STATISTICAL ANALYSIS PLAN

A Phase 1a/1b Study of FPT155 in Patients with Advanced Solid Tumors

PROTOCOLNUMBER: FPT155-001

PROTOCOL VERSION: AMENDMENT 4

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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
CD28	Cluster of Differentiation 28
CD80	Cluster of Differentiation 80
CI	Confidence Interval
CR	Complete Response
CRC	Cohort Review Committee
CSR	Clinical Study Report
CTCAE	Common Toxicity Criteria for Adverse Events
CTLA-4	Cytotoxic T-lymphocyte-associated protein 4
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
NK	Natural Killer Cells
ORR	Objective Response Rate
OS	Overall Survival
PD	Pharmacodynamic
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
Q3W	Once every 3 Weeks
RD	Recommended Dose
RECIST	Response Evaluation Criteria in Solid Tumors
RNA	Ribonucleic Acid
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
TNF	Tumor Necrosis Factor
WHO	World Health Organization
WHO-DD	World Health Organization Drug Dictionary

1 Introduction

The purpose of this statistical analysis plan (SAP) is to provide details of the statistical analyses that have been outlined within protocol Amendment 4 for study FPT155-001, which is entitled "A Phase 1a/1b Study of FPT155 in Patients with Advanced Solid Tumors" dated 14 September 2020. Any changes to the methods described in the final SAP will be documented in the clinical study report (CSR).

2 Study Design

This study is a Phase 1a/1b open-label, multicenter, dose escalation, dose exploration, and dose expansion study to evaluate the safety, tolerability, Pharmacokinetics (PK), Pharmacodynamics (PD), and preliminary efficacy of FPT155 in patients with advanced solid tumors. FPT155 (CD80-Fc) is a recombinant fusion protein composed of the Extracellular Domain (ECD) of human Cluster of Differentiation 80 (CD80) fused with the Fc domain of IgG1. It is designed to act as a potent stimulator of anti-tumor immunity. FPT155 as monotherapy and in combination with pembrolizumab will be evaluated.

2.1 General Study Design and Plan

2.1.1 FPT155 Monotherapy

FPT155 will be administered once every 3 weeks (Q3W) over approximately 60 minutes by intravenous (IV) infusion.

The monotherapy part of the study will initiate with Phase 1a dose escalation consisting of approximately 13 planned dose escalation cohorts, with the starting dose of 0.07 mg.

Phase 1a dose exploration consists of approximately 50 patients in total who may be enrolled at one or more dose levels to further evaluate safety, PK, PD, and clinical activity (conditional upon the dose levels clearing dose escalation criteria).

Phase 1b dose expansion consists of up to 8 tumor-specific expansion cohorts, enrolling approximately 30 patients each. Patients in Phase 1b will be treated with FPT155 at a recommended dose (RD) selected after assessment of data obtained in Phase 1a.

Treatment will continue until disease progression, unacceptable toxicity, consent withdrawal, or if any of the specified withdrawal criteria listed in Section 7.0 of the protocol are met.

2.1.2 FPT155 + Pembrolizumab

FPT155 will be administered Q3W over approximately 60 minutes by intravenous IV infusion

followed by 200 mg of pembrolizumab administered over 30 minutes by IV infusion a minimum of 30 minutes after the completion of FPT155. Eligible patients with advanced lung cancer will be enrolled for treatment with the combination of FPT155 and pembrolizumab.

Combination dose escalation will start with a FPT155 dose that is a minimum of two dose levels lower than the highest dose cleared in FPT155 monotherapy.

Combination dose exploration will include up to 30 patients who may be enrolled at one or more dose levels to further evaluate safety, PK, PD, and clinical activity (conditional upon the dose level clearing dose escalation criteria).

For patients enrolled for treatment with FPT155 and pembrolizumab, treatment will continue until disease progression, unacceptable toxicity or consent withdrawal. If one drug is discontinued, treatment may continue with the other alone for up to an additional 12 months.

2.1.3 Proposed FPT155 Dose Levels:

FPT155 will be initially administered Q3W, on Day 1 of each 21-day cycle. The anticipated dose levels are outlined in Table 1.

Table 1 Anticipated Dose Levels

Design	Cohort*	FPT155 Dose
Accelerated titration design	1aM1	0.07 mg
	1aM2	0.21 mg
	1aM3	0.70 mg
	1aM4	2.1 mg
3+3 design	1aM5	7 mg
	1aM6	21 mg
	1aM7	42 mg
	1aM8	70 mg
	1aM9	140 mg
	1aM10	280 mg
	1aM11	560 mg
	1aM12	840 mg
	1aM13	1260 mg

* Dose escalation cohorts, for example: 1aM1= Phase 1a FPT155 Monotherapy cohort 1.

