STATISTICAL ANALYSIS PLAN

A Phase 1a/1b Study of FPA150, an Anti-B7-H4 Antibody, in Patients with Advanced Solid Tumors

PROTOCOLNUMBER: FPA150-001

PROTOCOL VERSION: AMENDMENT 2

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LIST OF ABBREVIATIONS

ADA	Anti-drug antibodies
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
AUC	Area Under Curve
BLQ	Below the Limit of Quantification
BMI	Body Mass Index
BOR	Best Overall Response
CI	Confidence Interval
CR	Complete Response
CSR	Clinical Study Report
CTCAE	Common Toxicity Criteria for Adverse Events
DLT	Dose-Limiting Toxicity
DOR	Duration of Response
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
GC	Gastroesophageal Cancer
GI	Gastrointestinal
HR	Hazard Ratio
IHC	Immunohistochemistry
ITT	Intent to Treat
IV	Intravenous
LTFU	Long Term Follow-up
MedDRA	Medical Dictionary for Regulatory Activities
MTD	Maximum Tolerated Dose
NCI	National Cancer Institute
NE	Not Estimable
[redacted]	
ORR	Objective Response Rate
OS	Overall Survival
PD-1	Programmed cell Death protein 1
PFS	Progression-Free Survival
PK	Pharmacokinetics
PR	Partial Response
PT	Preferred Term
Q1, Q3	First Quartile, Third Quartile
RD	Recommended Dose
RECIST	Response Evaluation Criteria in Solid Tumors
[redacted]	
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan

SE	Standard Error
SOC	System Organ Class
StD	Standard Deviation
TEAE	Treatment-Emergent Adverse Event
TFLs	Tables, Figures, and Listings
[redacted]	
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

1 BACKGROUND AND RATIONALE

This statistical analysis plan (SAP) describes the statistical analysis methods and data presentations to be used in tables, figures and listings (TFLs) of the final analysis in the clinical study report (CSR) for study FPA150-001. This SAP is based on the study protocol Amendment 2 dated 04 February 2019. The SAP will be finalized prior to data finalization for the final analysis.

1.1 Study Design

This is a Phase 1a/1b open-label, multicenter study to evaluate the dosing, safety, tolerability, PK, pharmacodynamics, and preliminary efficacy of FPA150 as monotherapy and in combination with pembrolizumab, an anti-PD1 antibody, in patients with advanced solid tumors.

This study includes a Phase 1a FPA150 Monotherapy Dose Escalation, Phase 1a Monotherapy Dose Exploration, Phase 1a combination Safety Lead-in (FPA150 + pembrolizumab), a Phase 1b FPA150 Monotherapy Dose Expansion, and a Phase 1b combination Dose Expansion (FPA150 + pembrolizumab).

The Phase 1a Monotherapy Dose Escalation will include an initial accelerated titration design followed by a standard 3+3 dose escalation design until the MTD and/or RD for Phase 1b is determined. The Phase 1a combination Safety Lead-In will start enrolling once the FPA150 monotherapy RD is identified in Phase 1a monotherapy dose escalation and will continue until the FPA150 MTD/RD in combination is identified.

Phase 1a FPA150 monotherapy Dose Exploration may include cohorts that may enroll beyond 3 patients whose tumors express high levels of B7-H4 protein and/or have varying levels of B7H4 expression [redacted] to further evaluate safety, PK, pharmacodynamics, and clinical activity at that dose (to be conditional upon the dose level clearing DLT criteria).

Phase 1b will be the Dose Expansion (monotherapy and combination) portion of the study. Enrollment into Phase 1b Dose Expansion will begin after identification of the MTD and/or RD in Phase 1a (monotherapy and Safety Lead-in). Preliminary efficacy will be evaluated in Phase 1b in planned expansion cohorts that include patients with specific tumor types that are B7-H4+ advanced solid tumors.

