection	Pre				Pre		Pre		Pre		Pre		X	X	

On Day 1 of each cycle, PLD infusion precedes PF-07901801 infusion. Samples should be collected from the arm contralateral to that used for infusion. If a port is used for infusion, the port should be thoroughly flushed before sample collection.
Pre: Prior to initiation of any treatment on this study day
X: Anytime during the visit
1 Cycle 5, Cycle 7, Cycle 9 and every second cycle thereafter (Cycle 11, Cycle 13, etc.)
2 Participants with an unresolved AE at the Safety Follow-Up visit considered possibly related to ADA formation may be asked to return to the clinic for ADA blood sampling at approximately 3-month intervals (if feasible given the underlying disease) until the AE or its sequelae resolve or stabilize at a level acceptable to the investigator and sponsor up to a maximum of 12 months.
3 If Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg.

Table 32. Sample Collection Schedule for Analysis of PF-07901801 Biomarkers/Pharmacodynamics

Cycle	Screening	Cycle 1				Cycle 2		Cycle 3		Cycle 4		Cycle 5[1]	
		D1	D8	D15	D22	D1	D15	D1	D15	D1	D15	D1	D15
PLD Administration		●				●		●		●		●	
PF-07901801 Administration (Dose levels 12 mg/kg and 24 mg/kg)		●	●	●	●	●	●	●	●	●	●	●	●
PF-07901801 Administration (Dose level 48 mg/kg)[11]		●		●		●	●	●	●	●	●	●	●
Peripheral Receptor Occupancy[10] (Expansion cohort: if RP2D is 12 mg/kg or 24 mg/kg or the respective DL-1 or DL-2[10])		Pre[2] EOI[3]	Pre[2]			Pre[2] EOI[3]	Pre[2]	Pre[2]				Pre[2]	
Peripheral Receptor Occupancy[10] (Expansion cohort: if RP2D is 48 mg/kg or the respective DL-1 or DL-2[10])		Pre[2] EOI[3]		Pre[2]		Pre[2] EOI[3]	Pre[2]	Pre[2]				Pre[2]	

Table 32. Sample Collection Schedule for Analysis of PF-07901801 Biomarkers/Pharmacodynamics

Cycle	Screening	Cycle 1				Cycle 2		Cycle 3		Cycle 4		Cycle 5[1]	
		D1	D8	D15	D22	D1	D15	D1	D15	D1	D15	D1	D15
Cytokines		Pre[2] EOI[3] 2h[4] 4h[5]	Pre[2]					Pre[2] EOI[3] 2h[4]	Pre[2]				
Nanostring/RNA Sequencing		Pre[2]		Pre[2]		Pre[2]		Pre[2]		Pre[2]		Pre[2]	
TCRVβ		Pre[2]		Pre[2]		Pre[2]		Pre[2]				Pre[2]	
NGS		Pre[2]											
Adaptive and Innate Immunity		Pre[2]						Pre[2]				Pre[2,6]	
Tumor Biopsy	X[7]				Pre[2,8]			Pre[2,9]					

On Day 1 of each cycle, PLD infusion precedes PF-07901801 infusion. Samples should be collected from the arm contralateral to that used for infusion. If a port is used for infusion, the port should be thoroughly flushed before sample collection.

Table 32. Sample Collection Schedule for Analysis of PF-07901801 Biomarkers/Pharmacodynamics

Cycle	Screening	Cycle 1				Cycle 2		Cycle 3		Cycle 4		Cycle 5[1]	
		D1	D8	D15	D22	D1	D15	D1	D15	D1	D15	D1	D15

1. Cycles 5, 7, 9 and every second cycle thereafter (Cycle 11, Cycle 13, etc.), except for Adaptive and Innate Immunity sample[6].
2. Pre-dose samples are to be collected prior to any infusion of any study treatment on this indicated visit
3. Samples to be collected immediately after the end of infusion of PF-07901801 (i.e. post flush) (+ 5 min window)
4. Samples to be collected at PF-07901801 T0 + 2hr (±15 min window), where T0= start time of last PF-07901801 infusion
5. Samples to be collected at PF-07901801 T0 + 4hr (±15 min window), where T0= start time of last PF-07901801 infusion
6. Sample for adaptive and innate immunity to be collected every fourth cycle (Cycle 5, Cycle 9, Cycle 13, Cycle 17, etc.)
7. Newly-acquired FFPE/NBF tumor tissue (tumor block preferred; if tumor block is not available, unstained slides are acceptable). Tumor tissue to be collected anytime after signing of informed consent and prior to treatment on Cycle 1 Day 1. Archival tissue from most recent biopsy is acceptable if fresh tissue specimen is not available at screening. The baseline tissue chosen should be the most recently collected specimen before the start of the study therapy and after the most recent systemic therapy.
8. Target date for FFPE/NBF tumor tissue collection is Cycle 2 Day 1 but can be collected anytime within 7 days prior to and up to 14 days after Cycle 2 Day 1 (i.e. Tumor tissue should be collected within a 21-day window); other times may be acceptable after consultation with sponsor. Tumor block preferred; if block is not available, unstained slides are acceptable
9. FFPE/NBF Tumor biopsies may be collected at response, progression, at the time of any surgical intervention, end of treatment and at investigator's discretion; tumor block preferred; if tumor block is not available, unstained slides are acceptable
10. Peripheral Receptor Occupancy samples will only be collected from approximately 12 participants in the expansion cohort (at RP2D). Please refer to Section 10.3 and Table 15 for more details.
11. If Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg.

10.1 Pharmacokinetics

10.1.1 PF-07901801 Concentration

Blood samples for the PK analysis of PF-07901801 concentrations will be collected into appropriately labeled tubes for measurement of PF-07901801 concentrations at the times specified in the Schedule of Assessments (Table 28). Instructions for the collection and handling of biological samples will be provided in the laboratory manual or by the sponsor.

All efforts will be made to obtain the samples at the exact nominal time relative to dosing. Collection of samples within the sampling time window specified in the SoA will not be captured as a protocol deviation, as long as the exact time (24 hour clock time) of the collection is noted on the source document and the CRF.

If possible, all blood for PK should be taken from a peripheral vein or from the lumen of a central venous catheter of the contralateral infusion arm on dosing days.

Samples collected for measurement of PF-07901801 concentrations will be analyzed using validated analytical methods in compliance with applicable SOPs.

Samples collected for analyses of PF-07901801 concentrations may also be used to evaluate safety or efficacy aspects related to concerns arising during or after the study or evaluation of the bioanalytical method. These data will be used for internal exploratory purposes and not reported in the clinical study report.

The PK samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the PK sample handling procedure (eg, sample collection and processing steps, interim storage or shipping conditions), including any actions taken, must be documented and reported to the sponsor. On a case by case basis, the sponsor may make a determination as to whether sample integrity has been compromised.

10.2 Immunogenicity Assessments

10.2.1 Anti-PF-07901801 Antibody (ADA) and Neutralizing Anti-PF-07901801 Antibody (NAb)

Blood samples will be collected for determination of ADA and NAb for PF-07901801 into appropriately labeled tubes at times specified in the SoA. Instructions for the collection and handling of biological samples will be provided in the laboratory manual. The actual date and time (24 hour clock time) of each sample will be recorded.

Samples collected for determination of ADA and NAb will be analyzed using a validated analytical method in compliance with applicable SOPs. Samples determined to be positive for ADA may be further characterized for NAb.

Samples may also be used for additional characterization of the immune response and/or evaluation of the bioanalytical method, or for other internal exploratory purposes. These data will be used for internal exploratory purposes and not reported in the clinical study report.

The immunogenicity samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the immunogenicity sample handling procedure (eg, sample collection and processing steps, interim storage, or shipping conditions), including any actions taken, must be documented and reported to the sponsor. On a case by case basis, the sponsor may make a determination as to whether sample integrity has been compromised.

10.3 Biomarker and Pharmacodynamics Assessments

Unless prohibited by local regulations or ethics committee decision, blood and tumor biospecimens will be collected to analyze DNA, RNA, protein or metabolic biomarkers for achieving study objectives. Specific biomarker and pharmacodynamic analyses may not be performed if emerging data indicate that they would no longer support study objectives. Biomarker and pharmacodynamic analyses may include but are not limited to peripheral CD47 receptor occupancy, serum cytokines, nanostring/RNA sequencing, TCR sequencing, whole exome sequencing/NGS, multiplex immunohistochemistry and immune function assays.

Peripheral Receptor Occupancy samples will only be collected from approximately 12 participants in the expansion cohort (12mg/kg, 24mg/kg or 48mg/kg or their respective DL-1 or DL-2, ie the RP2D).

Refer to Table 32 for the schedule for collection of samples for biomarker/pharmacodynamics analyses and laboratory manual for sample collection, processing and shipping.

11 SCHEDULE OF PROCEDURES AND ASSESSMENTS

The following procedures and assessments will be performed at the indicated timepoints.

Screening Visit (Day -28 to -1)

- Informed consent
- Demographics
- Inclusion and exclusion criteria
- Medical history
- Cancer history
- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight), height
- LVEF by transthoracic echocardiogram or MUGA. Per investigator discretion, this can be performed anytime after screening if clinically indicated
- ECOG PS
- Serum chemistry
- Hematology
- Coagulation
- 12-lead ECG
- Serum pregnancy test and counseled on appropriate contraception (female participants of childbearing potential only)

- Radiologic assessment of disease status using CT, MRI or PET/CT; the method used at baseline should be used for the duration of participant participation
- Collection of FFPE/NBF tumor tissue for biomarkers/pharmacodynamics (tumor block preferred; if tumor block is not available, unstained slides are acceptable). Tumor tissue to be collected anytime after signing of informed consent and prior to treatment on Cycle 1 Day 1. Archival tissue from most recent biopsy is acceptable if fresh tissue specimen is not available at screening. The baseline tissue chosen should be the most recently collected specimen before the start of the study therapy and after the most recent systemic therapy

Cycle 1 Day 1

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Coagulation (unless previous assessment was performed within previous 72 hours)
- 12-lead ECG (unless previous assessment was performed within previous 72 hours)
- Urine or serum pregnancy test (female participants of childbearing potential only) must be performed and be negative prior to treatment and counseled on appropriate contraception
- Administer PLD
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- 60-minute observation period after PF-07901801 infusion; vital signs assessed in 30-minute intervals
- Adverse events
- Concomitant medications and procedures
- Blood collection for CA-125
- Blood collection for PF-07901801 concentration
- Blood collection for PLD concentration
- Blood collection for biomarkers/pharmacodynamics
- Blood collection for PF-07901801 anti-drug antibodies

Cycle 1 Day 8

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg)
- 60-minute observation period after PF-07901801 infusion; vital signs assessed in 30-minute intervals
- Adverse events

- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics

Cycle 1 Day 15

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- 60-minute observation period after PF-07901801 infusion; vital signs assessed in 30-minute intervals
- Adverse events
- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics

Cycle 1 Day 22

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg)
- 60-minute observation period after PF-07901801 infusion; vital signs assessed in 30-minute intervals
- Adverse events
- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration

Cycle 2 Day 1

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- 12-lead ECG (unless previous assessment was performed within previous 72 hours)
- Urine or serum pregnancy test (female participants of childbearing potential only) must be performed and be negative prior to treatment and counseled on appropriate contraception
- Administer PLD
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures

- Blood collection for CA-125
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics
- Blood collection for PF-07901801 anti-drug antibodies
- Collection of FFPE/NBF tumor tissue for biomarkers/pharmacodynamics (tumor block preferred; if tumor block is not available, unstained slides are acceptable). Target date for tumor tissue collection is Cycle 2 Day 1 but can collected anytime within seven days prior to and up to 14 days after this visit (ie, tumor tissue should be collected within a 21-day window), other times may be acceptable after consultation with sponsor.

Cycle 2 Day 8 (48 mg/kg dose level only)

- Hematology, unless previous assessment was performed within previous 72 hours, may be completed by a local lab.

Cycle 2 Day 15

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, and respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics

Cycle 2 Day 15 and Beyond (at any visit)

- FFPE/NBF Tumor biopsies may be collected at response, progression, at the time of any surgical intervention, end of treatment and at investigator's discretion for biomarkers/pharmacodynamics; tumor block preferred; if block is not available, unstained slides are acceptable

Cycle 2 Day 22 (48 mg/kg dose level only)

- Hematology, unless previous assessment was performed within previous 72 hours, may be completed by a local lab.