Planned dosing increments take into account conservative estimates of receptor occupancy (RO) and pharmacological activity (PA) through both Cluster of Differentiation 28 (CD28) and Cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Fixed 3-fold escalation increments are proposed while projected engagement of CD28 is low; more conservative increments (2-fold or less) are proposed at higher CD28 occupancy levels.

The Sponsor may add cohorts with alternative dose levels or dose regimens (e.g., different dosing frequency, intermediate dose levels) upon review of safety, PK, and PD profiles to achieve optimal target exposure with acceptable tolerability.

2.2 Treatment Assignment

2.2.1 Dose Escalation Decisions in Phase 1a FPT155 Monotherapy

An initial accelerated titration design enrolling at least 1 patient at each dose level is planned for dose levels 0.07, 0.21, 0.70, and 2.1 mg. Dose escalation to the next dose level may proceed after at least 1 patient completes the 21-day Dose-Limiting Toxicity (DLT) evaluation interval.

DLTs during Phase 1a dose escalation are defined as any of the following deemed by the investigator as related to FPT155:

- Absolute neutrophil count (ANC) < 1.0 x 109/L for > 5 days duration or Grade 3 febrile neutropenia (eg, ANC < 1.0 x 109/L with a single temperature of > 38.3°C or fever > 38°C for more than 1 hour)
- Platelets < 25 x 109/L or platelets < 50 x 109/L with clinically significant hemorrhage
- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) > 3 x upper limit of normal (ULN) with concomitant total bilirubin > 2 x ULN not related to liver involvement with cancer
- Grade 3-4 non-hematological toxicity except:
  - Grade 3 fatigue < 7 days
  - Grade 3 nausea and Grade 3-4 vomiting and diarrhea lasting < 72 hours in patients who have not received optimal anti-emetic and/or anti-diarrheal therapy
  - Grade 3 endocrinopathy that is adequately treated by hormone replacement
  - Laboratory value that may be corrected through replacement within 48 hours
- Grade 2 neurological toxicity except headache and peripheral neuropathy in patients with Grade 1-2 peripheral neuropathy at entry

If a single patient experiences a DLT during the 21-day DLT evaluation interval, standard 3+3 dose escalation criteria will apply for that cohort with enrollment of additional patients. All subsequent dosing cohorts will then follow standard 3+3 dose escalation criteria.

Alternatively, if 2 patients experience moderate AEs (at any planned accelerated titration dose level), standard 3+3 dose escalation criteria will apply for the highest dose level at which a moderate AE was experienced, with enrollment of additional patients. All subsequent dosing cohorts will then follow standard 3+3 dose escalation criteria. Moderate AEs are defined as ≥ Grade 2 AEs deemed by the investigator as related to FPT155. Grade 2 laboratory values will not be considered as moderate AEs for this purpose unless accompanied by clinical sequalae. The

algorithm outlined in the Table 2 will be used for all dose escalation decisions in Phase 1a. If not already applied at a lower dose level according to the criteria stated above, enrollment at all dose levels ≥ 7.0 mg will follow a standard 3+3 dose escalation design.

Table 2 Algorithm for 3+3 Dose Escalation Decisions in Phase 1a

Number of Patients with DLT at a Given Dose Level	Dose Escalation Decision Rule
0/3 or 1/6	Enroll 3 patients at next dose level (next/higher cohort)
1/3	Enroll 3 additional patients at current dose level (current cohort)
≥ 2	Stop enrollment. If at Cohort 1aM1, the study will be stopped. If at Cohort 1aM2 or above, enroll 3 more patients at the previous dose level (previous/lower cohort) if only 3 were previously enrolled, or at an intermediate dose level

Abbreviations: DLT = dose limiting toxicity.

The maximum tolerated dose (MTD) will be defined as the dose level below that in which ≥ 2 DLTs are identified. If dose escalation completes without the identification of 2 DLTs at a given dose level, no MTD will have been identified.

2.2.2 FPT155 Monotherapy Dose Exploration

Phase 1a dose exploration consists of up to approximately 50 patients in total who may be enrolled at one or more dose levels to further evaluate safety, PK, PD, and clinical activity (conditional upon the dose level clearing dose escalation criteria). Toxicities observed in these patients will contribute to the overall assessments of safety and tolerability, and may inform selection of the RD.

2.2.3 FPT155 Monotherapy Dose Expansion

Enrollment in Phase 1b dose expansion will begin when the MTD and/or RD has been identified by the Cohort Review Committee (CRC). Up to 8 tumor-specific cohorts consisting of approximately 30 patients each will evaluate the safety, efficacy, PK, and PD of FPT155 at the RD. Patients with advanced renal cell carcinoma (RCC) and melanoma that have failed prior anti-programmed death-ligand 1 (anti-PD[L]1) therapy will be enrolled in 2 of the 8 cohorts. Additional tumor types are specified in Table 3 for the remaining Phase 1b cohorts and will be determined based on emerging safety, translational, and clinical data for FPT155, as well as any potential new safety signals from other immunotherapies, such as significant changes to prescribing information for approved immunotherapies.