Figure 1: Study Schema- Monotherapy

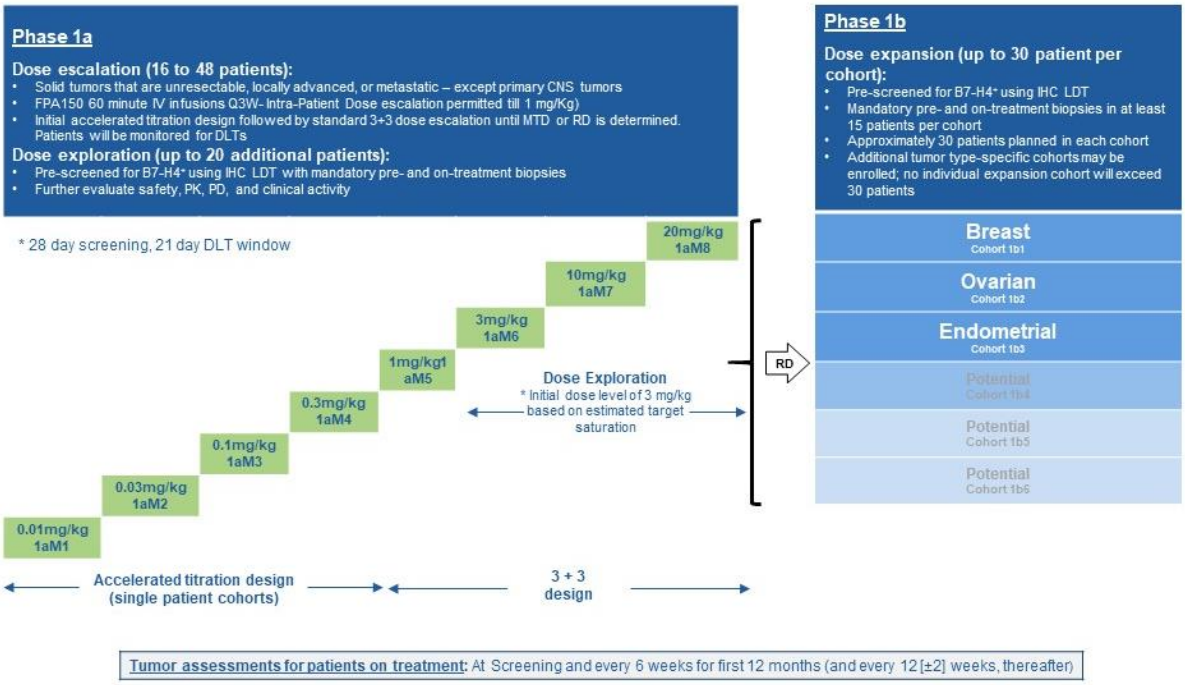
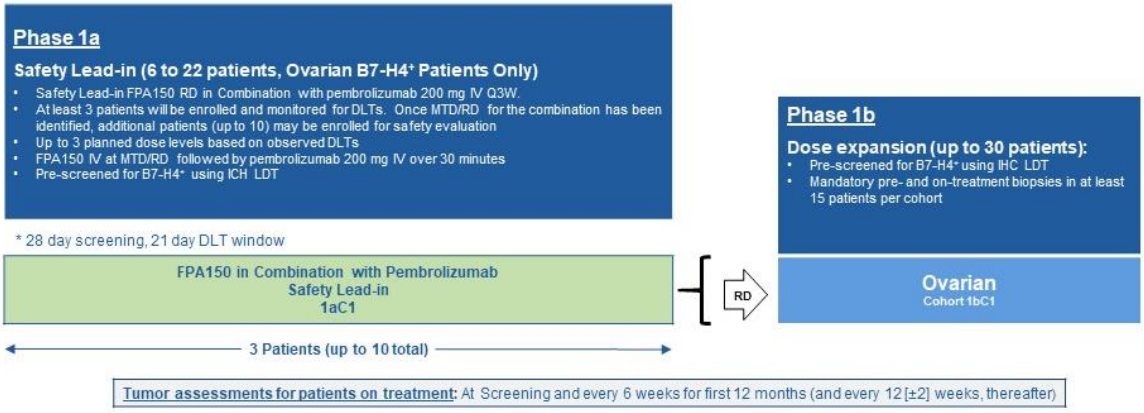


Figure 2: Study Schema - Combination



1.1.1 Study Design: Phase 1a Dose Escalation

Cohorts are planned at doses from 0.01 to 20 mg/kg, and enrollment will depend on safety and tolerability. Phase 1a Monotherapy Dose Escalation of the study will include an initial accelerated titration design followed by a standard 3+3 dose escalation design at dose levels ≥ 1 mg/kg until the MTD and/or RD for Phase 1b is determined. As of 28 January 2019, the RD for FPA150 monotherapy has been established as 20 mg/kg Q3W.

The proposed dosing cohorts are outlined in Table 1.

Table 1: Proposed Dose Levels for Phase 1a FPA150 Monotherapy

Dose Level	Cohort	Dose	Regimen
-1	-	FPA150 0.005 mg/kg	Q3W
1	1aM1	FPA150 0.01 mg/kg	Q3W
2	1aM2	FPA150 0.03 mg/kg	Q3W
3	1aM3	FPA150 0.1 mg/kg	Q3W
4	1aM4	FPA150 0.3 mg/kg	Q3W
5	1aM5	FPA150 1 mg/kg	Q3W
6	1aM6	FPA150 3 mg/kg	Q3W
7	1aM7	FPA150 10 mg/kg	Q3W
8	1aM8	FPA150 20 mg/kg	Q3W

Abbreviations: Q3W = once every 3 weeks.

Phase 1a Combination Safety Lead-in (Ovarian B7-H4$^+$ Patients Only)

Once the MTD and/or RD of FPA150 monotherapy in Phase 1a Dose Escalation is identified, the Sponsor will open a Safety Lead-in for the combination of FPA150 and pembrolizumab. At least 3 patients will be enrolled at the monotherapy RD of FPA150 in combination with pembrolizumab 200 mg IV Q3W and evaluated for DLTs by the CRC. If required due to the presence of DLTs, the dose of FPA150 will be reduced in accordance with the algorithm for de-escalation described in Table 2. The same dose levels that were assessed during dose escalation for FPA150 monotherapy will be evaluated for the combination in reverse order (from highest to lowest). Once the RD for the combination of FPA150 and pembrolizumab is identified the Sponsor may treat additional patients at that dose for additional safety assessment (up to 10 patients total).

Table 2: Proposed Dose Cohort/Levels for Phase 1a Combination Safety Lead-in (FPA150 in Combination with Pembrolizumab)

Cohort	Dose	Regimen
1aC1	FPA150 (RD) + pembrolizumab 200 mg IV	Q3W
1aC2	FPA150 (dose level -1) + pembrolizumab 200 mg IV	Q3W
1aC3	FPA150 (dose level -2) + pembrolizumab 200 mg IV	Q3W

Abbreviations: IV = intravenous; Q3W = once every 3 weeks; RD = recommended dose.

1.1.2 Study Design: Phase 1a Dose Exploration

Phase 1a includes a dose exploration cohort that may enroll beyond 3 patients (up to

20 additional patients across all dose levels). These 20 patients include 10 patients whose tumors express high levels of B7-H4 protein (3 mg and 10 mg), to further evaluate safety, PK, pharmacodynamics, and clinical activity at that dose (to be conditional upon the dose level clearing DLT criteria) of FPA150 monotherapy. It also includes up to 10 patients selected to have varying levels of B7-H4 expression [redacted] dosed at the FPA150 monotherapy MTD/RD.