Cycle 3 Day 1

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless previous assessment was performed within previous 72 hours)

- Hematology (unless previous assessment was performed within previous 72 hours)
- Urine or serum pregnancy test (female participants of childbearing potential only) must be performed and be negative prior to treatment and counseled on appropriate contraception
- 12-lead ECG (unless previous assessment was performed within previous 72 hours)
- Radiologic assessment of disease status (unless performed within previous 7 days)
- Administer PLD
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for CA-125
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics
- Blood collection for PF-07901801 anti-drug antibodies

Cycle 3 Day 8 (48 mg/kg dose level only)

- Hematology, unless previous assessment was performed within previous 72 hours, may be completed by a local lab

Cycle 3 Day 15

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, and respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics

Cycle 3 Day 22 (48 mg/kg dose level only)

- Hematology, unless previous assessment was performed within previous 72 hours, may be completed by a local lab.

Cycle 4 Day 1

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- 12-lead ECG (unless previous assessment was performed within previous 72 hours)

- Urine or serum pregnancy test (female participants of childbearing potential only) must be performed and be negative prior to treatment and counseled on appropriate contraception
- Administer PLD
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for CA-125
- Blood collection for PF-07901801 concentration
- Blood collection for PLD concentration
- Blood collection for biomarkers/pharmacodynamics
- Blood collection for PF-07901801 anti-drug antibodies

Cycle 4 Day 15

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration

Cycle 5 Day 1, Cycle 7 Day 1, Cycle 9 Day 1, etc. (every odd cycle)

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Urine or serum pregnancy test (female participants of childbearing potential only) must be performed and be negative prior to treatment and counseled on appropriate contraception
- 12-lead ECG (unless previous assessment was performed within previous 72 hours)
- Radiologic assessment of disease status (unless performed within previous seven days)
- Administer PLD
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for CA-125
- Blood collection for PF-07901801 concentration
- Blood collection for biomarkers/pharmacodynamics
- Blood collection for PF-07901801 anti-drug antibodies

Cycle 5 Day 1, Cycle 9 Day 1, Cycle 13 Day 1, Cycle 17 Day 1, etc. (every fourth cycle)

- Blood collection for biomarkers/pharmacodynamics

Cycle 5 Day 15, Cycle 7 Day 15, Cycle 9 Day 15, etc. (every odd cycle)

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration

Cycle 6 Day 1, Cycle 8 Day 1, Cycle 10 Day 1, etc. (every even cycle)

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Urine or serum pregnancy test (female participants of childbearing potential only) must be performed and be negative prior to treatment and counseled on appropriate contraception
- Blood collection for CA-125
- Administer PLD
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures

Cycle 6 Day 15, Cycle 8 Day 15, Cycle 10 Day 15, etc. (every even cycle)

- Brief physical examination
- Vital signs (temperature, blood pressure, pulse rate, and respiratory rate)
- Serum chemistry (unless previous assessment was performed within previous 72 hours)
- Hematology (unless previous assessment was performed within previous 72 hours)
- Administer PF-07901801 (12 mg/kg, 24 mg/kg, 48 mg/kg)
- Adverse events
- Concomitant medications and procedures

End-of-Treatment Visit (7 ± 3 days after last administration of study treatment)

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- Adverse events

- Concomitant medications and procedures
- Blood collection for PF-07901801 concentration
- Blood collection for PF-07901801 anti-drug antibodies

Safety Follow-Up Visit (30 + 5 days after last administration of study treatment or before initiation of subsequent anti-cancer therapy, whichever occurs soonest)

- Complete physical examination
- Vital signs (temperature, blood pressure, pulse rate, respiratory rate, weight)
- ECOG PS
- Serum chemistry (unless performed within previous 72 hours)
- Hematology (unless performed within previous 72 hours)
- 12-lead ECG
- Urine or serum pregnancy test (female participants of childbearing potential only) and counseled on appropriate contraception
- Radiologic assessment of disease status (unless performed within previous 7 days)
- Adverse events
- Concomitant medications and procedures
- Blood collection for CA-125
- Blood collection for PF-07901801 concentration
- Blood collection for PF-07901801 anti-drug antibodies

Long-Term Follow-Up Period

- Radiologic assessment of disease status (participants who have not experienced disease progression)
- Participants with an unresolved AE at the Safety Follow-Up visit considered possibly related to ADA formation may be asked to return to the clinic for ADA blood sampling at approximately 3-month intervals (if feasible given the underlying disease) until the AE or its sequelae resolve or stabilize at a level acceptable to the investigator and sponsor up to a maximum of 12 months.
- Survival and initiation of new anti-cancer therapies (assessed every 12 ± 2 weeks; telephone contact is acceptable)

12 STATISTICAL CONSIDERATIONS

12.1 Sample Size

12.1.1 Dose Escalation

The number of participants will depend on the number of dose cohorts that will be enrolled before reaching the MTD. It is anticipated that the study will evaluate three dose levels of PF-07901801 given in combination with a fixed dose of PLD. On the basis of emerging safety and/or clinical activity data, additional dose levels may be added. The size and design of the Phase 1 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-07901801 in combination with fixed-dose PLD and establishing PF-07901801 doses for further evaluation in the intended participant population. Based on a standard 3+3 design, up to approximately six DLT-evaluable participants may be enrolled in each dose level cohort during the Phase 1 dose escalation portion of the study; a minimum of nine and a maximum of 18 DLT-evaluable participants is anticipated.

12.1.2 Expansion Cohort

Phase 2 expansion cohort is planned to evaluate a selected PF-07901801 dose level in combination with a fixed dose of PLD. In this hypothesis-generating study, assuming an objective response rate of 10% with PLD monotherapy and an alternative of 30%, a power of 80% and one-sided Type 1 error set at 0.05, the combination will be considered worthy of further study if at least six responses are observed in the 25-participant cohort. If the dose level combination selected for further Phase 2 is determined to be not optimal or not well tolerated, an intermediate dose level, not to exceed the dose levels evaluated in Phase 1, may be implemented.

Other secondary endpoints, such as disease control, duration of response, progression-free survival and overall survival will be analyzed descriptively.

12.2 Analysis Populations

The following analysis populations are defined for the study:

Safety Population: all participants who received at least one dose of PF-07901801

DLT-Evaluable Population: all participants in Phase 1 who either experience DLT after at least one dose of PF-07901801 or did not experience a DLT and received the full dose of PLD and at least two infusions of PF-07901801 and completed safety evaluations during the 28-day Cycle 1 DLT period.

PF-07901801 and PLD Concentration Analysis Population: all participants who received at least one dose of PF-07901801 or PLD and have at least one evaluable blood sample for analysis collected.

12.3 Criteria for Evaluation

12.3.1 Safety

All participants who receive at least dose of PF-07901801 will be included in the safety analyses.

Adverse events, ECGs, laboratory data will be summarized and reviewed on an ongoing basis during the study. All adverse events, ECGs, LVEF assessments and safety laboratory abnormalities of potential clinical concern will be described. Safety data will be presented in tabular and/or graphical format and summarized descriptively by dose cohort and time where appropriate. Absolute value data and changes from baseline data will be summarized as appropriate.

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and severity of adverse events and laboratory abnormalities will be graded using NCI CTCAE v5 as appropriate. Incidence tables of participants with adverse events will be presented for all adverse events by maximum severity, serious adverse events, adverse events assessed as related to study drug and adverse events resulting in discontinuation of study drug.

For ECG analyses, the mean of the triplicate ECG parameters will be used as the observation for a participant at a nominal time point. Changes in ECG and laboratory measurements will be summarized.

Listings of all safety data sorted by dose cohort, participant and assessment date will be provided.

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The incidence, onset time and titer of PF-07901801 directed anti-drug antibodies will be summarized descriptively. Exploratory analysis may be conducted to evaluate the possible effects of anti-drug antibodies on PF-07901801 concentrations, efficacy and safety endpoints.

12.3.4 Disease Control

Clinical efficacy will be evaluated using overall tumor response for participants with measurable disease as assessed by the investigators using RECIST v1.1 (Appendix B). Duration of response will be calculated for participants 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 after achieving response. Progression-free survival will be calculated for all treated participants from the date of the first dose until the date of progression or death. Participants without progression or death will be censored at the date of last non-PD assessment. Overall survival will be calculated for all treated participants from the date of the first dose until date of death. Participants without death will be censored at the last date the participant was known to be alive. Disease control rate is defined as the percentage of participants who have achieved CR, PR, or SD lasting at least 12 weeks.

12.3.5 Biomarker and Pharmacodynamics Assessments

The details of biomarker and pharmacodynamic assessments will be described in the SAP or in a separate exploratory analysis plan. Results of biomarker and pharmacodynamic analyses will be described in the CSR to the extent possible. Due to the exploratory nature of these endpoints, the associated data analyses may not be completed at the time of the CSR preparation. If results of biomarker and pharmacodynamic analyses are not included in the CSR, they may be disseminated to the scientific community to the extent possible through presentation at scientific meetings and/or publication in peer-reviewed scientific journals.

12.4 Statistical Methods

Tabular summaries of data will be descriptive in nature (i.e., number of participants [n], mean, standard deviation, median, minimum and maximum for continuous variables and n and percent for categorical variables). For efficacy parameters, including objective response rate and disease control rate, 95% confidence intervals will be presented using the Wilson's score method. Time-to event endpoints such as DOR, PFS, and OS will be evaluated using Kaplan-Meier method.

Protocol deviations will be listed. Protocol deviations that might substantially affect efficacy analyses will be determined prior to database lock.

A more detailed description of analysis methods will be provided in the SAP to be completed prior to the clinical database lock.

13 SAFETY

Adverse events observed, mentioned on open questioning by a member of the investigator team, or spontaneously reported by the participantwill be documented. Adverse events will be documented event based. The observation phase for adverse events will start with signing the informed consent and will end at the completion of the active reporting period. Planned timepoints for all safety assessments are provided in the Study Assessments (Section 10). Unscheduled safety measurements may be obtained at any time during the study to assess any perceived safety issues.

13.1 Definition of Adverse Events

13.1.1 Adverse Event

An adverse event is any untoward medical occurrence or the worsening of a pre-existing medical condition following or during exposure to a pharmaceutical product, whether or not considered causally related to the product. Development of new disease lesions or disease progression is not considered an adverse event.

All AEs and SAEs occurring in a participant during the active collection period as described in Section 13.5.3 will be recorded on the appropriate CRF from the signature of the informed consent. All SAEs must be reported on the CT SAE Report Form to Pfizer Safety immediately upon awareness and under no circumstance should this exceed 24 hours. A worsening of a condition/disease recorded in the medical history is reportable as an AE. Documentation must be supported by an entry in the participant's source medical records. Laboratory abnormalities requiring treatment or considered by the investigator to be clinically relevant should be reported in the CRF as an AE. Each AE is to be evaluated for duration, severity and causal relationship with the IP.

For the purposes of this study, events that are unequivocally due to disease progression should not be reported as AEs unless the outcome is fatal within the active collection period. Hospitalization due to signs and symptoms of disease progression should not be reported as an SAE. If the malignancy has a fatal outcome during the study, the event leading to death must be recorded as an AE on the CRF, and as an SAE with CTCAE Grade 5 if it occurs during the active collection period. Symptoms of the disease under study/lack of efficacy should not be classified as AEs as long as they are within normal day-to-day fluctuations or expected progression of the disease.

The development of a new cancer should be regarded as an AE and will generally meet at least one of the SAE criteria. New cancers are those that are not the primary reason for study treatment and have been identified after the participant's inclusion in this study. They do not include metastases of the original cancer.

13.1.2 Serious Adverse Event

A serious adverse event is an adverse event occurring during any study at any dose of the investigational product(s) that fulfills one or more of the following:

- Results in death

- Is immediately life-threatening (the participant was at risk of death at the time of the event; this does not refer to an event which hypothetically might have caused death if it were more severe)
- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability or incapacity
- Results in a congenital abnormality or birth defect
- Is an important medical event that may jeopardize the participant or may require medical intervention to prevent one of the outcomes listed above

Medical or scientific judgment should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life threatening or result in death or hospitalization but may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious.

Examples of such events include invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

All serious adverse events that occur after any participant has signed informed consent, been enrolled, before treatment, during treatment, or within 30 days following the cessation of treatment, whether or not they are related to the study intervention, must be recorded on a Serious Adverse Event form.

13.2 Clarifications to Serious Adverse Event Reporting

- Death is an outcome of a serious adverse event and not a serious adverse event in itself. When death is an outcome, report the event(s) resulting in death as the serious adverse event term (e.g., “pulmonary embolism”). If the cause of death is unknown, report “Death, unknown cause” as the serious adverse event term.

- Pre-planned or elective hospitalizations including social and/or convenience situations (e.g., respite care) are excluded from serious adverse event reporting. In addition, emergency room visits and admission under 23-hour observation are excluded from serious adverse event reporting; however, such events should still be reported on the appropriate adverse event eCRF page.