Table 3 Additional Cohorts for Phase 1b Expansion

Phase 1b Cohort	Inclusion Criteria
1	Patients with advanced renal cell carcinoma as specified per Section 5.2 of the protocol.
2	Patients with advanced melanoma as specified per Section 5.2 of the protocol.
3	Patients with previously-treated unresectable or metastatic solid tumors with deficient mismatch repair (dMMR) or high microsatellite instability (MSI-H) and an absence of suitable standard treatment options.
4	Patients with previously-treated unresectable or metastatic non-small cell lung cancer and an absence of suitable standard treatment options.
5	Patients with previously-treated solid tumors with a response to prior PD-1 or PDL-1 directed treatment as defined by an objective response (partial or complete response) or a minimum of three months on prior PD-1 or PDL-1 directed therapy.

2.2.4 FPT155+Pembrolizumab Dose Escalation

FPT155 will start at a dose level a minimum of 2 levels below that cleared in dose escalation with FPT155 monotherapy.

Pembrolizumab will be administered Q3 weeks at 200mg over 30 minutes on Day 1 of each 21-day cycle.

Dose escalation decisions will follow the standard 3+3 algorithm described above and continue up to the dose level established as the MTD for FPT155 monotherapy. Additional intermediate dose levels or dose regimens may be considered upon review of emerging safety, PK and PD results.

2.2.5 FPT155 + Pembrolizumab Dose Exploration

Enrollment in combination dose exploration may occur at one more dose levels that have been cleared during combination dose escalation.

2.3 Sample Size Considerations

This study is designed as a dose escalation, dose exploration, and dose expansion study with objectives that include determination of an MTD and/or RD and assessments of the safety and tolerability of FPT155 as monotherapy and in combination with pembrolizumab. The sample size of Phase 1a is defined by the requirements of the 3+3 dose escalation design. The total number of patients planned for this study is estimated to be approximately 408.

The sample size of Phase 1a is defined by the requirements of the accelerated titration and 3+3 dose escalation design. Approximately up to 108 patients will participate in Phase 1a monotherapy, depending on the number of dose levels evaluated and the incidence of DLTs; this

includes up to 58 patients in the Phase 1a monotherapy dose escalation portion and allows for up to approximately 50 patients in the Phase 1a monotherapy dose exploration to further explore safety, PK, PD, and clinical activity at one or more dose levels (conditional upon the dose level clearing dose escalation criteria). Approximately up to 60 patients will participate in Phase 1a combination, depending on the number of dose levels evaluated and the incidence of DLTs; this includes up to 30 patients in the Phase 1a combination dose escalation, and up to 30 patients in the Phase 1a combination dose exploration.

For the objective of estimating the ORR of FPT155 in Phase 1b monotherapy, it is estimated that up to 30 patients will be enrolled to ensure 25 evaluable patients in each cohort. Table 4 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 in each cohort.

Approximately 240 patients will participate in Phase 1b monotherapy. Phase 1b monotherapy will consist of up to 8 cohorts of approximately 30 patients each.

Table 4 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.

3 Study Objectives and Endpoints

3.1 FPT155 Monotherapy Phase 1a Dose Escalation/Exploration Objectives and Endpoints

The objectives and endpoints for Phase 1a Monotherapy Dose Escalation/Exploration are summarized in Table 5.

Table 5 Objectives and Endpoints: FPT155 Monotherapy Phase 1a Dose Escalation/Exploration

OBJECTIVES	ENDPOINTS
PRIMARY	

OBJECTIVES	ENDPOINTS
Safety • To assess the safety and tolerability of FPT155 as monotherapy in patients with advanced solid tumors • To determine the RD of FPT155 as monotherapy	**Safety** • The incidence of adverse events (AEs), serious adverse events (SAEs), clinical laboratory abnormalities, and electrocardiogram (ECG) abnormalities • The incidence of AEs defined as dose limiting toxicities (DLTs), clinical laboratory abnormalities defined as DLTs, and overall assessment of pharmacokinetics (PK) and pharmacodynamics (PD)
SECONDARY	
Pharmacokinetics • To characterize the PK profile of FPT155 as monotherapy in patients with advanced solid tumors	**Pharmacokinetics** The following PK parameters will be derived from concentration-time data for FPT155 when appropriate and applicable. • Area under serum concentration-time curve (AUC) • Maximum observed serum concentration (C_{max}) • Trough observed serum concentration at the end of each dose interval (C_{trough}) • Clearance (CL) • Terminal 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
Immunogenicity • To characterize the immunogenicity of FPT155 as monotherapy in patients with advanced solid tumors	**Immunogenicity** • Incidence of treatment emergent anti-FPT155 antibody response
EXPLORATORY	
[redacted]	

OBJECTIVES	ENDPOINTS
[redacted]	

3.2 FPT155 Monotherapy Phase 1b Dose Expansion Objectives and Endpoints

The objectives and endpoints for Phase 1b Monotherapy Dose Expansion are summarized in Table 6.