Table 3: Proposed Dose Cohort/Level for Phase 1a Dose Exploration

Cohort	Dose/Regimen	B7-H4 Status
1aE1	FPA150 3 mg/kg	High
1aE2	FPA150 10mg/kg	High
1aE3	FPA150 monotherapy MTD/RD	[redacted]

Abbreviations: MTD = maximum tolerated dose; Q3W = once every 3 weeks; RD = recommended dose

Toxicities observed in these patients will contribute to the overall assessment of safety and tolerability, but will not be included in the formal DLT calculations per Protocol.

1.1.3 Study Design: Phase 1b Dose Expansion

Enrollment in Phase 1b monotherapy and in combination with pembrolizumab will begin when the MTD and/or RD has been identified by the CRC (refer to Protocol Section 4.1.1), based on overall safety, tolerability, objective response, PK, pharmacodynamics from the Phase 1a part of the study.

Phase 1b will consist of tumor-specific cohorts of up to 30 patients each.

During the Screening Period, the patient will undergo protocol-specified screening procedures to ensure all eligibility criteria are met. Enrollment in Phase 1b will initially occur in 3 monotherapy cohorts and one cohort with FPA150 in combination with pembrolizumab (once the Safety Lead-in is completed and the MTD/RD for the combination is identified) as outlined in Table 4.

Table 4: Phase 1b Expansion Cohorts and Tumor Types

Cohort	Tumor Type	Therapy Type (Monotherapy or Combination)
1b1	Breast cancer	Monotherapy: FPA150
1b2	Ovarian cancer	Monotherapy: FPA150
1b3	Endometrial cancer	Monotherapy: FPA150
1bC1	Ovarian cancer	Combination: FPA150 with pembrolizumab

1.2 Study Objectives and Endpoints

1.2.1 Phase 1a Objectives and Endpoints

The objectives and endpoints for Phase 1a of the study are summarized in Table 5.

Table 5: Objectives and Endpoints: Phase 1a

OBJECTIVES	ENDPOINTS
PRIMARY - SAFETY	
FPA150 Monotherapy • To evaluate the safety and tolerability of FPA150 as monotherapy in patients with advanced solid tumors treated at the MTD and/or RD • To determine the MTD and/or RD of FPA150	**FPA150 Monotherapy** • The incidence of Grade 3 and Grade 4 AEs and clinical laboratory abnormalities defined as DLTs • The incidence of AEs, clinical laboratory abnormalities, and ECG abnormalities
FPA150 in Combination with Pembrolizumab • To evaluate the safety and tolerability of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer • To determine the MTD and/or RD of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer	**FPA150 in Combination with Pembrolizumab** • The incidence of AEs, clinical laboratory abnormalities, and ECG abnormalities • The incidence of Grade 3 and Grade 4 AEs and clinical laboratory abnormalities defined as DLTs
SECONDARY - PHARMACOKINETIC	
FPA150 Monotherapy • To characterize the PK profile of FPA150 as monotherapy in patients with advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • AUC • Maximum serum concentration (C_{max}) • Trough serum concentration at the end of a dose interval (C_{trough}) • Clearance (CL) • Termina half-life ($t_{1/2}$) • Volume of distribution at steady state (V_{ss}) • Other parameters, such as dose proportionality, accumulation ratio, attainment of steady state, will also be calculated if the data are available
SECONDARY - IMMUNOGENICITY	
FPA150 Monotherapy • To characterize the immunogenicity of FPA150 as monotherapy in patients with advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • Immune response (ADAs) to FPA150

OBJECTIVES	ENDPOINTS
EXPLORATORY - EFFICACY	
FPA150 Monotherapy • To evaluate the clinical benefit of FPA150 as monotherapy	**FPA150 Monotherapy** • ORR defined as the total number of patients with confirmed responses of either CR or PR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 divided by the total number of patients who are evaluable for a response • Duration of response (DOR), defined as the time from onset of response (CR or PR) that is subsequently confirmed to the first observation of progressive disease or death due to any cause • Progression free-survival (PFS), defined as the time from the patient's first dose to the first observation of progressive disease or death
FPA150 in Combination with Pembrolizumab • To evaluate the clinical benefit of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer	**FPA150 in Combination with Pembrolizumab** • ORR, defined as the total number of patients with confirmed responses of either CR or PR per RECIST v1.1 divided by the total number of patients who are evaluable for a response • DOR, defined as the time from onset of response (CR or PR) that is subsequently confirmed to the first observation of progressive disease or death due to any cause • PFS, defined as the time from a patient's first dose to the first observation of progressive disease or death due to any cause.
EXPLORATORY - Pharmacokinetics	
FPA150 in Combination with Pembrolizumab • To characterize the pharmacokinetic (PK) profile of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer	**FPA150 in Combination with Pembrolizumab** The following PK parameters will be derived from concentration-time data for FPA150 in combination with pembrolizumab when appropriate and applicable: • AUC • C_{max} • C_{trough} • Clearance (CL) • $t_{1/2}$ • V_{ss} • Other parameters, such as dose proportionality, accumulation ratio, attainment of steady state, will also be calculated if the data are available for FPA150 • C_{max} and C_{trough} as well as accumulation ratio of C_{max} and C_{trough} for pembrolizumab may be calculated if the data are available