- An isolated laboratory abnormality is not reportable as a serious adverse event unless the investigator assesses that the event meets the standard ICH criteria for a serious adverse event.

13.3 Assessment of Causality

The relationship of each adverse event to administration of the study drug(s) will be assessed by the investigator after careful consideration of all relevant factors such as (but not limited to) the underlying study indication, co-existing disease, concomitant medication, relevant history, pattern of the adverse event, temporal relationship to receipt of the study medication(s) and de-challenge or re-challenge.

Study drug or study treatment refers to intravenously-administered PLD and intravenously-administered PF-07901801. The assessment of relationship to study drug or study treatment will be done for each drug separately. If the investigator feels such a distinction cannot be made, the assessment will be based on the combination of the two drugs.

The assessment of causality is based on the question of whether there was a reasonable causal relationship to the study drug in question according to the following guidelines:

RELATED: there is a reasonable possibility that the study treatment caused the event; one or more of the following criteria apply:

- The event follows a reasonable temporal sequence from administration of study treatment
- The event could not be reasonably attributed to the known characteristics of the participant's clinical state, environment or toxic factors or other modes of therapy administered to the participant
- The event follows a known pattern of response to study treatment
- The event disappears or decreases on cessation or reduction in dose of the study treatment. In some situations, an adverse event will not disappear or decrease in intensity upon discontinuation of the study treatment despite other clear indications of relatedness

UNRELATED: there is no reasonable possibility that the study treatment caused the event; one or more of the following criteria apply:

- The event does not follow a reasonable temporal sequence from administration of study treatment
- The event could be reasonably attributed to known characteristics of the participant's clinical state, concurrent illness, environment or toxic factor or other therapies administered to the participant
- The event does not follow a known pattern of response to study treatment
- The event does not disappear or decrease on cessation or reduction in dose of the study treatment, and it does not reappear or worsen when the study treatment is re-administered
- There is a clear alternative explanation

13.4 Assessment of Severity

The severity rating of an adverse event refers to its intensity. The severity of each adverse event will be categorized using the NCI CTCAE v5. For any term that is not specifically listed in the CTCAE scale, intensity should be assigned a grade of 1 through 5 using the following CTCAE guidelines:

Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated

Grade 2: Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental activities of daily living

Grade 3: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living

Grade 4: Life-threatening consequences; urgent intervention indicated

Grade 5: Death related to adverse event

It is important to distinguish between serious adverse events and severe adverse events. Severity is a measure of intensity whereas seriousness is defined by the criteria under Section 13.1.2. An adverse event of severe intensity may not be considered a serious adverse event.

13.5 Action Taken

Any action with study treatment to resolve the adverse event is to be documented using the categories listed below. The study drug action should be recorded separately for each component as detailed in the eCRF.

- Drug withdrawn
- Drug interrupted
- Dose reduced
- Dose not changed
- Not applicable
- Unknown

13.5.1 Other Specific Treatments of Adverse Event

- None
- Remedial drug therapy
- Other

13.5.2 Outcome of Adverse Event

The outcome of the adverse event is to be documented as follows:

- Recovered / resolved
- Recovering / resolving
- Recovered / resolved with sequelae
- Not recovered / not resolved
- Fatal
- Unknown

13.5.3 Time Period and Frequency for Collecting AE and SAE Information

The time period for actively eliciting and collecting AEs and SAEs ("active collection period") for each participant begins from the time the participant provides informed-consent, which is obtained before undergoing any study-related procedure and/or receiving study intervention, through and including a minimum of 30 calendar days after the last administration of the study intervention.

For participants who are screen failures, the active collection period ends when screen failure status is determined.

If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.

If a participant permanently discontinues or temporarily discontinues study intervention because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE reported using the CT SAE Report Form.

Investigators are not obligated to actively seek information on AEs or SAEs after the participant has concluded study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has completed the study, and they consider the event to be reasonably related to the study intervention, the investigator must promptly report the SAE to Pfizer using the CT SAE Report Form.

13.5.4 Documentation

All AEs (serious and non-serious) occurring within the period of observation for the study must be documented in the CRF with the following information, where appropriate. (The period of observation for the study is described in Section 13.5.3).

- AE name or term
- When the AE first occurred (start date)
- When the AE stopped (stop date or an indication of "ongoing")
- Severity of the AE
- Seriousness (hospitalization, death, etc.)
- Actions taken
- Outcome
- Investigator opinion regarding the AE relationship to the IP(s)

All nonserious AEs and SAEs occurring in a participant during the active collection period which begins after obtaining informed consent as described in Section 13.5.3, will be recorded on the AE section of the CRF.

The investigator or designee is to record on the CRF all directly observed and all spontaneously reported AEs and SAEs reported by the participant.

The investigator must record his or her reasoning for this decision in the participant's medical record and as a comment on the CRF.

Reporting of AEs and SAEs for participants who fail screening are subject to the CRF requirements as described in Section 13.5.3.

As part of ongoing safety reviews conducted by the sponsor, any nonserious AE that is determined by the sponsor to be serious will be reported by the sponsor as an SAE. To assist in the determination of case seriousness, further information may be requested from the investigator to provide clarity and understanding of the event in the context of the clinical study.

If a participant begins a new anti-cancer therapy, the recording period for nonserious AEs ends at the time the new treatment is started; however, SAEs must continue to be recorded on the CRF during the above indicated active collection period. Note that a switch to a commercially available version of the study intervention is considered as a new anti-cancer therapy for the purposes of SAE reporting.

13.5.5 Follow-Up

Follow-up by the investigator continues throughout and after the active collection period and until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator.

If a participant is lost to follow-up, this should be captured accordingly within the adverse event eCRF and on the follow-up serious adverse event report.

When a clinically important AE remains ongoing at the end of the active collection period, follow-up by the investigator continues until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator and Pfizer concurs with that assessment.

After the initial AE or SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. For each event, the investigator must pursue and obtain adequate information until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow up.

In general, follow up information will include a description of the event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare providers.

All findings relevant to the final outcome of an AE must be reported in the participant's medical record and recorded on the eCRF page.

New and ongoing treatment-related serious adverse events should be followed beyond the 30-day Safety Follow-Up Visit. If the participant dies, this should be captured as the outcome of the adverse event unless no link between the adverse event and the participant death can be established, in which case the adverse event will be marked as ongoing and the death will be reported as a separate event. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer Safety.

13.5.6 Notification

Serious Adverse Events

The investigator or designee must report all SAEs (related and unrelated) promptly to Pfizer Safety within 24 hours of the knowledge of the occurrence.

To report the SAE, complete the CT SAE form electronically in the Pfizer SAE Submission Assistant (PSSA) tool. When the form is completed, Pfizer Safety personnel will be notified electronically. If the event meets serious criteria and it is not possible to access the PSSA tool, then fax the completed paper CT SAE form to Pfizer Safety within 24 hours of awareness. When the PSSA tool becomes available, the SAE information must be entered within 24 hours of the PSSA system becoming available.

At the time of first notification, the investigator or designee should provide the following information, if available:

- Protocol number
- Reporter (study site and investigator)
- Participant's study number
- Participant's year of birth
- Participant's gender
- Date of first dose of IP(s)
- Date of last dose of IP(s), if applicable
- AE term
- Date of occurrence of the event
- A brief description of the event, outcome to date, and any actions taken
- The seriousness criteria(on) that were met
- Concomitant medication at onset of the event
- Relevant medical history information
- Relevant laboratory test findings
- Investigator's opinion of the relationship to IP(s). ("Is there a reasonable possibility that the IP caused the SAE? Yes or No?")

It should be noted that the CT SAE Report Form for reporting of SAE information is not the same as the AE page of the CRF. When the same data are collected, the forms must be completed in a consistent manner. AEs should be recorded using concise medical terminology and the same AE term should be used on both the CRF and the CT SAE Report Form for reporting of SAE information.

13.5.7 Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The

sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRBs/ECs, and investigators.

Investigator safety reports must be prepared for SUSARs according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives SUSARs or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the SRSD(s) for the study and will notify the IRB/EC, if appropriate according to local requirements.

13.6 Adverse Events of Special Interest

N/A

13.7 Lack of Efficacy

The investigator must report signs, symptoms, and/or clinical sequelae resulting from lack of efficacy. Lack of efficacy or failure of expected pharmacological action is reportable to Pfizer Safety only if associated with an SAE.

13.8 Environmental Exposure, Exposure during Pregnancy, or Breastfeeding, and Occupational Exposure

Environmental exposure, occurs when a person not enrolled in the study as a participant receives unplanned direct contact with or exposure to the study intervention. Such exposure may or may not lead to the occurrence of an AE or SAE. Persons at risk for environmental exposure include healthcare providers, family members and others who may be exposed. An environmental exposure may include Exposure During Pregnancy (EDP), Exposure During Breastfeeding (EDB) and occupational exposure. Any such exposure to the study intervention under study are reportable to Pfizer Safety within 24 hours of investigator awareness.

13.8.1 Exposure During Pregnancy (EDP)

An EDP occurs if:

- A female participant is found to be pregnant while receiving or after discontinuing study intervention for at least 45 days after last dose of PF-07901801 AND for combination therapy with PLD, during and for 6 months after treatment which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s).

- A female nonparticipant is found to be pregnant while being exposed or having been exposed to study intervention because of environmental exposure. Below are examples of environmental EDP:

    - A female family member or healthcare provider reports that she is pregnant after having been exposed to the study intervention by ingestion, inhalation or skin contact.

- A male family member or healthcare provider who has been exposed to the study intervention by ingestion, inhalation or skin contact then inseminates his female partner prior to or around the time of conception.

The investigator must report EDP to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The initial information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

- If EDP occurs in a participant or participant's partner, the investigator must report this information to Pfizer Safety through PSSA, on the CT SAE Report Form and an EDP Supplemental Form regardless of whether an SAE has occurred. Details of the pregnancy will be collected after the start of study intervention until 45 days after the last dose of PF-07901801 and for combination therapy with PLD, during and for 6 months after treatment.

- If EDP occurs in the setting of environmental exposure, the investigator must report information to Pfizer Safety through PSSA using the CT SAE Report Form and EDP Supplemental Form. Since the exposure information does not pertain to the participant enrolled in the study, the information is not recorded on a CRF, however, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

Follow-up is conducted to obtain general information on the pregnancy and its outcome for all EDP reports with an unknown outcome. The investigator will follow the pregnancy until completion (or until pregnancy termination) and notify Pfizer Safety of the outcome as a follow-up to the initial EDP Supplemental Form. In the case of a live birth, the structural integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless pre-procedure test findings are conclusive for a congenital anomaly and the findings are reported).

Abnormal pregnancy outcomes are considered SAEs. If the outcome of the pregnancy meets the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death or congenital anomaly), the investigator should follow the procedures for reporting SAEs. Additional information about pregnancy outcomes that are reported to Pfizer Safety as SAEs follows:

- Spontaneous abortion including miscarriage, and missed abortion should be reported as an SAE

- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to the study intervention.

Additional information regarding the EDP may be requested by the sponsor. Further follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on preterm infants to identify developmental delays). In the case of paternal exposure, the investigator will provide the participant with the Pregnant Partner Release of Information Form (PPRIF) to deliver to his partner. The investigator must document in the source documents that the participant was given the Pregnant Partner Release of Information Form to provide to his partner.

13.8.2 Exposure During Breastfeeding (EDB)

An EDB occurs if:

A female participant is found to be breastfeeding while receiving or after discontinuing study intervention until 45 days after the last dose of PF-07901801 and for combination therapy with PLD, during and for 6 months after treatment.

A female non-participant is found to be breastfeeding while being exposed or having been exposed to study intervention (ie, environmental exposure). An example of environmental EDB is a female family member or healthcare provider who reports that she is breastfeeding after having been exposed to the study intervention by ingestion, inhalation or skin contact.

The investigator must report EDB to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The information must be reported through PSSA. When EDB occurs in the setting of environmental exposure, the exposure information does not pertain to the participant enrolled in the study, so the information is not recorded on a CRF. However, a copy of the completed CT SAE Report Form (extracted from PSSA) is maintained in the investigator site file.

An EDB report is not created when a Pfizer drug specifically approved for use in breastfeeding women (eg, vitamins) is administered in accordance with authorized use. However, if the infant experiences an SAE associated with such a drug, the SAE is reported together with the EDB.

13.8.3 Occupational Exposure

The investigator must report any instance of occupational exposure to Pfizer Safety within 24 hours of the investigator's awareness using the CT SAE Report Form regardless of whether there is an associated SAE. Since the information about the occupational exposure does not pertain to a participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form (extracted from PSSA) must be maintained in the investigator site file.

13.8.4 Cardiovascular and Death Events

Not Applicable

13.8.5 Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs

Not applicable

13.9 Medication Error

Medication errors may result from the administration or consumption of the study intervention by the wrong participant, or at the wrong time, or at the wrong dosage strength.