Table 6 Objectives and Endpoints: FPT155 monotherapy Phase 1b dose expansion

OBJECTIVES	ENDPOINTS
PRIMARY	
Safety • To evaluate the safety and tolerability of FPT155 as monotherapy in patients with selected advanced solid tumors treated at the RD	**Safety** • The incidence of AEs, SAEs, clinical laboratory abnormalities, and ECG abnormalities • The incidence of treatment discontinuations, modifications, and interruptions due to AEs
SECONDARY	
Efficacy • To evaluate the clinical benefit of FPT155 as monotherapy in patients with selected advanced solid tumors treated at the RD through the analysis of ORR, DOR., PFS, and DCR	**Efficacy** • ORR, DOR, and PFS • Disease Control Rate (DCR) defined as total number of patients with confirmed responses of either CR, PR, or stable disease as determined by the investigator per RECIST v1.1, divided by the total number of patients who are evaluable for a response

OBJECTIVES	ENDPOINTS
Pharmacokinetics • To characterize the PK profile of FPT155 as monotherapy in patients with selected advanced solid tumors treated at the RD	**Pharmacokinetics** The following PK parameters will be derived from concentration-time data for FPT155 when appropriate and applicable. • AUC • C_{max} • C_{trough} • 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. Assessment of time-dependence of PK, the effect of body weight as well as other covariates on PK, and the exposure-response relationship, when the data allow, will be conducted to determine the appropriate dosing approach (eg, body weight-based or fixed dosing) for future trials.
Immunogenicity • To characterize the immunogenicity of FPT155 as monotherapy in patients with selected advanced solid tumors treated at the RD	**Immunogenicity** • Incidence of treatment emergent anti-FPT155 antibody response
EXPLORATORY	
[redacted]	

3.3 FPT155 + Pembrolizumab Phase 1a Dose Escalation/Exploration Objectives and Endpoints

The objectives and endpoints for FPT155 + Pembrolizumab Phase 1a Combination Dose

Escalation/Exploration are summarized in Table 7:

Table 7 Objectives and Endpoints: FPT155 + Pembrolizumab Phase 1a Dose escalation/Exploration

OBJECTIVES	ENDPOINTS
PRIMARY	
• To evaluate the safety and tolerability of FPT155 in combination with pembrolizumab in patients with advanced non-small cell lung cancer • To determine the RD of FPT155 in combination with pembrolizumab in patients with advanced non-small cell lung cancer	• The incidence of adverse events (AEs), serious adverse events (SAEs), clinical laboratory abnormalities, and electrocardiogram (ECG) abnormalities • The incidence of dose limiting toxicities (DLTs)
SECONDARY	
• To evaluate the preliminary clinical response rate of FPT155 in combination with pembrolizumab in patients with non-small cell lung cancer	• Objective Response Rate (ORR), defined as the total number of patients with responses of either CR or PR, as determined by the investigator per RECIST v1.1, divided by the total number of patients who are evaluable for a response
[redacted]	

OBJECTIVES	ENDPOINTS
[redacted]	

4 Analysis Population

4.1 Enrolled Population

All patients who sign informed consent and are registered as enrolled in IVRS/IWRS.

4.2 Efficacy Population

All patients who have received any portion of at least one dose of study drug.

4.3 DLT-Evaluable Population

All patients enrolled into Phase 1a dose escalation portion of the study who received at least 1 dose of all assigned study drug(s) and remain on study for the 21-day DLT evaluation period, or who experienced a DLT before clearing the 21-day DLT evaluation interval.

4.4 Safety Population

All patients who have received any portion of at least one dose of any study.

4.5 Response-Evaluable Population

All patients who met eligibility criteria, received at least one dose of any study drug, have measurable tumor lesions at baseline, and have at least one post-baseline disease assessment unless the death and clinical progressive disease occurred prior to the first post baseline disease assessment.

4.6 PK-Evaluable Population

All patients who have received at least one dose of study drug and have had sufficient PK sample for the calculation of at least one PK parameter on at least one Study Day.

5 General Considerations

All programming of tables, listings and figures (TLFs) will be performed using the statistical software package SAS® version 9.4 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. Confident intervals (CI) may be included as appropriate.

Patient data listings will be based on all enrolled patients, unless specified otherwise and will be sorted by Phase, Treatment Group, Patient Identifier and Visit. Study day relative to first dose of study drug may be presented.