OBJECTIVES	ENDPOINTS
EXPLORATORY - Immunogenicity	
FPA150 in Combination with Pembrolizumab • To characterize the immunogenicity of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer	**FPA150 in Combination with Pembrolizumab** • Immune response (ADAs) to FPA150 • Immune response (ADAs) to pembrolizumab
EXPLORATORY – Pharmacodynamic Biomarkers	
FPA150 Monotherapy • To characterize the pharmacodynamic profile of FPA150 through an analysis of the immune cell infiltrate in pre-treatment and on-treatment tumor biopsies • To characterize the pharmacodynamic profile of FPA150 through evaluation of exploratory biomarkers in peripheral blood samples	**FPA150 Monotherapy** • Changes in markers of tumor immune infiltrate • [redacted] • Changes in selected pharmacodynamic biomarkers in peripheral blood samples
FPA150 in Combination with Pembrolizumab • To characterize the pharmacodynamic profile of FPA150 in combination with pembrolizumab through an analysis of the immune cell infiltrate in pre-treatment and on-treatment tumor biopsies • To characterize the pharmacodynamic profile of FPA150 in combination with pembrolizumab through evaluation of exploratory biomarkers in peripheral blood samples	**FPA150 in Combination with Pembrolizumab** • Changes in markers of tumor immune infiltrate [redacted] • Changes in selected additional pharmacodynamic markers in peripheral blood in patients treated with FPA150 in combination with pembrolizumab

1.2.2 Phase 1b Objectives and Endpoints

The objectives and endpoints for Phase 1b of the study are summarized in Table 6.

Table 6: Objectives and Endpoints: Phase 1b

OBJECTIVES	ENDPOINTS
PRIMARY - SAFETY	
FPA150 Monotherapy • To evaluate the safety and tolerability of FPA150 as monotherapy in patients with B7-H4+ advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • The incidence of AEs, clinical laboratory abnormalities, and ECG abnormalities
FPA150 Combined with Pembrolizumab • To evaluate the safety and tolerability of FPA150 in combination with pembrolizumab in selected	**FPA150 Combined with Pembrolizumab** • The incidence of AEs, clinical laboratory abnormalities, and ECG abnormalities in patients

OBJECTIVES	ENDPOINTS
patients with B7-H4+ ovarian cancer treated at the MTD and/or RD	treated with FPA150 in combination with pembrolizumab
SECONDARY - EFFICACY	
FPA150 Monotherapy • To evaluate the clinical benefit of FPA150 as monotherapy in patients with B7-H4+ advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • ORR, defined as the total number of patients with confirmed responses of either CR or PR per RECIST v1.1 divided by the total number of patients who are evaluable for a response • DOR, defined as the time from onset of response (CR or PR) that is subsequently confirmed to the first observation of progressive disease or death due to any cause • PFS, defined as the time from the patient's first dose to the first observation of progressive disease or death due to any cause)
FPA150 in Combination with Pembrolizumab • To evaluate the clinical benefit of FPA150 in combination with pembrolizumab in patients with B7-H4 + ovarian cancer treated at the MTD and/or RD	**FPA150 in Combination with Pembrolizumab** • ORR, defined as the total number of patients with confirmed responses of either CR or PR per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 divided by the total number of patients who are evaluable for a response to FPA 150 combined with pembrolizumab • DOR, defined as the time from onset of response (CR or PR) that is subsequently confirmed to the first observation of progressive disease or death due to any cause to FPA150 combined with pembrolizumab • PFS, defined as the time from the patient's first dose to the first observation of progressive disease or death due to any cause to FPA150 combined with pembrolizumab
SECONDARY - PHARMACOKINETICS	
FPA150 Monotherapy • To characterize the PK profile of FPA150 as monotherapy in patients with B7-H4+ advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • AUC • C_{max} • C_{trough} • CL • $t_{1/2}$ • V_{ss} • Other parameters, such as accumulation ratio, attainment of steady state, will also be calculated if the data are available

OBJECTIVES	ENDPOINTS
SECONDARY - IMMUNOGENICITY	
FPA150 Monotherapy • To characterize the immunogenicity of FPA150 as monotherapy in patients with B7-H4+ advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • Immune response (ADAs) to FPA150
EXPLORATORY - PHARMACOKINETICS	
FPA150 in Combination with Pembrolizumab • To characterize the PK profile of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer treated at the MTD and/or RD • To characterize the PK profile of pembrolizimab in combination with FPA150 in patients with ovarian cancer	**FPA150 in Combination with Pembrolizumab** The following PK parameters will be derived from concentration-time data for FPA150 in combination with pembrolizumab when appropriate and applicable: • AUC • C_{max} • C_{trough} • CL • $t_{1/2}$ • V_{ss} • Other parameters, such as accumulation ratio, attainment of steady state, will also be calculated if the data are available for patients treated with FPA150 combined with pembrolizumab • C_{max} and C_{trough} as well as accumulation ratio of C_{max} and C_{trough} for pembrolizumab may be calculated if the data are available
EXPLORATORY - IMMUNOGENICITY	
FPA150 in Combination with Pembrolizumab • To characterize the immunogenicity of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer treated at the MTD and/or RD • To characterize the immunogenicity of pembrolizumab in combination with FPT150 patients with with B7-H4+ ovarian cancer treated at the MTD and/or RD	**FPA150 in Combination with Pembrolizumab** • Immune response (ADAs) to FPA150 • Immune response (ADAs) to pembrolizumab
EXPLORATORY – PHARMACODYNAMIC BIOMARKERS	
FPA150 Monotherapy • To characterize the pharmacodynamic profile of FPA150 through an analysis of the immune cell infiltrate in pre-treatment and on-treatment tumor biopsies • To characterize the pharmacodynamic profile of FPA150 through evaluation of exploratory biomarkers in peripheral blood samples	**FPA150 Monotherapy** • Changes in markers of tumor immune infiltrate [redacted] • [redacted] • Changes in selected pharmacodynamic biomarkers in peripheral blood samples