Medication errors include:

- Medication errors involving participant exposure to the study intervention
- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the study participant
- The administration of expired study intervention
- The administration of an incorrect study intervention
- The administration of an incorrect dosage
- The administration of study intervention that has undergone temperature excursion from the specified storage range, unless it is determined by the sponsor that the study intervention under question is acceptable for use.

In the event of a medication dosing error, the sponsor should be notified within 24 hours.

Whether or not the medication error is accompanied by an AE, as determined by the investigator, the medication error and associated AE(s), serious and non-serious, are recorded on the AE page of the CRF. Medication errors should be reported to Pfizer Safety within 24 hours through PSSA only when associated with an SAE.

13.10 Laboratory Abnormalities

To the extent possible, all laboratory abnormalities observed during the course of the study will be included under a reported adverse event term describing a clinical syndrome (e.g., elevated blood urea nitrogen and creatinine in the setting of an adverse event of “renal failure”). In these cases (e.g., an adverse event of renal failure), the laboratory abnormality itself (e.g., elevated creatinine) does not need to be recorded as an adverse event.

If a laboratory abnormality cannot be reported as a clinical syndrome, AND if the laboratory abnormality results in a therapeutic intervention (i.e., concomitant medication or therapy), is a dose-limiting toxicity or is judged by the investigator to be of other particular clinical relevance, then the laboratory abnormality should be reported as an adverse event. Laboratory Abnormalities requiring treatment or considered by the investigator to be clinically-relevant should be reported in the CRF as an AE.

See APPENDIX D for suggested actions and follow-up assessments in the event of potential drug induced liver injury.

See APPENDIX E for instructions for laboratory testing to monitor kidney function and reporting laboratory test abnormalities.

Participants experiencing adverse events or clinically-significant laboratory abnormalities will be assessed and appropriate evaluations performed until all parameters have returned to baseline levels or are consistent with the participant's then-current physical condition.

13.11 Sponsor Safety Review

The medical monitor or designee will be responsible for the ongoing review and evaluation of safety throughout the study (this includes all laboratory, ECG and echocardiogram/MUGA data as well as all adverse events).

13.12 Overview of Safety Monitoring

Throughout the study, investigators, site staff and the study sponsor will meet regularly to review the status of all active participants on study. During the dose escalation portion of the study, a regularly scheduled safety and information call will be held with participating investigators and site staff to discuss safety, review any questions, provide updates and to share information across sites. At the completion of each dose escalation cohort, safety data will be summarized and presented for discussion with all investigators for the purpose of determining whether the observed safety in each cohort warrants escalation to the next higher dose level or whether an alternate dose level or other action should be considered.

During the dose expansion portion of the study, these regularly-scheduled safety and information calls will continue; the calls will initially be held regularly although *ad hoc* meetings may be held as necessary to review specific safety or other issues that might arise during the course of the study. As the study progresses, the frequency of these safety and information calls may be adjusted to reflect need on the basis of safety observations observed, the rate of enrollment and investigator or sponsor request or need.

14 ETHICAL AND ADMINISTRATIVE CONSIDERATIONS

This study will be conducted in accordance with applicable national and local regulations and guidelines, Good Clinical Practice (GCP), including ICH guidelines (Integrated Addendum To ICH E6[R1]: Guideline For Good Clinical Practice, E6[R2], Current Step 4 version [2016]), the National Statement on Ethical Conduct in Human Research 2007, and The Declaration of Helsinki (Brazil, 2013).

14.1 Regulatory Authority Approvals

The sponsor or designee will submit the study protocol plus all relevant study documents to applicable regulatory agencies for approval , as appropriate, before the study start. No participant will be admitted to the study until regulatory submissions are complete and approvals, where appropriate, have been received.

Each investigator must complete a Form FDA 1572 or equivalent and provide the completed form according to written instructions to the sponsor (or designee). Each investigator must submit to the sponsor (or designee) financial disclosure information according to national law and/or local regulations.

Data generated in the US will be handled in accordance with the Health Information Portability and Accountability Act (HIPAA). The study will be registered at www.clinicaltrials.gov using the Protocol Registration System.

14.2 Institutional Review Board

This protocol and any material to be provided to the participant (such as advertisements, patient information sheets, informed consent document or descriptions of the study used to obtain informed consent) will be submitted by the investigator to an IRB. This also applies to protocol amendments.

The sponsor will supply relevant data for the investigator to submit the study protocol and additional study documents to the IRB. The principal investigator will submit the study protocol for review and approval by an IRB, according to national law and/or local regulations, and will provide the IRB with all appropriate materials.

Verification of the IRB's unconditional approval of the study protocol and the written ICF will be transmitted to the sponsor. This approval must refer to the study by exact study protocol title and number, identify the documents reviewed, and state the date of the review.

No patient will be admitted to the study until appropriate IRB approval of the study protocol and the informed consent document has been received, the investigator has obtained the signed and dated ICF, and the sponsor is notified.

The principal investigator will submit appropriate reports on the progress of the study to the IRB at least annually in accordance with applicable national law and/or local regulations and in agreement with the policy established by the IRB and sponsor.

The IRB must be informed by the principal investigator of all subsequent study protocol amendments and of serious adverse events or SUSARs occurring during the study that are likely to affect the safety of the participants or the conduct of the study.

14.3 Confidentiality of Information

The investigator must ensure that participants' anonymity is strictly maintained and that their identities are protected from unauthorized parties. Only participant initials and an identification code (i.e., not names) should be recorded on any form submitted to the sponsor and the IRB. The investigator must keep logs on screened and enrolled participants. In addition, the investigator must have a list where the identity of all treated participants can be found.

The investigator agrees that all information received from the sponsor, including, but not limited to, the Investigator's Brochure, this protocol, eCRFs, the protocol-specified treatment, and any other study information, remain the sole and exclusive property of the sponsor during the conduct of the study and thereafter. This information is not to be disclosed to any third party (except employees or agents directly involved in the conduct of the study or as required by law) without prior written consent from the sponsor. The investigator further agrees to take all reasonable precautions to prevent the disclosure by any employee or agent of the study center to any third party or otherwise into the public domain. The investigator shall be under

additional obligations related to non-disclosure confidential information and the handling of intellectual property as set forth in the Clinical Trial Agreement.

14.4 Patient Informed Consent

All information about the clinical study, including the participant information and the informed consent form, is prepared and used for the protection of the human rights of the participant according to ICH GCP guidelines and the Declaration of Helsinki.

It is the responsibility of the investigator to obtain signed informed consent forms from each participant participating in this study after adequate explanation of the aims, methods, objectives, and potential hazards of the study and before undertaking any study-related procedures.

The informed consent form, prepared by the investigator with the assistance of the sponsor, must be approved along with the study protocol by the IRB and be acceptable to the sponsor.

The participant must be provided with the patient information and informed consent form consistent with the study protocol version used and approved by the relevant IRB. The informed consent form must be in a language fully-comprehensible to the prospective participant. Participants (and/or relatives, guardians, or legal representatives, if necessary) must be given sufficient time and opportunity to inquire about the details of the study and to discuss with the investigator and decide on their participation in the study. The participant and the person explaining about the study and with whom they discuss the informed consent will sign and date the informed consent form. A copy of the signed informed consent form will be retained by the participant and the original will be filed in the investigator file unless otherwise agreed. The consenting process will be documented.

14.5 Study Monitoring

On behalf of the sponsor, a clinical research organization monitor will contact and visit the investigator at the study center as necessary before the entry of the first participant and at predetermined appropriate intervals during the study until after the last participant has completed. The clinical research organization will use centralized remote monitoring and on-site monitoring activities including source document verification to support and oversee activities being undertaken at the study center. The monitor will also perform a study closure visit.

In accordance with ICH GCP guidelines, the investigator must ensure provision of sufficient time, reasonable space, and adequate qualified personnel for the monitoring visits. The visits are for the purpose of verifying adherence to the study protocol and the completeness, consistency, and accuracy of data entered on the eCRF and other documents.

The investigator will make all source data (i.e, the various study records, the eCRFs, laboratory test reports, other participant records, drug accountability forms, and other pertinent data) available for the monitor and allow access to them throughout the entire study period. Monitoring is done by comparing the relevant site records of the participants with the entries on the eCRF (i.e., source data verification). It is the monitor’s responsibility to verify the

adherence to the study protocol and the completeness, consistency, and accuracy of the data recorded on the eCRFs.

By agreeing to participate in the study, the investigator agrees to cooperate with the monitor to ensure that any problems detected in the course of the monitoring visits are resolved. Contact information for the study monitor is located in the investigator file. Representatives from the sponsor may also contact and visit the investigators and monitor data during the study.

14.6 Clinical Supplies

The principal investigator will be responsible for the dispensing, inventory and accountability of all clinical supplies, ensuring that accepted medical and pharmaceutical practices are followed. An accurate and timely accountability record of the disposition of all clinical supplies must be maintained. The supplies and inventory record must be made available for inspection by the sponsor or the designated sponsor's representative upon request. Under no circumstances will the principal investigator allow the investigational product to be used other than as directed by this protocol.

14.7 Electronic Case Report Form

The data will be collected using an electronic data capture (EDC) system by remote data entry on eCRFs and by agreeing to participate in the study, the investigator agrees to maintain accurate eCRF and source documents as part of the case history for each participant who participates in the study. Sites will receive training on the EDC system. All users will be supplied with unique login credentials.

Before study start, the investigator will prepare a list showing the signature and handwritten initials of all individuals authorized to make or change entries on eCRFs. This "study center personnel and delegation list" must be kept current throughout the study.

For each participant enrolled, an eCRF must be completed, reviewed, signed and dated by the principal investigator or Co-investigator. Data entry into the CRF should be completed within a reasonable time period after data collection, generally on the order of approximately two weeks. This also applies to records for those participants who fail to complete the study. If a participant withdraws from the study, the reason must be noted on the eCRF. If a participant is withdrawn from the study because of a treatment-limiting adverse event, thorough efforts should be made to clearly document the outcome.

All laboratory data and investigator observations on the results and any other clinically significant test results must be documented on eCRFs. Full information regarding EDC and completing eCRFs is included in the investigator files. All questions or comments related to electronic data capture should be directed to the assigned study monitor.

14.8 Study Termination and Site Closure

Both the sponsor and the investigator reserve the right to terminate the study at any time. Should this be necessary, both parties will arrange discontinuation procedures. In terminating the study, the sponsor and the investigator will ensure that adequate consideration is given to the protection of the participants' interests.

The sponsor reserves the right to discontinue the study at any time for medical or administrative reasons. When feasible, a 30-day written notification will be given.

The entire study will be stopped if:

- The protocol-specified treatment is considered too toxic to continue the study
- Evidence has emerged that, in the opinion of the sponsor or the investigator(s), makes the continuation of the study unnecessary or unethical
- The stated objectives of the study are achieved
- The sponsor discontinues the development of study drug

Regardless of the reason for termination, all data available for the participant at the time of discontinuation of follow-up must be recorded on the eCRF. All reasons for discontinuation of treatment must be documented. In terminating the study, the investigator will ensure that adequate consideration is given to the protection of the participants' interests.

14.9 Modification of the Study Protocol

Protocol amendments, except when necessary to eliminate an immediate hazard to participants, must be made only with the prior approval of the sponsor. Agreement from the investigator must be obtained for all protocol amendments and amendments to the informed consent document. The IRB must be informed of all amendments and give approval before their implementation. The sponsor will submit any study protocol amendments to the concerned regulatory authorities for approval and keep the investigator(s) updated as detailed in the ICH GCP guidelines.

14.10 Retention of Study Documents

The study site will maintain a study file, which should contain, at minimum, the IB, the protocol and any amendments, drug accountability records, correspondence with the IRB and the sponsor, and other study-related documents.

The investigator agrees to keep records and those documents that include (but are not limited to) the identification of all participating participants, medical records, study-specific source documents, source worksheets, all original signed and dated ICFs, copies of all eCRFs, query responses, and detailed records of drug disposition to enable evaluations or audits from regulatory authorities and the sponsor or its designees.

The investigator shall retain records required to be maintained for a period of 5 years after the date a marketing application in an ICH region is approved for the drug for the indication for which it is being investigated or, if no application is to be filed or if the application is not approved for such indication, until at least 5 years after the investigation is discontinued. However, these documents should be retained for a longer period if required by the applicable regulatory requirement(s) or if needed by the sponsor. In addition, the investigator must make provision for the participants' medical records to be kept for the same period of time.

No data should be destroyed without the agreement of the sponsor. Should the investigator wish to assign the study records to another party or move them to another location, the sponsor

must be notified in writing of the new responsible person and/or the new location. The sponsor will inform the investigator, in writing, when the study-related records are no longer needed.