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

- Phase 1a Monotherapy Dose Escalation/Exploration
- Phase 1b Monotherapy Dose Expansion
- Phase 1a Combination Dose Escalation/Exploration

Decimal places originally recorded in the data will be displayed in the listings. In general, the number of decimal places should not exceed 3 decimal places in the listings unless appropriate. In the summaries, values that are directly from the original value, such as range (minimum and maximum) will be reported in the original significant decimal places and not exceed 3 decimal places. Values that are calculated directly from the original value such as mean and median are reported in the original significant decimal places + 1 more decimal place. Values that are calculated from calculated values such as standard deviation and standard error will be reported in the original significant decimal places + 2 more decimal places. A full set of summary statistics will only be presented if there are 3 or more values available. If there is only 1 available value, standard deviation will be denoted as “NE” (Not Estimable). Percentages will be rounded to one decimal place. Confidence intervals (CIs) will be provided and will be rounded to 1 decimal place, unless otherwise specified, in the table and listing shell.

5.1 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 Phase 1a for combination will be combined for summary.

5.2 Handling Dropouts and Missing Values

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

The following imputation rules in will be used to impute start date and stop date of adverse event and concomitant medication.

- For stop date: If the month and year are present, impute the last day of the month. If only the year is present, impute December 31 of that year. If the stop date is entirely missing, assume the event or medication is ongoing. If a partial or complete stop date is present and the 'ongoing' or 'continuing' box is checked, then it will be assumed that the adverse event or concomitant medication stopped and the stop date will be imputed, if partial. If imputed stop date is after end of study (EOS)/Death date then EOS/Death date will be used as stop date.
- For start date: please refer to Table 8 below.

Table 8 Imputation Rules for Start Date of Adverse Event and Concomitant Medication.

Missing	Imputation	Exception
Day	01	Default to Study Day 1 if an adverse event starts the same year and month as Study Day 1 and the flag indicates that the adverse event started on or after the first dose on the Adverse Events eCRF
Day/Month	01 JAN	Default to Study Day 1 if an adverse event started the same year as Study Day 1 and the flag indicates that the adverse event started on or after the first dose on the Adverse Events eCRF
Day/Month/Year	If complete stop date present Stop date < first dosing date: Impute January 1 of the stop year Stop date ≥ first dosing date: Impute the date of first dose If partial stop date present ie, YYYYMM Partial Stop date < first dosing date: Impute January 1 of the stop year Partial Stop date ≥ first dosing date: Impute the date of first dose If partial stop date present ie, YYYY	

	Partial Stop date < first dosing date: Impute January 1 of the stop year Partial Stop date ≥ first dosing date: Impute the date of first dose If stop date is completely missing: Impute the date of first dose	

Date of disease diagnosis, prior anti-cancer therapy and new anticancer therapy will be imputed using the same rule when only the date is missing (no imputation when month or year is missing).

The following imputation rules in will be used for partial or missing death dates.

- If death year and month are available but day is missing:
    - If yyyymm for the date last known to be alive equals yyyymm for death date, set death date to the day after the date last known to be alive.
    - If yyyymm for the date last known to be alive is less than the yyyymm for death date, set death date to the first day of the death month.
    - If yyyymm for the date last known to be alive is greater than yyyymm for death date, assume death date is in error, do not impute and censor the subject survival time.
- If month and day are missing and year of death is known:
    - If yyyy for the date last known to be alive equals yyyy for death date, set death date to the day after last known to be alive date.
    - If yyyy for the date last known to be alive is less than yyyy for death date, set death date to the first day of the death year.
    - If yyyy for the date last known to be alive is greater than yyyy for death date, assume death date is in error, do not impute and censor the subject survival time.
- If a death date is totally missing:
    - Set death date to the day after the date last known to be alive. If the date last known to be alive is a partial date, set it to the first day of the month last known to be alive or first day of the year last known to be alive if month is also missing.

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.

5.3 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 Cycle 1 Day 1 pre-dose timepoint, and treated as missing for other timepoints in the concentration summaries.

5.4 Definition of Baseline

When appropriate, baseline is defined as the last non-missing result with a collection date-time less than the date-time of the first dose of study medication.

For continuous measurements before the first dose, 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, the last non-missing value will be used as baseline. For categorical measurements before the first dose, 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 last non-missing value will be considered as the baseline value.

Measurements occurred after first dose date will be considered post baseline values.

5.5 Analysis Visit Windows

5.5.1 Study Day Calculation

Study day relative to first dose will be calculated as: event date - first dose date in the study + 1 (if event date ≥ first dose date in the study) and event date - first dose date in the study (if event date < first dose date in the study).

5.5.2 Visit Windows

Visit windows are presented in the Appendix 1 and Appendix 2.

6 Statistical Analysis

6.1 Subject Information

Subject information data will be performed on the Safety Population, except the subject disposition summary and listing will be based on the Enrolled Population.

6.1.1 Subject Enrollment and Disposition

The number and percentage of patients for each of the following will be provided.

- Patients enrolled
- Patients who received study treatment
- Patients who completed the treatment
- Patients discontinued from treatment prematurely, overall and by reasons of discontinuation
- Patients who completed the study
- Patients discontinued from study, overall and by reasons of discontinuation
- Analysis populations

Listings will be provided for discontinued patients and patients completing the study. The summaries and listing will be based on all enrolled patients.