OBJECTIVES	ENDPOINTS
FPA150 in Combination with Pembrolizumab • To characterize the pharmacodynamic profile of FPA150 in combination with pembrolizumab through an analysis of the immune cell infiltrate in pre-treatment and on-treatment tumor biopsies • To characterize the pharmacodynamic profile of FP150 in combination with pembroliumab through evaluation of exploratory biomarkers in peripheral blood samples	**FPA150 in Combination with Pembrolizumab** • Changes in markers of tumor immune infiltrate, [redacted] • [redacted] • Changes in selected additional pharmacodynamic biomarkers in peripheral blood samples for patients treated with FPA150 in combination with pembrolizumab
EXPLORATORY - EFFICACY	
FPA150 Monotherapy • To evaluate the clinical benefit of FPA150 as monotherapy in patients with B7-H4+ advanced solid tumors treated at the MTD and/or RD	**FPA150 Monotherapy** • OS, defined as time from patient's first dose to death due to any cause
FPA150 in Combination with Pembrolizumab • To evaluate the clinical benefit of FPA150 in combination with pembrolizumab in patients with B7-H4+ ovarian cancer treated at the MTD and/or RD	**FPA150 in Combination with Pembrolizumab** • OS, defined as time from patient's first dose to death due to any cause

1.3 Sample Size

For Phase 1a, this study is designed as a dose escalation study with objectives that include determination of an MTD and/or RD for FPA150 monotherapy and FPA150 combined with pembrolizumab. It will also include assessments of the safety and tolerability of FPA150 monotherapy and in combination with pembrolizumab. The sample size of this study was not determined by strict statistical considerations. The total number of patients planned for this study is estimated to be up to 278.

Phase 1a will enroll up to 68 patients. The 68 patients include 23 to 26 patients in the Phase 1a Monotherapy Dose Escalation cohorts, 6 to 22 patients in the Phase 1a Combination Safety Lead-in cohort and up to 20 additional patients in the Phase 1a Monotherapy Dose Exploration cohorts to further evaluate safety, PK, pharmacodynamics, and clinical activity at 1 or more dose levels (to be conditional upon the dose level clearing DLT criteria).

For the objective of estimating the ORR of FPA150 in the Phase 1b Monotherapy and Combination Dose Expansion cohorts, it is estimated that up to 30 patients will be enrolled to ensure 25 evaluable patients in each cohort. The following table displays the corresponding 2-sided 90% confidence interval (CI) and the precision for the various observed response rates based on 25 evaluable patients. The sample size of 25 is chosen to ensure that it will allow to

exclude 10% when the observed ORR is 24% or higher (Agresti 1998).

Phase 1b will enroll up to 210 patients with specific tumor types. Up to 30 patients are planned for each of the 3 FPA150 Monotherapy Dose Expansion cohorts, and one additional cohort of FPA150 in combination with pembrolizumab. Additional cohorts of up to 30 patients each may be enrolled, based on emerging clinical and translational data.

Table 7: Two-Sided 90% Confidence Intervals of the Observed Response Rates

Sample Size	Observed Response Rate	90% CI	Precision (longest one-sided CI length*)
25	5/25 (20%)	(8%, 38%)	18%
	6/25 (24%)	(11%, 42%)	18%
	7/25 (28%)	(14%, 46%)	18%
	8/25 (32%)	(17%, 50%)	18%
	9/25 (36%)	(20%, 54%)	18%
	10/25 (40%)	(24%, 58%)	18%

Abbreviations: CI = confidence interval.
*Distance from the observed response rate to the lower or upper CI boundary.

Considering it is possible to open successive cohorts after data is reviewed, up to 210 patients may be enrolled in Phase 1b (not to exceed 30 patients in any individual cohort).

A 2-stage design will be used to determine the actual enrolled subjects. Sponsor will evaluate efficacy in phase 1b on an ongoing basis and may suspend or terminate enrollment in specific cohorts if <=1 response (CR or PR per RECIST 1.1) is observed in the first 16 patients enrolled in each cohort. In this case, the probability of early termination is 0.81 with 0.05 responder rate for futility and 0.2 responder rate for efficacy.

2 TYPE OF PLANNED ANALYSES

The final analysis of the data will be performed after all patients completed or discontinued the study. At the time of the final analysis, outstanding data queries will be resolved or adjudicated as unresolvable, and the data will be cleaned and finalized.

3 GENERAL CONSIDERATIONS

All statistical tabulations and analyses will be done using SAS®, Version 9.3 or higher.

Unless otherwise noted, continuous variables will be summarized using the number of subjects (n), mean, standard error (SE) or standard deviation (StD), median, minimum, and maximum; categorical variables will be summarized using the number and percentage of subjects in each category.

By-subject listings will be presented for all subjects in the Safety Analysis Set and sorted by phase, treatment group, subject ID number, visit date, and time (if applicable). Data collected on log forms, such as AEs, will be presented in chronological order within the subject. The treatment group to which subjects were enrolled will be used in the listings. Age, sex at birth, race, and ethnicity will be included in the listings, as space permits.

The summaries of the efficacy data will be presented by treatment group.

Unless stated otherwise, summaries will be provided separately for the following 3 groups of subjects:

- Phase 1a (Dose Escalation + Exploration)
- Phase 1b (Monotherapy)
- Phase 1a (Combination Safety Lead-in) and Phase 1b (Combination)

3.1 Analysis Sets

3.1.1 Safety Analysis Set

The Safety Analysis Set includes all subjects who have received any portion of at least 1 dose of FPA150.