Participants' medical records and other original data will be archived in accordance with the archiving regulations or facilities of the investigational site.

14.11 Clinical Study Report

A clinical study report will be prepared under the responsibility and supervision of the sponsor and signed by a sponsor representative, thereby indicating their agreement with the analyses, results, and conclusions of the clinical study report.

14.12 Study Publication

The conditions regulating dissemination of the information derived from this study are described in the Clinical Trial Agreement.

14.13 Quality Assurance Audits

An audit visit to clinical centers may be conducted by a quality assurance auditor appointed by the sponsor. The purpose of an audit, which is independent of and separate from routine monitoring or quality control functions, is to evaluate study conduct and compliance with the protocol, standard operating procedures, ICH GCP and the applicable regulatory requirements. The investigator and the sponsor may also be subject to an inspection by the US Food and Drug Administration (FDA), Health Canada, European regulatory authorities or other applicable regulatory authorities at any time.

The auditor and regulatory authorities will require authority from the investigator to have direct access to the participants' medical records. It is important that the investigator(s) and their staff cooperate with the auditor or regulatory authorities during this audit or inspection.

14.14 Dissemination of Clinical Study Data

Pfizer fulfills its commitment to publicly disclose clinical study results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the EudraCT/CTIS, and/or www.pfizer.com, and other public registries and websites in accordance with applicable local laws/regulations. In addition, Pfizer reports study results outside of the requirements of local laws/regulations pursuant to its SOPs.

In all cases, study results are reported by Pfizer in an objective, accurate, balanced and complete manner and are reported regardless of the outcome of the study or the country in which the study was conducted.

www.clinicaltrials.gov

Pfizer posts clinical trial results on www.clinicaltrials.gov for Pfizer-sponsored interventional studies (conducted in participants) that evaluate the safety and/or efficacy of a product, regardless of the geographical location in which the study is conducted. These results are submitted for posting in accordance with the format and timelines set forth by US law.

EudraCT/CTIS

Pfizer posts clinical trial results on EudraCT/CTIS for Pfizer-sponsored interventional studies in accordance with the format and timelines set forth by EU requirements.

www.pfizer.com

Pfizer posts CSR synopses and plain-language study results summaries on www.pfizer.com for Pfizer-sponsored interventional studies at the same time the corresponding study results are posted to www.clinicaltrials.gov. CSR synopses will have personally-identifiable information anonymized.

Documents within Marketing Authorization Applications

Pfizer complies with applicable local laws/regulations to publish clinical documents included in marketing applications. Clinical documents include summary documents and CSRs including the protocol and protocol amendments, sample CRFs, and SAPs. Clinical documents will have personally identifiable information anonymized.

Data Sharing

Pfizer provides researchers secure access to participant-level data or full clinical study reports for the purposes of "bona-fide scientific research" that contributes to the scientific understanding of the disease, target or compound class. Pfizer will make data available from these trials 24 months after study completion. Participant-level data will be anonymized in accordance with applicable privacy laws and regulations. Clinical study reports will have personally-identifiable information anonymized.

Data requests are considered from qualified researchers with the appropriate competencies to perform the proposed analyses. Research teams must include a biostatistician. Data will not be provided to applicants with significant conflicts of interest, including individuals requesting access for commercial/competitive or legal purposes.

14.15 Finance and Insurance

Details on finance and insurance will be provided in a separate agreement between the investigator and the sponsor.

14.16 Retention of Biological Specimens

Biological specimens collected during the course of this study may be used for purposes related to this research. Specimens will be stored until the sponsor has determined that specimens are no longer needed and the decision has been made that none of the samples need to be re-analyzed. Identifiable specimens can be destroyed at any time at the request of the participant.

15 REFERENCES

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16 APPENDIX A
ECOG Performance Status Assessment Scale

ECOG Performance Status	Description
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work.
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours.
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours.
4	Completely disabled. Cannot carry on selfcare. Totally confined to bed or chair.

17 APPENDIX B
Response Evaluation Criteria in Solid Tumor (RECIST) Version 1.1

RECIST guidelines (Version 1.1) are described in Eisenhauer (2009) and at https://recist.eortc.org/recist-1-1-2/; a short summary is given below.

Measurable Disease

Tumor lesions: measurable lesions are defined as those that can be accurately measured in at least one dimension (longest diameter to be recorded) with the following:

- A minimum size of 10 mm by CT scan (CT scan thickness no greater than 5 mm);
- A minimum size of 10 mm caliper measurement by clinical exam (lesions that cannot be accurately measured with calipers should be recorded as nonmeasurable);
- A minimum size of 20 mm by chest X-ray.

All tumor measurements must be recorded in millimeters (or decimal fractions of centimeters).

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- A minimum size of 20 mm by chest X-ray.

All tumor measurements must be recorded in millimeters (or decimal fractions of centimeters).

Malignant lymph nodes: to be considered pathologically enlarged and measurable, a lymph node must be ≥15 mm in short axis when assessed by CT scan (CT scan slice thickness recommended to be not greater than 5 mm). At baseline and in follow up, only the short axis will be measured and followed.

Non-measurable Disease

All other lesions (or sites of disease), including small lesions (longest diameter < 10 mm or pathological lymph nodes with ≥ 10 to < 15 mm short axis), as well as truly non-measurable lesions, are considered non-measurable disease. Lesions considered truly non-measurable include leptomeningeal disease, ascites, pleural/pericardial effusions, inflammatory breast disease, lymphangitic involvement of skin and lung, and abdominal masses/abdominal organomegaly identified by physical exam that is not measurable by reproducible imaging techniques.

Bone Lesions

Bone lesions, cystic lesion, and lesions previously treated with local therapy require particular comment. Bone scan, PET scan or plain films are not considered adequate imaging techniques to measure bone lesions. However, these techniques can be used to confirm the presence or disappearance of bone lesions.

Lytic bone lesions or mixed lytic-blastic lesions with identifiable soft tissue components that can be evaluated by cross-sectional imaging techniques such as CT or MRI can be considered as measurable lesions if the soft tissue component meets the definition of measurability described above. Blastic bone lesions are non-measurable.

Cystic Lesions

Lesions that meet the criteria for radiographically defined simple cysts should not be considered as malignant lesions (neither measurable nor non-measurable) because they are, by definition, simple cysts.

Cystic lesions thought to represent cystic metastases can be considered as measurable lesions if they meet the definition of measurability described above. However, if non-cystic lesions are present in the same patient, these are preferred as target lesions.

Lesions with Prior Local Treatment

Tumor lesions situated in a previous irradiated area or in an area subjected to other locoregional therapy are usually not considered measurable unless there has been demonstrated progression in the lesion.

Target Lesions

All measurable lesions up to a maximum of 2 lesions per organ and 5 lesions in total, representative of all involved organs, should be identified as target lesions and recorded and measured at baseline. Target lesions should be selected on the basis of their size (lesions with the longest diameter) and their suitability for accurate repeated measurements (either by imaging techniques or clinically). A sum of the longest diameter (LD) for all target lesions will be calculated and reported as the baseline sum LD. The baseline sum LD will be used as reference by which to characterize the overall tumor response.

Non-Target Lesions

RECIST criteria require unequivocal quantification of the changes in tumor size for adequate interpretation of the sum of target lesions. Consequently, when the boundaries of the primary are difficult to delineate, this tumor should not be considered a target lesion.

Guidelines for Evaluation of Measurable Disease

The same method of assessment and the same technique should be used to characterize each identified and reported lesion at baseline and during follow up. Imaging-based evaluation is

preferred to evaluation by clinical examination when both methods have been used to assess the antitumor effect of a treatment.

Evaluation of Target Lesions

Complete Response	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	At least a 30% decrease in the sum of the LD of target lesions, taking as reference the baseline sum LD.
Stable Disease	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	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 progression.

Evaluation of Non-Target Lesions

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

If tumor markers are initially above the institutional ULN, they must normalize for a patient to be considered a complete responder.

Evaluation of Best Overall Response

The best overall response is the best response recorded from the start of the treatment until disease progression/recurrence (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.

Timepoint Response

A response assessment will occur at the protocol-specified timepoints. The tables below provide a summary of the overall response status calculation at each timepoint for patients who have measurable and non-measurable disease (non-target disease only).

Timepoint Response: Patients with Target (± Non-Target) Disease

Target Lesions	Non-target Lesions	New Lesions	Overall Response
CR	CR	No	CR
CR	Non-CR/non-PD	No	PR
CR	Not evaluated	No	PR
PR	Non-PD or not evaluated	No	PR
SD	Non-PD or not evaluated	No	SD
Not Evaluated	Non-PD	No	NE
PD	Any	Yes or No	PD
Any	PD	Yes or No	PD
Any	Any	Yes	PD

CR, complete response; PD, progressive disease; PR, partial response; SD, stable disease; NE, Not evaluable.

Evaluation of Best Overall Response When Confirmation of CR and PR Required

Overall Response First Timepoint	Overall Response Subsequent Timepoint	Best Overall Response
CR	CR	CR
CR	PR	SD, PD or PR[a]
CR	SD	SD provided minimum criteria for SD duration met, otherwise, PD

Overall Response First Timepoint	Overall Response Subsequent Timepoint	Best Overall Response
CR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
CR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
PR	CR	PR
PR	PR	PR
PR	SD	SD
PR	PD	SD provided minimum criteria for SD duration met, otherwise, PD
PR	NE	SD provided minimum criteria for SD duration met, otherwise, NE
NE	NE	NE

a. If a CR is truly met at first timepoint, then any disease seen at a subsequent timepoint, even disease meeting PR criteria relative to baseline, makes this disease PD at that point (since disease must have reappeared after CR). Best response would depend on whether minimum duration for SD was met. However sometimes 'CR' may be claimed when subsequent scans suggest small lesions were likely still present and in fact the patient had PR, not CR at the first time point. Under these circumstances, the original CR should be changed to PR and the best response is PR.

Timepoint Response: Patients with Non-Target Lesion Assessments

Non-Target Lesions	New Lesions	Overall Response	Best Response for this Category also Requires
CR	No	CR	Normalization of tumor markers, tumor nodes < 10 mm
Non-CR/non-PD	No	Non-CR/non-PD	
Not all evaluated	No	NE	
Unequivocal PD	Any	PD	
Any	Yes	PD	

Note: Patients with a global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression at that time should be reported as "symptomatic deterioration". This is a reason for stopping therapy, but is NOT objective PD. Every effort should be made to document the objective progression even after discontinuation of treatment.

Missing Assessments and Not Evaluable Designation

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.

Patients with a global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression at that time should be classified as having symptomatic deterioration. Every effort should be made to document the objective progression, even after discontinuation of treatment.

In some circumstances, it may be difficult to distinguish residual disease from normal tissue. When the evaluation of CR depends on this determination, it is recommended that the residual lesion be investigated (fine needle aspiration/biopsy) before confirming the CR status.

Confirmatory Measurement/Duration of Response

Confirmation

Radiographic tumor assessments are required. 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.

Duration of Overall Response

The duration of overall response is measured from the time measurement criteria are met for CR or PR (whichever is first recorded) until the first date that recurrent or PD is objectively documented (taking as reference for PD the smallest measurements recorded since the treatment started).

The duration of overall CR is measured from the time measurement criteria are first met for CR until the first date that recurrent disease is objectively documented.

Duration of Stable Disease

Stable disease is measured from the start of the treatment until the criteria for progression are met, taking as reference the smallest measurements recorded since the treatment started.

Reference: 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.

18 APPENDIX C: CONTRACEPTIVE AND BARRIER GUIDANCE

- Female Participant Reproductive Inclusion Criteria

The criteria below are part of Inclusion Criteria (Section *Contraception*) and Section 6.6 and specify the reproductive requirements for including female participants.

A female patient is eligible to participate if she (a) is not pregnant or breastfeeding; (b) agrees to not donate eggs (ova, oocytes) for the purpose of reproduction from the time of screening through 45 days after the last dose of PF-07901801 AND, for combination therapy with PLD, during and for 6 months after treatment; and (c) at least one of the following conditions applies:

- Is not a WOCBP

  OR

- Is a WOCBP who agrees to use a highly effective contraceptive method (failure rate of <1% per year) with low user dependency during the intervention period and for at least 45 days after the, last dose of PF-07901801 AND for combination therapy with PLD, during and for 6 months after treatment, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

  OR

- Is a WOCBP and agrees to use a highly effective (failure rate of <1% per year) user-dependent method of contraception during the intervention period and for at least 45 days after the last dose of PF-07901801 AND for combination therapy with PLD, during and for 6 months after treatment, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). In addition to her use of the highly effective method above, she agrees to concurrently use an effective barrier method. The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

The investigator is responsible for reviewing the woman's medical history, menstrual history, and recent sexual activity in order to decrease the risk of enrolling a woman with an early, undetected pregnancy.