6.1.2 Protocol Deviations

A summary of the number and percentage of patients with protocol deviations by type of deviation will be provided. A listing of protocol deviations will be presented. All protocol deviations felt to be significant enough to impact the interpretation of the results will be presented in the data listings.

Possible protocol deviations will include but are not limited to:

- Violations of eligible criteria
- Disallowed medications or procedures
- Issues regarding informed consent form

6.1.3 Treatment Exposure and Compliance

6.1.3.1 Treatment Exposure

Descriptive statistics will be provided by treatment for the following

- Number of FPT155 Administered
- Cumulative dose (mg)
- Total duration of exposure to study drug (weeks)

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 population. A by-subject listing of study drug administration will be provided.

6.1.3.2 Treatment Compliance

The treatment compliance (%) and dose intensity (%) will be summarized. Compliance is defined as the sum of all numbers of doses administered across the treatment phase and divided by the planned numbers of doses for the patient for phase.

Compliance (%) = Actual numbers of doses received / Scheduled numbers of doses * 100%

Dose intensity is defined as actual total dosage received divided by planned total dosage. The planned total dosage is determined by the numbers of planned dosing visit*assigned dose level.

Intensity (%) = Actual doses received / Scheduled doses * 100%

6.1.4 Demographics and Baseline Characteristics

Demographic data will be summarized using descriptive summary statistics by cohort and overall in the safety population. A by-subject listing will be provided for demographic data.

6.1.4.1 Demographics

The demographic characteristics include

- Age (continuous), age is calculated based on year of informed consent and year of birth per EDC system.
- Sex (Male, Female) and Childbearing Potential Status for Female
- Race
- Ethnicity
- Baseline Height (in cm)
- Baseline Weight (in kg)
- Baseline Body Mass Index (BMI; in kg/m^2)

6.1.4.2 Disease-Specific Baseline Disease Characteristics

Disease-specific baseline characteristics include:

- Number of Anti-Cancer Regimens
- Time Since Completion of Last Regimen in Months

- Best Response of Last Regimen
- Time Since Initial Diagnosis of Cancer in Months
- ECOG Performance Status
- Stage at Diagnosis
- Stage at Study Entry
- Primary Site of Cancer
- Specific Histology

6.1.5 Medical History

Medical history will be coded using MedDRA 21.1 or later, sorted alphabetically by system organ class and preferred term, summarized for the safety population. By-subject listings will be provided for medical history.

6.1.6 Prior and Concomitant Medications

The World Health Organization Drug Dictionary (WHODrug-Global-B3) will be used to classify concomitant medications by therapeutic class and generic name.

Prior and concomitant medications, defined below, are summarized by Preferred Term (PT) for Safety Population.

- Medication started prior to first dose of any study drug will be considered as prior medication.
- Concomitant medication is defined as all medications used on or after the first dose of any study drug, through the treatment phase and for 30 days following the last dose of any study drug. A medication can be classified as both prior and concomitant medication.

Subjects reporting more than one use of the same medication will be counted only once in the summary tables. All medications will be sorted by descending total frequency of PT.

All prior and concomitant medications will be provided in a by-subject listing for Safety Population.

6.1.7 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 population as part of the disease-specific baseline characteristics.

The anti-cancer treatment, anti-cancer radiotherapy, anti-cancer surgery and procedures will be provided separately in a by-subject listing for Safety Population.

6.2 Efficacy Analyses

Tumor response assessment will be performed by the investigator per RECIST v1.1 guidelines. The tumor response will be classified to: complete response [CR], partial response [PR], stable disease [SD], or progressive disease [PD].

The Efficacy analyses listed in the Table 9 will be performed on the efficacy population as primary analysis, and on the response-evaluable population as a sensitivity analysis. Efficacy analysis will be performed separately for Phase 1a Monotherapy Dose Escalation/Exploration, Phase 1b Monotherapy Dose Expansion and Phase 1a Combination Dose Escalation/Exploration.

Table 9 Efficacy analysis

Phase	Efficacy Endpoint	Efficacy Analysis
Phase 1a Monotherapy Dose Escalation/Exploration	Exploratory	[redacted]
Phase 1b Monotherapy Dose Expansion	Secondary	ORR, DOR, PFS, DCR
	Exploratory	[redacted]
Phase 1a Combination Dose Escalation/Exploration	Secondary	ORR
	Exploratory	[redacted]

6.2.1 Efficacy Endpoint: ORR

Objective Response Rate (ORR) is defined as the total number of patients with confirmed responses of either complete response (CR) or partial response (PR), as determined by the investigator per RECIST v1.1, divided by the total number of patients who are evaluable for a response. The best overall response (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.

For the confirmed BOR, the algorithm below should be followed. The hierarchy of the categories for confirmed BOR is in the order listed.