The Safety Analysis Set will be used in the summary of subject disposition, demographics and baseline characteristics, as well as safety data and study treatment administration.

3.1.2 Efficacy-Evaluable Analysis Set

The Efficacy-Evaluable Analysis Set includes all subjects received at least 1 dose of FPA150, had at least 1 postbaseline evaluable tumor assessment unless death or clinical progressive disease occurred prior to the first post baseline disease assessment.

The Efficacy-Evaluable Analysis Set will be used in the summary of efficacy data.

3.1.3 DLT-Evaluable Analysis Set

The DLT-Evaluable Analysis Set includes all enrolled subjects in Phase 1 monotherapy and in combination with pembrolizumab who received at least 2 doses of FPA150, and completed Cycles 1 of treatment, or who experienced a DLT in Cycle 1.

3.1.4 PK Analysis Set

The PK Analysis Set is defined as all subjects who have received at least one dose of FPA150 and have at least 1 PK sample collected. These subjects will be evaluated for PK analysis unless the number of data points required for analysis is not enough, or significant protocol deviations have affected the data or if key dosing or sample information is missing. The PK Analysis Set is the primary analysis set for all PK analyses.

3.1.5 ADA Analysis Set

The ADA Analysis Set includes all enrolled subjects who received at least 1 dose of FPA150 and have at least 1 ADA sample drawn at any timepoint.

3.2 Subject Grouping

Subjects will be grouped according to the actual treatment they received. Subjects with the same dose level from the dose escalation and exploratory in Phase 1a for monotherapy and safety lead-in in Phase 1a and Phase 1b for combination will be combined for summary.

3.3 Examination of Subject Subgroups

There are no prespecified subject subgroupings for efficacy and safety analyses.

3.4 Multiple Comparisons

Adjustments for multiplicity will not be made, because no formal statistical testing will be performed in this study.

3.5 Missing Data and Outliers

3.5.1 Missing Data

In general, missing data will not be imputed unless methods for handling missing data are specified.

The handling of missing or incomplete dates for disease diagnosis and prior anticancer therapy is described in Section 5.3; for prior and concomitant medications in described in Section 5.4; for new anticancer therapy is described in Section 6.1, for AE onset is described in Section 7.1.5.

3.5.2 Outliers

Outliers will be identified during the data management and data analysis process, but no sensitivity analyses will be conducted. All data will be included in the data analysis.

3.6 Data Handling Conventions and Transformations

In PK analysis, natural logarithm transformation will be used for serum concentration and analysis of PK parameters. Concentration values that are below the limit of quantitation (BLQ) will be presented as "BLQ" in the listing. Values that are BLQ will be treated as 0 at pre-dose timepoints, and one-half the value of the lower limit of quantitation (LLOQ) at postbaseline timepoints in the concentration summaries.

The following conventions will be used in the summary of concentration data:

- If at least 1 subject has a concentration value of BLQ for the timepoint, the minimum will be displayed as "BLQ".
- If more than 25% of the subjects have a concentration value of BLQ for the timepoint, the minimum and Q1 values will be displayed as "BLQ".
- If more than 50% of the subjects have a concentration value of BLQ for the timepoint, the minimum, Q1, and median values will be displayed as "BLQ".
- If more than 75% of the subjects have a concentration value of BLQ for the timepoint, the minimum, Q1, median, and Q3 values will be displayed as "BLQ".
- If all subjects have a concentration value of BLQ for the timepoint, all summary statistics (minimum, Q1, median, Q3, and maximum) will be displayed as "BLQ".

3.7 Analysis Visit Windows

3.7.1 Definition of Study Day

Study day will be calculated from the first dosing date of any portion of the study drug:

- Postdose Study Days = Assessment Date – First Dosing Date + 1
- Study Day prior to First Dose = Assessment Date – First Dosing Date

3.7.2 Analysis Visit Windows

No analysis visit window will be assigned in the analysis as no summary by visit is planned.

3.7.3 Selection of Data

In general, the baseline value will be the last non-missing value on or prior to the first dosing date of study drug unless specified differently.

For continuous measurements, if multiple measurements occur on the same day, the last non-missing value will be considered as the baseline value. If these multiple measurements occur at the same time or the time is not available, the average of these measurements will be considered the baseline value. For categorical measurements, if multiple measurements occur on the same day, the last non-missing value will be considered as the baseline value. If these multiple measurements occur at the same time or the time is not available, the value with the lowest severity will be considered the baseline value.

Measurements occurred after first dose date will be considered postbaseline values.

4 SUBJECT DISPOSITION

4.1 Subject Enrollment and Disposition

A summary of subject disposition will be provided by treatment group. Percentages will be based on the Safety Analysis Set. The number of subjects in the following categories will be provided:

- Signed the inform consent
- Received any study treatment
- Continuing study treatment
- Discontinued from study treatment with reasons for treatment discontinuation
- Continuing study
- Discontinued from study with reasons for study discontinuation

4.2 Extent of Exposure and Adherence

Descriptive statistics of extent of exposure will be presented by treatment group for FPA150:

- Duration of exposure (weeks)
- Cumulative exposure by week
- Number of infusions

Total duration of exposure to study drug (in weeks) will be defined as (last available dosing date – first dosing date + 21)/7, regardless of any temporary interruptions in study drug administration.

The number and percentage of subjects who have dose reduction, dose delay or interruption, and infusion interruption will be summarized with reasons.

Summaries of exposure will be performed with the Safety Analysis Set. A by-subject listing of study drug administration will be provided.