- Woman of Childbearing and Non-Childbearing Potential

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

If fertility is unclear (eg, amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before the first dose of study intervention, additional evaluation should be considered.

Women in the following categories are not considered WOCBP:

1. Pre-menopausal female with 1 of the following:

    - Documented hysterectomy
    - Documented bilateral salpingectomy
    - Documented bilateral oophorectomy

    For individuals with permanent infertility due to a medical cause other than the above (eg, mullerian agenesis, androgen insensitivity), investigator discretion should be applied to determining study entry.

    Note: Documentation for any of the above categories can come from the site personnel's review of the participant's medical records, medical examination or medical history interview. The method of documentation should be recorded in the participant's medical record for the study.

2. Post-menopausal female:

    - A post-menopausal state is defined as no menses for 12 months without an alternative medical cause. In addition
    - A high FSH level in the post-menopausal range must be used to confirm a post-menopausal state in women under 60 years of age and not using hormonal contraception or HRT
    - A female on HRT and whose menopausal status is in doubt will be required to use one of the highly effective non-estrogen hormonal contraception methods if she wishes to continue her HRT during the study. Otherwise, she must discontinue HRT to allow confirmation of post-menopausal status before study enrollment

- Contraception Methods

Contraceptive use by women should be consistent with local availability/regulations regarding the use of contraceptive methods for those participating in clinical trials.

The following contraceptive methods are appropriate for this study:

Highly Effective Methods That Have Low User Dependency

1. Implantable progestogen-only hormone contraception associated with inhibition of ovulation
2. Intrauterine device
3. Intrauterine hormone-releasing system
4. Bilateral tubal occlusion
5. Vasectomized partner

- Vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used. The spermatogenesis cycle is approximately 90 days.

Highly Effective Methods That Are User-Dependent

6. Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation:

- Oral + barrier*
- Intravaginal + barrier*
- Transdermal + barrier*

7. Progestogen-only hormone contraception associated with inhibition of ovulation:

- Oral + barrier*
- Injectable + barrier*

Sexual Abstinence

8. Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.

* Acceptable barrier methods to be used concomitantly with options 6 or 7 for the study include any of the following:

- Male or female condom with or without spermicide;
- Cervical cap, diaphragm, or sponge with spermicide;
- A combination of male condom with either cervical cap, diaphragm or sponge with spermicide (double-barrier methods).

19 APPENDIX D: LIVER SAFETY: SUGGESTED ACTION AND FOLLOW-UP ASSESSMENTS

Potential Cases of Drug Induced Liver Injury

Humans exposed to a drug who show no sign of liver injury (as determined by elevations in transaminases) are termed “tolerators,” while those who show transient liver injury but adapt are termed “adaptors.” In some participants, transaminase elevations are a harbinger of a more serious potential outcome. These participants fail to adapt and therefore are "susceptible" to progressive and serious liver injury, commonly referred to as DILI. Participants who experience a transaminase elevation above 3 × ULN should be monitored more frequently to determine if they are “adaptors” or are “susceptible.”

In the majority of DILI cases, elevations in AST and/or ALT precede T bili elevations (>2 × ULN) by several days or weeks. The increase in T bili typically occurs while AST/ALT is/are still elevated above 3 × ULN (i.e., AST/ALT and T bili values will be elevated within the same laboratory sample). In rare instances, by the time T bili elevations are detected, AST/ALT values might have decreased. This occurrence is still regarded as a potential DILI. Therefore, abnormal elevations in either AST OR ALT in addition to T bili that meet the criteria outlined below are considered potential DILI (assessed per Hy’s law criteria) cases and should always be considered important medical events, even before all other possible causes of liver injury have been excluded.

The threshold of laboratory abnormalities for a potential DILI case depends on the participant’s individual baseline values and underlying conditions. Participants who present with the following laboratory abnormalities should be evaluated further as potential DILI (Hy’s law) cases to definitively determine the etiology of the abnormal laboratory values:

- Participants with AST/ALT and T bili baseline values within the normal range who subsequently present with AST OR ALT values ≥3 × ULN AND a T bili value ≥2 × ULN with no evidence of hemolysis and an alkaline phosphatase value <2 × ULN or not available.

For participants with baseline AST OR ALT OR T bili values above the ULN, the following threshold values are used in the definition mentioned above, as needed, depending on which values are above the ULN at baseline:

- Pre-existing AST or ALT baseline values above the normal range: AST or ALT values ≥2 times the baseline values AND ≥3 × ULN; or ≥8 × ULN (whichever is smaller)

- Pre-existing values of T bili above the normal range: T bili level increased from baseline value by an amount of >1 × ULN or if the value reaches ≥3 × ULN (whichever is smaller)

Rises in AST/ALT and T bili separated by more than a few weeks should be assessed individually based on clinical judgment; any case where uncertainty remains as to whether it represents a potential Hy’s law case should be reviewed with the sponsor.

The participant should return to the investigator site and be evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation should include laboratory tests, detailed history and physical assessment.

In addition to repeating measurements of AST and ALT and T bili for suspected Hy's law cases, additional laboratory tests should include albumin, CK, direct and indirect bilirubin, GGT, PT/INR, total bile acids, and alkaline phosphatase. Consideration should also be given to drawing a separate tube of clotted blood and an anti-coagulated tube of blood for further testing, as needed, for further contemporaneous analyses at the time of the recognized initial abnormalities to determine etiology.

A detailed history, including relevant information, such as review of ethanol, acetaminophen/paracetamol (either by itself or as a co-formulated product in prescription or over-the-counter medications), recreational drug or supplement (herbal) use and consumption, family history, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and potential occupational exposure to chemicals, should be collected. Further testing for acute hepatitis A, B, C, D and E infection, liver imaging (eg, biliary tract) and collection of serum samples for acetaminophen/paracetamol drug and/or protein adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and T bili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the LFT abnormalities has yet been found. Such potential DILI (Hy's law) cases are to be reported as SAEs, irrespective of availability of all the results of the investigations performed to determine etiology of the LFT abnormalities.

A potential DILI (Hy's law) case becomes a confirmed case only after all results of reasonable investigations have been received and have excluded an alternative etiology.

20 APPENDIX E: KIDNEY SAFETY: MONITORING GUIDELINES

Laboratory Assessment of Change in Kidney Function and Detection of Kidney Injury

Standard kidney safety monitoring requires assessment of baseline and post-baseline (Scr measurement to eGFR [Scr-based eGFR]) or eCrCl. Baseline and post baseline Scys makes it feasible to distinguish acute kidney injury (AKI) from other causes of Scr increase. If Scr increase is confirmed after baseline, then reflex measurement of Scys is indicated to estimate the combined Scr-Scys eGFR calculation (for adults only).

Regardless of whether kidney function monitoring tests are required as a routine safety monitoring procedure in the study, if the investigator or sponsor deems it necessary to further assess kidney safety and quantify kidney function, then these test results should be managed and followed per standard of care.

Age-Specific **Kidney Function Calculation Recommendations**

Adults (18 Years and Above)—2021 CKD-EPI Equations

2021 CKD-EPI Scr only	Scr *(mg/dL)*	Scys *(mg/L)*	Recommended eGFR Equation
Female	if ≤ 0.7	N/A	$eGFR = 143 \times (Scr/0.7)^{-0.241} \times (0.9938)^{Age}$
Female	if > 0.7	N/A	$eGFR = 143 \times (Scr/0.7)^{-1.200} \times (0.9938)^{Age}$
Male	if ≤ 0.9	N/A	$eGFR = 142 \times (Scr/0.9)^{-0.302} \times (0.9938)^{Age}$
Male	if > 0.9	N/A	$eGFR = 142 \times (Scr/0.9)^{-1.200} \times (0.9938)^{Age}$
2021 CKD-EPI Scr-Scys Combined	Scr *(mg/dL)*	Scys *(mg/L)*	Recommended eGFR Equation
Female	if ≤ 0.7	if ≤ 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.219} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Female	if ≤ 0.7	if > 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.219} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Female	if > 0.7	if ≤ 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.544} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Female	if > 0.7	if > 0.8	$eGFR = 130 \times (Scr/0.7)^{-0.544} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Male	if ≤ 0.9	if ≤ 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.144} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Male	if ≤ 0.9	if > 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.144} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$
Male	if > 0.9	if ≤ 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.544} \times (Scys/0.8)^{-0.323} \times (0.9961)^{Age}$
Male	if > 0.9	if > 0.8	$eGFR = 135 \times (Scr/0.9)^{-0.544} \times (Scys/0.8)^{-0.778} \times (0.9961)^{Age}$

Inker LA et al. (2021)[42]

Adolescents (12 Years to <18 Years)—Cockcroft-Gault Formula

CrCl (mL/min)

Males: CrCl = [(140-age) × body weight (in kg)] / [Scr (in mg/dL) × 72]

Females: CrCl = 0.85 × [(140-age) x body weight (in kg)] / [Scr (in mg/dL) × 72]

Children (2 years to <12 years)—Modified Schwartz Equation

CrCl normalized to BSA (mL/min/1.73 m^2) = (K × Ht)/ Scr

Ht in cm; Scr in mg/dL.

K (proportionality constant): Female Child < 12 years: K = 0.55. Male Child < 12 years: K = 0.70

Infants (1 month to <2 years) and Neonates (<1 month)—Bedside Schwartz Equation

eGFR (mL/min/1.73 m^2) = 0.413 × (Ht/Scr)

Ht in cm ; Scr in mg/dL.

Adverse Event Grading for Kidney Safety Laboratory Abnormalities

AE grading for decline in kidney function (ie, eGFR or eCrCl) will be according to CTCAE criteria.

21 APPENDIX G: DOCUMENT HISTORY

Version	Date
1.3	26-Aug-2021
2.0	07-Dec-2022

SUMMARY OF CHANGES IN VERSION 2

Section (s)	Change	Rationale	Substantial or Non-Substantial
Synopsis/ Section 3.7.1 (PF-07901801)/ Section 5.1 (Study Design)/ Section 6.2 (Inclusion Criteria)	Updated and added text: Participants with ~~prior~~ exposure to ~~anthracyclines~~ ~~including~~ PLD **while platinum-resistant or in the treatment regimen immediately prior to enrollment in this study,** will ~~be~~ not be eligible for treatment under this protocol**; however, earlier exposure to PLD, including while platinum-sensitive, or for an indication other than recurrent platinum-resistant EOC, eg, breast cancer, will be allowed for participants in the Phase 1 dose escalation portion of the study. In the Phase 2, dose expansion portion of the study, depending on clinical benefit during Phase 1, earlier exposure to PLD, including while platinum-sensitive, may be allowed if agreed upon by the investigators and Pfizer. Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin.** Up to approximately 18 participants are planned to be enrolled in this portion of the study to evaluate three dose levels of PF-07901801: 12 mg/kg (Dose Level 1), **24**~~18~~ mg/kg (Dose Level 2) and **48**~~24~~ mg/kg (Dose Level 3). In Cycle 1 **for dose levels 1 and 2,** PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 in combination with PLD on Day 1 of 28-day cycle**.** Beginning with Cycle 2 **at dose levels 1 and 2**, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow PF-07901801 levels to more quickly reach steady state**. For dose level 3, PF-07901801 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles.** **Dose level 3 will be biweekly regimen from the start.**	This criterion update releases the barrier to enrollment: it allows earlier anthracyclines under the limitation of total cumulative doses associated with increased risk of cardiomyopathy in a manner that is considered not anticipated to impact efficacy and safety	Substantial
Synopsis and/or	Added, revised and updated text in the objectives and endpoints:	Updated information	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
Section 5.1 (Study design)	Secondary objectives include further evaluation of the safety of the combination and assessment of other indicators of ~~clinical benefit~~ **disease control**, including progression-free survival, overall survival, duration of response, and ~~clinical benefit~~ **disease control (CR, PR, or SD ≥12 weeks)** ~~rate~~ as defined by RECIST v1.1 criteria. ~~and assessment of overall response and other markers of clinical benefit as defined by immune-related RECIST (irRECIST) criteria.~~ Exploratory objectives include ~~assessment of the pharmacodynamic effects of PF-07901801(TTI-622) in combination with PLD in peripheral blood samples and tumor tissue~~, evaluation of CA-125 levels, characterization **of PF-07901801 and PLD pharmacokinetics** ~~concentrations in serum~~ when **co-**administered ~~in combination with PLD~~, evaluation of development of antibodies directed against PF-07901801; exploration of possible relationships between PF-07901801 exposure and clinical outcome, safety and pharmacodynamics observations, and **to understand the relationship between the therapeutic intervention(s) being studied and the biology of participant's disease** ~~assessment of possible relationships between CD47 expression on tumor cells and clinical outcome, safety and pharmacodynamic observations~~. Exploratory endpoints ~~may~~ include but are not limited to **PK and immunogenicity of PF-0790180~~1,~~ PK of PLD, CA-125 levels** ~~assessment of correlation between CD47 expression by immunohistochemistry and clinical outcome; evaluation of associations between clinical activity and selected biomarkers measured in serial peripheral blood samples, such as T-cell receptor clonality, immunophenotyping of circulating immune cells, circulating cytokines, immune function assays; and evaluation of the association between clinical activity and selected biomarkers measured in tumor tissue, such as immune infiltrate by IHC (including CD68 and CD163), somatic mutations utilizing high-throughput sequencing, and gene expression profiling.~~ **measurements of biomarkers/pharmacodynamics, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study, as well as the single and multiple dose pharmacokinetics of PF-07901801.**		