- Confirmed CR: Check if the longest consecutive duration of CR (allow NE in between; duration starts at CR and ends at CR) is >=4 weeks, if yes, set BOR to CR; otherwise:
- Confirmed PR: Check if the longest consecutive duration of PR (allow NE or CR in between; duration starts at PR and ends at PR/CR) is >=4 weeks, if yes, set BOR to PR; otherwise:
- SD: Check if the best time-point response is CR or PR or SD, if yes, set BOR to SD; otherwise:

- PD: Check if the best time-point response is PD, set confirmed BOR to PD.
- NE: Otherwise set to NE.

Estimate of ORR and corresponding 2-sided exact 90% CI using the Clopper-Pearson method will be provided by treatment and overall. The Clopper-Pearson exact 90% CIs will be from SAS FREQ procedures with option BINOMIAL (EXACT). Patients who don't have any postbaseline adequate tumor assessments will be counted as non-responders.

6.2.2 Efficacy Endpoint: DCR

Disease Control Rate (DCR) is defined as total number of patients with confirmed responses of either CR, PR, or stable disease as determined by the investigator per RECIST v1.1, divided by the total number of patients who are evaluable for a response.

Estimate of DCR and corresponding 2-sided exact 90% CI using the Clopper-Pearson method will be provided by treatment and overall. The Clopper-Pearson exact 90% CIs will be from SAS FREQ procedures with option BINOMIAL (EXACT).

6.2.3 Efficacy Endpoint: DOR

Duration of Response (DOR) is defined as the time from first response (CR or PR determined by the investigator per RECIST v1.1) that is subsequently confirmed until the onset of progressive disease or death from any cause, whichever comes first.

DOR in months will be calculated as: (date of first progression or death from any cause – date of first confirmed CR or PR + 1)/30.4375. Patients who are alive and progression-free at the time of data analysis will be censored at the time of their last assessment for tumor response. DOR for CR and PR patients will be summarized using 25th, 50th (median), and 75th percentiles with associated 2-sided 90% CIs, as well as percentage of censored observations. The median will be estimated by using the Kaplan-Meier method and corresponding 2-sided 90% CI using Brookmeyer and Crowley methodology (using log-log transformation). The detailed censoring rules are displayed in Table 10.

Table 10 Censoring Rules for DOR

Situation	Outcome	Date of Progression or Censoring	Event Description/ Censoring Reason
No baseline tumor assessments	Censored	Date of first dose	No baseline tumor assessment
No baseline tumor assessment, but death within two consecutive tumor assessments period after first dose	Censored	First tumor assessment date	No baseline tumor assessment
No post-baseline tumor assessments and no death	Censored	Date of first dose	No post-baseline tumor assessment

No post-baseline tumor assessment and death after two or more consecutive missing tumor assessments from first dose	Censored	Date of first dose	No post-baseline tumor assessment
Disease progression before receiving subsequent anticancer therapy or data cutoff, which ever happens first	Event	Date of first documented progression per RECIST v1.1 (excludes clinical progression)	PD
Death without documented PD and not receiving new anticancer therapy on or before data cutoff	Event	Date of death	Death
Disease progression or death after two or more consecutive missing tumor assessments	Censored	Date of last evaluable tumor assessment prior to disease progression or death	Two or more consecutive missing tumor assessments
Subsequent anticancer therapy received without documented PD or death prior or on the same day	Censored	Date of last evaluable tumor assessment prior to the date of initiation of subsequent anticancer therapy	Started new anti-myeloma treatment before PD or death.
Alive and without progression	Censored	Date of last evaluable tumor assessment	Alive and without progression

6.2.4 Efficacy Endpoint: PFS

Progression Free Survival (PFS) defined as time from the first dose of study treatment until the first documentation by the investigator of disease progression per RECIST v1.1 or death from any cause, whichever comes first.

PFS in months will be calculated as: (date of first progression or death from any cause - date of first dose + 1)/30.4375. Patients who are alive and progression-free at the time of data analysis will be censored at the time of their last assessment for tumor response. PFS will be summarized using 25th, 50th (median), and 75th percentiles with associated 2-sided 90% CIs, as well as percentage of censored observations. The median will be estimated by using the Kaplan-Meier method and corresponding 2-sided 90% CI using Brookmeyer and Crowley methodology (using log-log transformation). The same censoring rules as DOR will be applied. See details in Table 10.

6.2.5 Efficacy Endpoint: OS

Overall Survival (OS), defined as the time from the first dose of study treatment until death from any cause.

OS in months will be calculated as: (date of death from any cause - date of first dose + 1)/30.4375. Patients who are known alive as of their last known status will be censored at the date

of their last known to be alive. OS for patients will be summarized using 25th, 50th (median), and 75th percentiles with associated 2-sided 90% CIs, as well as percentage of censored observations. The median will be estimated by using the Kaplan-Meier method and corresponding 2-sided 90% CI using Brookmeyer and Crowley methodology (using log-log transformation). Number and percent of survival subject at 1 year will be estimated. The detailed censoring rules are displayed in Table 11.