5 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

5.1 Demographics

Demographic data will be summarized using descriptive summary statistics for the Safety Analysis Set. The demographic characteristics include age, sex, race, ethnicity, body height (in cm), body weight (in kg) and body mass index (BMI; in kg/m^2).

A by-subject listing will be provided for demographic data.

5.2 Other Baseline Disease Characteristics

Other baseline characteristics include baseline ECOG PS and B7-H4 expression level by IHC. Summary of ECOG PS by treatment group for the Safety Analysis Set will be provided as part of the disease-specific baseline characteristics. A by-subject listing will be provided for B7-H4 expression level by IHC.

5.3 Medical History

Medical history will be collected at screening for disease-specific and general conditions (ie, conditions not specific to the disease being studied).

A summary of disease-specific medical history will be provided for the Safety Analysis Set as part of the disease-specific baseline characteristics. Time since initial diagnosis of cancer (months) and time since diagnosis of unresectable disease (months) will be calculated by (date of first dose – date of diagnosis) / 30.4375. They will be summarized using summary statistics for a continuous variable. Disease stage at diagnosis and at screening will be summarized using summary statistics for a categorical variable.

In deriving the time since diagnosis, all partial dates of diagnosis and last regimen will be identified, and the partial dates will be imputed as follows:

- If day and month are missing but year is available, then the imputed day and month will be 01 Jan.
- If day is missing but the month and year are available, then the imputed day will be the first day of the month.
- Partial date will not be imputed if the year is missing.

General medical history data will be listed only. By-subject listings will be provided for disease-specific medical history and general medical history.

5.4 Prior and Concomitant Medications

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary –WHODD and classified according to ATC codes levels 2 (therapeutic sublevel) and 4 (chemical sublevel).

All medications with an end date prior to the first dose of any study drug will be considered as prior medication regardless of the stop date. If a partial start date is entered the medication will be considered prior unless the month and year (if day is missing) or year (if day and month are missing) of the start date are after the first dosing date. Medications with a completely missing start date will be considered as prior medication, unless otherwise specified.

Concomitant medications are defined as medications taken while a subject took study drug. If a partial stop date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) prior to the date of first study drug administration will not be considered as concomitant medication. If a partial start date is entered, any medication with the month and year (if day is missing) or year (if day and month are missing) after the study drug stop date will not be considered as concomitant medication. Medications with completely missing start and stop dates will be considered as concomitant medication, unless otherwise specified.

All prior and concomitant medications (other than per-protocol study drugs) will be provided in a by-subject listing.

5.5 Prior Anticancer Therapy

Number of prior regimens, time since the completion of last regimen will be summarized by treatment group using descriptive statistics. The best response to the last regimen will be summarized using summary statistics for a categorical variable. The summaries will be based on the Safety Analysis Set as part of the disease-specific baseline characteristics. A partial completion date will be imputed using the algorithm defined in Section 5.3. The prior anticancer therapy will be listed by subject.

6 EFFICACY ANALYSES

Efficacy summaries will be presented by treatment group based on the Efficacy-Evaluable Analysis Set.

6.1 Objective Response Rate

ORR is defined as the proportion of subjects who achieve best overall response (BOR) of either complete response (CR) or partial response (PR) based on investigator assessment tumor lesions per RECIST v1.1. The BOR is the best response documented from first dose until the end of study, first disease progression, death, or start of new anti-cancer therapy, whichever is earlier. Subjects, who do not have sufficient baseline or on-study tumor status information to be adequately assessed for response status (i.e., those with BOR of not evaluable [NE]), or received anticancer therapy other than the study treatment, will be considered as non-responders and will be included in the denominators in calculations of response rates.

When the date of initiation of new anticancer therapy other than the study treatment is incomplete or missing, the following algorithm will be followed:

- If the day is missing but the month and year are available, then the imputed day will be the last day of the month.
- If day and month are missing but year is available, then the imputed day and month will be the last day of the month for the last adequate disease assessment if they have the same year.

The analysis of ORR will be performed based on the Efficacy-Evaluable Analysis Set. ORR with corresponding 2-sided 95% CI based on Clopper-Pearson method along with each category of BOR will be summarized by treatment group. Patients who don't have any postbaseline adequate tumor assessments will be counted as non-responders.

By-subject listings will be provided for target lesion, nontarget lesion, new lesion, and investigator-assessed timepoint response. A by-subject listing of new anticancer therapy will also be provided.

6.2 ECOG Performance Status Score

The ECOG performance status score has a range from 0 (Fully active; able to carry on all pre-disease performance without restriction) to 5 (Dead). The baseline ECOG performance status is summarized in the disease-specific baseline characteristics as specified in Section 5.2. A listing of ECOG performance status will be provided.

6.3 Changes from Protocol-Specified Efficacy Analysis

Analysis and summary will not be provided for time to duration of response and progression-free

survival due to limitation of the data.

7 SAFETY ANALYSES

Unless otherwise specified, all analyses will be performed using the Safety Analysis Set.

No formal comparisons of safety endpoints are planned.

7.1 Adverse Events and Deaths

7.1.1 Adverse Event Dictionary

All AEs will be coded to SOC and PT using Medical Dictionary for Regulatory Activities (MedDRA Version 21).

7.1.2 Adverse Event Severity

Adverse events are graded for severity by the investigators using the National Cancer Institute Common Toxicity Criteria for Adverse Events (NCI-CTCAE) Version 4.03. The severity grade of events for which the investigator did not record severity will be categorized as "missing" for tabular summaries and data listings.