Section (s)	Change	Rationale	Substantial or Non-Substantial
	~~PLD should be administered through a freeflowing catheter as a 1 mg/min intravenous infusion. After Cycle 1, PLD can be delivered as a 1 hour infusion as tolerated in accordance with institutional guidelines for use of PLD in this patient population. TTI-622 will be administered by intravenous infusion; the duration of infusion is dependent on dose level with dose levels <24 mg/kg infused over 60 minutes and the dose level of 24 mg/kg infused over 90 minutes.~~ ~~In Cycle 1 only, TTI-622 will be administered by intravenous infusion on Day 1, Day 8, Day 15 and Day 22 in combination with PLD on Day 1 of 28-day cycles. Beginning with Cycle 2, TTI-622 will be administered on Day 1 and Day 15 in combination with PLD on Day 1 of 28-day cycles. The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow TTI-622 levels to more quickly reach steady state. For the purposes of safety decisions that guide cohort expansion and considerations of TTI-622 dose adjustment in the dose escalation portion of the study,~~ The dose-limiting toxicity ~~safety~~ evaluation period will consist of the 28-day Cycle 1 **or until participants experience a DLT in Cycle 1.** A participant who withdraws from the study during Cycle 1 in the absence of ~~objective disease progression or~~ DLT **evaluable (ie, not receiving PLD and at least two doses of PF-07901801)** will be replaced. Objective disease assessments will be performed **every 8 (±1) weeks through week 48, or until participant has been on study for one year, and every 12 (±2) weeks thereafter** ~~after every second cycle of treatment for approximately 50 weeks and after every third cycle thereafter. A patient enrolled in an expansion cohort who withdraws or is withdrawn from the study prior to completion of two cycles of treatment and objective disease assessment after the second cycle for a reason other than disease progression or safety will be replaced in order to meet the statistical criteria for the Simon two-stage study design.~~		

Section (s)	Change	Rationale	Substantial or Non-Substantial
	~~The mechanism of immunotherapy is mechanistically distinct from other types of therapy. The patterns of response and progression to immunotherapeutic agents, such as TTI-622, often differ temporally, qualitatively and quantitatively from those observed with cytotoxic and targeted agents. The goal of immunotherapy is to overcome immunosuppression induced by a tumor and its microenvironment, thereby allowing the immune system to develop or activate an immune response that targets and kills cancer cells. Some patients have experienced pseudo-progression or immune-mediated inflammation, in which areas of disease showed an initial surge followed by shrinkage that led to development of immune-related disease response criteria that supports continued treatment beyond progression in patients whose clinical conditions have not worsened and who have not experienced severe toxicities. Recognizing that immunotherapy represents a paradigm shift in oncology treatment, patients with a early observation of disease progression but without deterioration in clinical conditions or unacceptable toxicity and who consent should continue treatment until disease progression is verified by a repeated disease assessment at least four weeks later.~~		
Synopsis/ Section 6.2 (Inclusion criteria)	Removal of # 13 in the inclusion criteria: •~~INR ≤ 1.5 x ULN (≤ 2.5 x ULN if on anti-coagulants) and PTT ≤ 5 seconds above the ULN unless receiving anti-coagulation therapy; patients on full-dose anti-coagulation must be on a stable dose of oral anti-coagulant or low-molecular-weight heparin, have therapeutic INR, no active bleeding (defined as within 14 days prior to first dose of study medication) and no pathological condition that carries a high risk of bleeding (e.g., tumor involving major vessels or known varices)~~	Not applicable	Substantial
Synopsis/Section 5.1 (Overall Study Design)/ Section 6.2 (Inclusion Criteria)	Added, revised and updated text in the Previous Therapy section: **15. Unlimited lines of therapies in the platinum-sensitive setting are allowed. Once a participant becomes platinum-resistant** no more than 4 prior treatment regimens for platinum-resistant disease **are allowed.** ~~including lines of therapy in the recurrent setting. NOTE: frontline treatment/maintenance therapy does not count towards the 4-line maximum~~ 16. **Participants with exposure to PLD while platinum-resistant or in the treatment regimen immediately prior to enrollment in this study, will not be eligible for treatment under this protocol; however, earlier exposure to PLD, including while**	Updated to reflect new information	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	platinum-sensitive, or for an indication other than recurrent platinum-resistant EOC, eg, breast cancer, will be allowed for participants in the Phase 1 dose escalation portion of the study. In the Phase 2, dose expansion portion of the study, depending on clinical benefit during Phase 1, earlier exposure to PLD, including while platinum-sensitive, may be allowed if agreed upon by the investigators and Pfizer. Prior treatment with doxorubicin or other anthracyclines' equivalents at total cumulative doses must not be greater than 320 mg/m^2 for doxorubicin, and calculated using doxorubicin equivalent doses: 1 mg doxorubicin= 1 mg pegylated liposomal doxorubicin (PLD)= 1.8 mg epirubicin= 0.3 mg mitoxantrone= 0.25 mg idarubicin. ~~Anthracycline naïve (anthracycline in any prior setting, including the neoadjuvant/adjuvant or advanced stage settings, renders the participant ineligible for participation)~~		
Synopsis/ Section 6.3 (Exclusion Criteria)	Revised, added and updated text in the exclusion criteria: ~~Non-epithelial histology, including m~~**M**alignant mixed Mullerian tumors **Investigator site staff directly involved in the conduct of the study and their family members, site staff otherwise supervised by the investigator, and sponsor and sponsor delegate employees directly involved in the conduct of the study and their family members.** Any comorbidity or concomitant medication or other **medical or psychiatric** condition **including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation** that in the opinion of the investigator and/or **sponsor** medical monitor renders the participant unsuitable for participation in the trial or unlikely to fully comply with study procedures, restrictions and/or requirements that are considered relevant for evaluation of the efficacy or safety of the trial drug. ~~Consideration should be given to SARS-CoV-2 vaccination status as a condition that may render a patient unsuitable for participation in the trial or unlikely or unable to fully comply with study procedures, restrictions and/or requirements that are considered relevant for the evaluation of the efficacy or safety of study treatment~~	Updated information	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	Uncontrolled intercurrent illness, including active or chronic ~~infection~~ **uncontrolled bacterial, fungal, or viral infection, including (but not limited to) HBV, HCV, and known HIV or AIDS related illness** ~~infection~~ requiring systemic therapy or oral or systemic antibiotics within 14 days prior to study start. **Participants with HIV with an undetectable viral load and a CD4 count ≥400 µL are eligible.** **COVID-19/SARS-CoV-2: While SARS-CoV-2 testing is not mandated for entry into this study, testing should follow local clinical practice standards. If a participant has a positive test result for SARS-CoV-2 infection, is known to have asymptomatic infection or is suspected of having SARS-CoV-2, the participant is excluded until a negative antigen test and resolution of symptoms if applicable.** Significant bleeding disorders, vasculitis or a significant bleeding episode ~~from the GI tract~~ within three months prior to study entry. **Ongoing prophylactic anticoagulation therapy at a stable dose for prevention of VTE (Venous Thromboembolism) are allowed. Note: Participant on therapeutic anticoagulation must not be started on study before therapy is completed and prophylactic anticoagulation is established.** **Chronic** ~~S~~**s**ystemic steroid therapy (> 10 mg daily prednisone or equivalent) or any other form of immunosuppressive therapy within seven days prior to the first dose of study treatment; topical, inhaled, nasal and ophthalmic steroids are not prohibited; **Intermittent prophylaxis per site institutional policy is not prohibited as long as it does not exceed chronic daily use of >10 mg prednisone or equivalent eg, prophylactic use of steroids for Palmar Plantar Erythrodysesthesia (PPE) toxicity with PLD is allowed.**		
Synopsis/ Section 4.5 (Exploratory Objectives)	Some minor editorial clarifications made in the primary and secondary objectives are not described in this Summary of Change. Revised and added text in the exploratory objectives:	Updated information	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	• ~~Assess the pharmacodynamic effects of TTI-622 in combination with PLD in peripheral blood samples and tumor tissue~~ • **Characterize the PLD concentration in plasma when administered in combination with PF-07901801** • **Assess DDI potential between PF-07901801 and PLD** • **Understand the relationship between the therapeutic intervention(s) being studied and the biology of the participant's disease.** ~~Explore possible relationships between CD47 expression on tumor cells and clinical outcome, safety and pharmacodynamics observations~~		
Synopsis/ Section 4.2 (Primary Endpoints)/ Section 4.4 (Secondary Endpoints)/Section 4.6 (Exploratory Endpoints)	Added, updated and revised text: Primary: • ~~Overall safety profile as assessed by the type, frequency, severity, timing and causal relationship of any adverse events, changes in vital signs, ECG, serum chemistry or other laboratory assessment, treatment delays or discontinuations~~ **DLTs during the DLT observation period (28 days following C1D1).** • ~~The percentage of patients with o~~ Objective response (CR, **PR**) as defined by RECIST v1.1 criteria Secondary: • PFS, OS, disease control ~~rate~~ (DC [CR ~~+~~**or** PR ~~+~~ **or** SD]), **and** 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~~ • ~~Response rate and other markers of clinical benefit as defined by immune related RECIST (irRECIST) criteria~~ Exploratory: All the evaluations of selected biomarkers have been removed and the text was updated: • **Measurements of biomarkers/pharmacokinetics, which may consist of DNA, RNA, protein or defined cell types, resulting from analyses of peripheral blood and/or tumor tissue biospecimen obtained at baseline, on treatment and/or at end of study.**	Updated information on primary, secondary and exploratory endpoints	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	• **Immunogenicity: Incidence and titers of ADA and neutralizing antibodies against PF-7901801** • **PF-07901801 PK: Single and multiple Dose C_{max},** CCI [redacted] **, and clearance.** • **PLD PK: Single and multiple dose C_{max} and C_{trough}.**		
Synopsis/ Section 3.7.1 (PF-07901801)/ Section 5.1 (Overall Study design)/ Section 5.2.2 (PF-07901801)	Updated text: The dose of PF-07901801 will be based upon the dose level cohort to which the participant is assigned; the duration of infusion is dependent on dose level: dose levels ~~<24 mg/kg are infused over 60 minutes and the >24 mg/kg dose level is infused over 90 minutes~~ **less than or equal to 33 mg/kg infused over 60 min and doses greater than 33 mg/kg infused over 90 minutes and will have doses equal to or less than 2500 mg in 250 mL and doses 2501 mg or more in 500 mL or neat drug if the drug volume is over 500 mL.** In Cycle 1 **for dose levels 12 mg/kg and 24 mg/kg only,** PF-07901801 will be administered on Day 1, Day 8, Day 15 and Day 22 of a 28-day cycle. **The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow PF-07901801 levels to more quickly reach steady state.** **For dose level 48 mg/kg , PF-07901801 will be administered on Day 1 and Day 15 of a 28-day cycle. Loading doses (Day 8 and Day 22) may be considered for Cycle 1 at the 48 mg/kg dose level if found to be safe and offer clinical benefit for participants. If Cycle 1 loading doses are implemented, all dosing and lab draw schedules for the 48 mg/kg dose will follow the schedules for dose levels 12 mg/kg and 24 mg/kg.** ~~The enhanced dosing in Cycle 1 represents a loading cycle and is intended to allow TTI-622 levels to more quickly reach steady state.~~	Updated information	Substantial
Section 3.5.2.2	Revised and updated text with tables provided for single and multiple dose PK parameters of PF-07901801 for this Section 'Pharmacokinetics and Immunogenicity in Humans'.	Updated information	Substantial
Section 3.7.1/ Section 5.2.2	Dose levels of PF-07901801 have been updated in Table 10 and in Table 12.	Updated dose levels	Substantial
Section 4.	Updated and revised text for the primary objectives and endpoints, secondary objectives and endpoints, and exploratory objectives and endpoints.	Revised information	Substantial
Section 8.3.1	Revised text for the Section 'PF-07901801	Updated information	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
Section 8.7.2	Revised text	Updated information	Substantial
Section 8.7.4	Addition of Section 8.7.4 'Prohibited Medication and Potential Drug-Drug Interactions (DDI)	Updated information	Substantial
Section 9.2.5	Revised and updated text	Updated information	Substantial
Section 10	Updated and revised Table 28, Table 29, Table 30, Table 31, and Table 32. Addition of Subheadings 10.1; 10.2; 10.3	Updated information	Substantial
Section 11	Updated and revised text	Updated information	Substantial
Section 12.1.2	Added language **If the dose level combination selected for further Phase 2 is determined to be not optimal or not well tolerated, an intermediate dose level, not to exceed the dose levels evaluated in Phase 1, may be implemented.**	Updated information	Substantial
Section 12.3.3	Addition of Section 12.3.3 'PLD Concentration'	Updated information	Substantial
Section 13.1.1	Added language on AEs and SAEs	Updated information	Substantial
Section 13.5.3	Addition of Section 13.5.3 'Time period and Frequency for Collecting AE and SAE Information'	Updated information	Substantial
Section 13.5.4	Addition of Section 13.5.4 'Documentation'	Updated information	Substantial
Section 13.5.5	Addition of Section 13.5.5 'Follow-Up'	Update information	Substantial
Section 13.5.6	Addition of Section 13.5.6 'Notification'	Updated information	Substantial
Section 13.5.7	Addition of Section 13.5.7 'Regulatory Reporting Requirements for SAEs	Updated information	Substantial
Section 13.6	Addition of Section 13.6 'Adverse Events of Special Interest	Updated information	Substantial
Section 13.7	Addition of Section 13.7 'Lack of Efficacy'	Updated information	Substantial
Section 13.8, Section 13.8.1, Section 13.8.2	Section 'Pregnancy or Drug Exposure during Pregnancy' has been divided in 2 sections:'Exposure during Pregnancy', and 'Exposure During Breastfeeding'. The text was also updated.	Updated information	Substantial
Section 13.8.5	Addition of Section 13.8.5 'Disease-related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs'	Updated information	Substantial
Section 13.9	Addition of Section 13.9 'Medication Error'	Updated information	Substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
Section 'Reporting Adverse Events'	Removal of the section 'Reporting Adverse Events'	Updated information	Substantial
Section 13.12	Addition of Section 10.12 'Overview of Safety Monitoring'	Updated information	Substantial
Section 14.14	Addition of language on Dissemination of Clinical Study, Documents within Marketing Authorization Applications, and Data Sharing,	Updated information	Substantial
Appendices C, E, F	Addition of Appendix C: Contraceptive and Barrier Guidance Addition of Appendix E: Liver Safety Addition of Appendix F: Kidney Safety	Contraceptive guidance, liver and kidney safety guidance have been updated for harmonization across sponsor studies.	Substantial
All Sections	Minor editorial modifications in the text, which are not provided in this summary of changes, were made for additional clarity.	Clarification	Non-substantial
Synopsis/ Section 5.1 (Overall Study Design)	Revised/added text: This study will investigate a new therapeutic regimen for participants with platinum-resistant **recurrent** epithelial ovarian cancer **(EOC),** defined as disease progression ~~>1 month and~~ ≤ 6 months after ~~at least four cycles of~~ the most recent platinum-based treatment regimen or participants who were no longer able to receive or declined treatment with platinum-based chemotherapy, and who have not received more than four regimens for platinum-resistant disease.	Updated information	Non-substantial
Synopsis/ Section 6.1 (Inclusion Criteria)	Revised text for clarification of number of participants per phase: Up to approximately 50 **participants**, including up to ~~approximately~~ 18 **DLT-evaluable** in the **Phase 1** dose escalation portion of the study and up to ~~approximately~~ 30 **treated** in the **Phase 2** expansion ~~cohort~~ **portion**.	Updated for clarification	Non-substantial
Synopsis	Removal of the 'Enrollment Period' row:~~The enrollment period is anticipated to be approximately 15 months in duration, with the first patient anticipated to be enrolled in September 2021 and completion of enrollment anticipated for December 2022.~~	Information not required	Non-substantial
Synopsis/ Section 5.1 Overall Study Design/Section 12.2	Updated text in the paragraph: A participant will be evaluable for dose-limiting toxicity if ~~she has~~ **the participant experiences a DLT during Cycle 1 or did not experience a DLT and** received PLD on	Updated information	Non-substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
Analysis Populations	Day 1 **and**, ~~received~~ at least two infusions of PF-07901801 (TTI-622) in the 28-day Cycle 1 and ~~were evaluable for safety for~~ the complete**d** 28-day cycle **safety evaluation period**. ~~The requirement for a minimum of two infusions of PF-07901801 during Cycle 1 is based on the infusion schedule for all cycles beyond Cycle 1, in which PF-07901801 (TTI-622) will be administered only on Day 1 and Day 15 of each 28-day cycle~~. A participant who withdraws from the study during Cycle 1 in the absence of ~~objective disease progression or~~ **DLT evaluable (ie, not receiving PLD and at least two doses of PF-07901801)** will be replaced.		
Synopsis/ Section 5.4 (Dose limiting toxicity criteria)	Added and updated text in the CCI paragraph: ○ CCI	Updated information	Non-substantial
Synopsis/ Section 6.2 (Inclusion criteria)	Revised text and updated text: ~~17. If sexually active, the patient must be post-menopausal, surgically sterile or using effective contraception. Effective contraception for women of child-bearing potential is defined as one barrier method (e.g., condom) and one additional method (e.g., hormonal) of contraception during the study and for at least three months from the last administration of TTI-622 and six months from the last administration of PLD (abstinence is acceptable if this is the usual lifestyle and preferred method of contraception for the subject)~~ ~~18. Women of child-bearing potential may not be breastfeeding and must have a negative serum pregnancy test within 72 hours prior to start of study treatment~~ **Female participants of childbearing potential must have a serum pregnancy test at screening (Appendix D). Following Screening, pregnancy tests may be urine or serum tests, and must have a sensitivity of at least 25 mIU/mL. A negative pregnancy test result at screening and at baseline is required before the first study drug administration.**	Contraceptive requirements have been updated and harmonized across sponsor studies.	Non-substantial
Synopsis/ Section 12.1.2 (Expansion Cohort)	Revised and updated text: Based on a standard 3+3 design, up to approximately six **DLT-evaluable** participants may be enrolled in each dose level cohort evaluated during the **Phase 1** dose escalation portion	Updated information	Non-substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	of the study; a minimum of nine and a maximum of 18 **DLT-evaluable** participants ~~who complete the safety review~~ period is anticipated. The **Phase 2** expansion cohort is anticipated to provide a reasonable estimate of disease control, defined for this study as **objective** response rate among 25 **treated** participants, defined by RECIST v1.1 criteria, to support planning of future studies. ~~Because this endpoint is based on these statistical considerations, a patient who is withdrawn from the expansion arm of the study for a reason other than safety or objective disease progression and is not evaluable for response, defined as having completed at least two cycles of treatment as described in this protocol and having a post-treatment objective disease assessment, will be replaced in order to have at least 25 patients available for evaluation of response.~~ Other evidence of clinical activity, such as duration **of response**, progression-free survival, **and overall survival will be evaluated descriptively.** ~~and time to progression which are poor in this patient population, will be considered although the sample size is not anticipated to be sufficiently large to allow statistical evaluation of these endpoints in this hypothesis-generating study.~~		
Section 5.2	Updated text for the dose escalation	Updated information	Non-substantial
Section 5.3	Updated text: Any treatment-related adverse event that is deemed life-threatening, regardless of grade. **For Grade 4 adverse events, discontinuation must be considered unless the adverse event is transient and/or monitorable and manageable, asymptomatic and/or not clinically significant. If the participant is receiving disease control and the investigator judges that continued treatment may be in the participants best interest, PF-07901801 treatment can be resumed when the adverse event resolves to a level that meets re-treatment criteria. In consultation with the sponsor medical monitor, the dose level may be resumed** Addition of this paragraph which was previously in the synopsis:	Updated information	Non-substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	The mechanism of immunotherapy is mechanistically distinct from other types of therapy. The patterns of response and progression to immunotherapeutic agents, such as TTI-622, often differ temporally, qualitatively and quantitatively from those observed with cytotoxic and targeted agents. The goal of immunotherapy is to overcome immunosuppression induced by a tumor and its microenvironment, thereby allowing the immune system to develop or activate an immune response that targets and kills cancer cells. Some patients have experienced pseudo-progression or immune-mediated inflammation, in which areas of disease showed an initial surge followed by shrinkage that led to development of immune-related disease response criteria that supports continued treatment beyond progression in patients whose clinical conditions have not worsened and who have not experienced severe toxicities. Recognizing that immunotherapy represents a paradigm shift in oncology treatment, patients with an early observation of disease progression but without deterioration in clinical conditions or unacceptable toxicity and who consent should continue treatment until disease progression is verified by a repeated disease assessment at least four weeks later.		
Section 6.5	Revised text: ~~In general, waivers of inclusion or exclusion criteria will not be granted; the Investigator may consult with the Medical Monitor on a case-by-case~~. **Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.**	Updated information	Non-substantial
Section 6.6	Revised text for the Section 'Patients of Reproductive Potential'	Updated information	Non-substantial
Section 8.3.2	Revised text for Section Pegylated Liposomal Doxorubicin	Updated information	Non-substantial
Section 8.7	Removal of the following paragraphs: ~~Patients must not receive live, attenuated vaccines (e.g., FluMist) within four weeks prior to first day of study treatment, at any time during the study, or through 90 days after the last dose of TTI-622. Inactivated vaccines are allowed. Influenza vaccination should be given during influenza season only (approximately October to March).~~	Revised text due to updated information	Non-substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	~~Doxorubicin, the active component of PLD, is a major substrate of cytochrome P450 CYP3A4 and CYP2D6, and P-glycoprotein (P-gp). Clinically significant interactions have been reported with inhibitors of CYP3A4, CYP2D6, and/or P-gp (e.g., verapamil), resulting in increased concentration and clinical effect of doxorubicin. Inducers of CYP3A4 (e.g., phenobarbital, phenytoin, St. John's Wort) and P-gp inducers may decrease the concentration of doxorubicin. While the Prescribing Information for PLD does not carry these statements, the Investigator may consider whether concurrent use of inhibitors and inducers of CYP3A4, CYP2D6 or P-gp is warranted or should be avoided when PLD is being administered or may wish to employ alternate medications when possible. The Investigator may consult with the Medical Monitor when considering use of one of these agents.~~		
Section 8.7.1	Added text: **Intermittent prophylaxis per site institutional policy is not prohibited as long as it does not exceed chronic daily use of >10 mg prednisone or equivalent e.g. prophylactic use of steroids for Palmar Plantar Erythrodysesthesia (PPE) toxicity with PLD is allowed.**	Updated information	Non-substantial
Section 9.2.6	Added text: Note: Stimulating factors such as hematopoietic growth factors to stimulate white cell, red cell, or platelet production and transfusions are prohibited concomitant medications during cycle 1 (DLT period)	Updated information	Non-substantial
Section 12.3.2	Updated and revised text	Updated information	Non-substantial
Section 12.3.4	Revised and updated text	Updated information	Non-substantial
Section 12.3.5	Updated text	Updated information	Non-substantial
Section 13	Revised text The observation phase for adverse events will start with signing the informed consent and will end ~~in general with the last follow up visit. Adverse events occurring after signing of~~	Updated information	Non-substantial

Section (s)	Change	Rationale	Substantial or Non-Substantial
	~~the informed consent but prior to administration of any study treatment or prophylaxis will be considered medical history unless related to performance of a screening procedure. Adverse events still present at the end of the observation phase will be followed as long as possible.~~ **at the completion of the active reporting period. Planned timepoints for all safety assessments are provided in the Study Assessments (Section 10). Unscheduled safety measurements may be obtained at any time during the study to assess any perceived safety issues.**		
Section 13.1.2	Revised language	Update for clarification	Non-substantial
Section 13.2	Updated text	Updated information	Non-substantial
Section 13.8.3	Addition of Section 13.8.3 ‘Occupational Exposure’	Updated information	Non-substantial
Section 13.8.4	Addition of Section 13.8.4 ‘Cardiovascular and Death Events’	Updated information	Non-substantial
Section 13.10	Provided clarification	Updated information	Non-substantial
Appendices C	Removal of Appendix C	Updated information	Non-substantial
Appendix G	Removal of Appendix G ‘Principal Investigator Acknowledgement Form’ and replaced by ‘Document History’	Updated information	Non-substantial