7.1.3 Relationship of Adverse Event to Study Drug

A treatment related AE is an AE noted as related to FPA150 or pembrolizumab by the investigator. Events for which the investigator did not record relationship to study drug will be considered related to study drug for summary purposes. However, by-subject data listings will show the relationship as missing.

7.1.4 Serious Adverse Events

Serious adverse events (SAEs) will be identified and captured as SAEs if the AEs met the definitions of SAEs that were specified in the study protocol.

7.1.5 Treatment-Emergent Adverse Events (TEAE)

A treatment-emergent AE (TEAE) is defined as an AE that was not present prior to the start date of study drug or was worsened during treatment and 28 days after permanent discontinuation of study drug. An AE that was present at treatment initiation but resolved and then reappeared and the event severity increase while the subject was on treatment is also a TEAE.

If the onset date of the AE is incomplete and the AE stop date is not prior to the first dosing date of study drug, then the month and year (or year alone if month is not recorded) of onset determine whether an AE is treatment emergent. The event is considered treatment emergent if both of the following 2 criteria are met:

- The AE onset is the same as or after the month and year (or year) of the first dosing date of study drug, and

- The AE onset date is the same as or before the month and year (or year) of the date corresponding to 28 days after the date of the last dose of study drug

An AE with completely missing onset and stop dates, or with the onset date missing and a stop date later than the first dosing date of study drug, will be considered treatment emergent. In addition, an AE with the onset date missing and incomplete stop date with the same or later month and year (or year alone if month is not recorded) as the first dosing date of study drug will be considered treatment emergent.

7.1.6 Summary of Adverse Events and Deaths

The number and percentage of subjects who experienced at least 1 TEAE will be provided and summarized by SOC, PT, and treatment group. For other AEs described below, summaries will be provided by SOC, PT, maximum severity, and treatment group

- TEAE
- TE SAE
- Summary of TEAE of Grade 3-5
- TEAE related to FPA150
- TEAE leading to FPA150 treatment discontinuation
- TEAE leading to death
- TEAE of dose limiting toxicity

A brief, high-level summary of AEs described above will be provided by treatment group and by the number and percentage of subjects who experienced the above AEs.

Multiple events will be counted only once per subject in each summary. AEs will be summarized in alphabetic order of SOC and then by PT in descending order of total frequency within each SOC. For summaries by severity, the most severe severity will be used for those AEs that occurred more than once in a subject.

In addition to the above summary tables, TEAEs will be summarized by PT only in descending order of total frequency.

All AE and recorded deaths for the safety population will be listed.

7.1.7 Dose-Limiting Toxicity

The summary and listing of DLTs will be performed on the DLT-Evaluable Analysis Set. A summary of DLT will be provided by SOC, PT, and severity. All DLTs will be listed.

7.2 Clinical Laboratory Evaluations

Summaries of laboratory data will be provided in the Safety Analysis Set and will include data collected up to the last dose of study drug plus 28 days for subjects who have discontinued study drug, or all available data at the time of the final analysis data-cut for subjects who are ongoing at the time of the final analysis.

Treatment-emergent laboratory abnormalities are defined as values that increase at least 1 toxicity grade from baseline at any postbaseline time point. If the relevant baseline laboratory value is missing, any abnormality of at least Grade 1 observed within the time frame specified above will be considered treatment emergent.

Summary of laboratory abnormalities with CTCAE v4.03 will be provided by lab test and treatment group. Subjects will be categorized according to the most severe postbaseline abnormality grade for a given laboratory test.

A by-subject listing of laboratory test results collected throughout the study will be provided.

7.3 Body Weight and Vital Signs

Descriptive statistics will be provided by treatment group for body weight and vital signs as follows:

- Baseline
- Postbaseline maximum
- Postbaseline minimum
- Change and percentage change from baseline to postbaseline maximum
- Change and percentage change from baseline to postbaseline minimum

A baseline value is defined as the last available value collected on or prior to the first dose of study drug.

A by-subject listing of body weight and vital signs will be provided by subject ID and time point in chronological order.

7.4 Electrocardiograms

Subjects with abnormal ECG findings will be listed.

7.5 Other Safety Measures

By-subject listings for pregnancy report will be provided.

8 PHARMACOKINETIC (PK) AND IMMUNOGENICITY ANALYSES

8.1 PK Analysis

Nominal sampling times will be used for concentration-time plots and tables. Actual dose administered, and actual sampling times will be used for the calculation of PK parameters for each subject. The reasons for excluding any sample from the analyses will be provided.

Individual concentration-time data and PK parameters will be tabulated and presented. Summary of PK concentration over time and PK parameters will be provided. Mean concentration-time profiles for each dose will be provided. PK parameters will include, but will not be limited to, maximum observed concentration (C_{max}), time to maximum concentration (t_{max}) and area under the concentration-time curve (AUC), observed concentration at the end of a dose interval (C_{trough}). Other PK parameters such as clearance (CL) and terminal half-life ($t_{1/2}$) may be analyzed. PK parameters will be estimated using standard non-compartmental approaches based on the PK Analysis Set and summarized by dose level using descriptive statistics including, but not limited to means, standard deviations, geometric means, geometric CV (%), medians, minimums, and maximums.

8.2 Immunogenicity Analysis

Postbaseline treatment induced ADA positive is derived as subjects with

- ADA negative at baseline and ADA positive at any postbaseline timepoint, or
- ADA positive at baseline and ADA positive with titer of at least 4-fold of the baseline titer at one or more postbaseline timepoint

The summary of immunogenicity and by-subject listings of FPA150 ADA will be provided.

9 REFERENCE

Clopper CJ, Person ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometricka. 1934;26:404-413.

10 SOFTWARE

SAS® Software Version 9.4. SAS Institute Inc., Cary, NC, USA