Table 11 Censoring Rules for OS

Situation	Outcome	Date of Progression or Censoring	Event Description/ Censoring Reason
Death before data cutoff	Event	Date of death	Death
Death after data cutoff	Censored	Date of data cutoff	Alive on or before data cutoff
No death before data cutoff	Censored	Date subject last known to be alive	Alive on or before data cutoff
Discontinued from study without death prior to data cutoff	Censored	Date subject last known to be alive	Discontinued from study

By-subject listings will be provided for target lesion, nontarget lesion, new lesion, and tumor response assessment. A by-subject listing of subsequent anti-cancer treatment will also be provided. By-subject listings for the efficacy endpoints above will also be provided.

6.2.6 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 6.1.4.2. A listing of ECOG performance status will be provided.

6.3 Safety Analyses

Safety analyses will be performed separately for Phase 1a Monotherapy Dose Escalation/Exploration, Phase 1b Monotherapy Dose Expansion, Phase 1a Combination Dose Escalation/Exploration and for all patients combined. AEs, clinical laboratory information, vital signs, ECOG performance status, weight, ECGs, and concomitant medications/procedures will be tabulated and summarized for the Safety Population. In addition, the incidence of DLTs in Phase 1a will be summarized using DLT-Evaluable Population. Unless otherwise specified, all analyses will be performed using the Safety Population.

6.3.1 Adverse Event

All AEs were collected from the start of study treatment (Cycle 1 Day 1) through completion of study, at the time points specified in the Appendix 1 and Appendix 2.

6.3.1.1 Adverse Event Dictionary

All AEs will be coded to SOC and PT using Medical Dictionary for Regulatory Activities (MedDRA Version 21.1 or later).

6.3.1.2 Adverse Event Severity

Adverse events will be 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.

- Grade 1: Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated; mild AE
- Grade 2: Moderate; minimal, local or non-invasive intervention indicated; limiting age-appropriate instrumental activities of daily living; moderate AE
- Grade 3: Severe or medically significant but non-immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living; severe AE
- Grade 4: Life-threatening consequences; urgent intervention indicated
- Grade 5: Fatal AE

6.3.1.3 Relationship of Adverse Event to Study Drug

A treatment related AE is an AE noted as related to FPT155 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.

6.3.1.4 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. All SAEs will be collected from the start of study treatment (Cycle 1 Day 1). In addition, any SAE occurring between signing of ICF and start of treatment will be recorded if it is due to a study related procedure. The SAEs will be collected through the Day 100 End of Treatment (EOT) visit.

6.3.1.5 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 100 days after last dose of treatment. 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.

6.3.1.6 Summary of Adverse Events and Deaths

An overall summary of TEAEs will summarize the number (%) of patients by the treatment group and overall with: all TEAEs, TEAEs with grade 3 or higher, TEAEs related to FPT155-001, TEAEs related to FPT155-001 with grade 3 or higher, TEAEs leading to study drug discontinuation, serious TEAEs, serious TEAEs related to FPT155-001, TEAEs leading to death. For the Phase 1a Combination Dose Escalation/Exploration, the TEAEs related to pembrolizumab, TEAEs related to pembrolizumab with grade 3 or higher and serious TEAEs related to pembrolizumab will also be included in the overall summary table.

The number and percentage of subjects who experienced at least 1 TEAE will be provided and summarized by SOC, PT, maximum severity, and treatment group. 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 maximum severity will be used for those AEs that occurred more than once in a subject. A subject with multiple adverse events within a SOC is only counted once in this SOC. Similarly, a subject with multiple adverse events within a PT is only counted once in this PT.

- TEAEs
- TEAEs with grade 3 or higher
- TEAEs related to FPT155
- TEAEs related to pembrolizumab (for Phase 1a Combination Dose Escalation/Exploration only)
- TEAEs leading to drug discontinuation of FPT155
- TEAEs leading to drug discontinuation of pembrolizumab (for Phase 1a Combination Dose Escalation/Exploration only)
- Serious TEAEs
- Serious TEAEs related to FPT155
- Serious TEAEs related to pembrolizumab (for Phase 1a Combination Dose Escalation/Exploration only)
- TEAEs leading to death

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.

6.3.1.7 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. The DLTs will also be summarized by PT only in descending order of total frequency. All DLTs will be listed.

6.3.2 Deaths

All deaths during the study, deaths within 28 days after the last dose of treatment, deaths within 100 days after the last dose of treatment and deaths beyond 100 days after the last dose of treatment will be summarized, the cause of deaths will also be included. All recorded deaths for safety population will be listed.

6.3.3 Clinical Laboratory Evaluations

Observed and absolute change from baseline of continuous clinical laboratory values (chemistry, hematology) for each parameter will be summarized at each scheduled time point in the Safety Population.

Shift tables displaying subject counts and percentages classified by baseline grade and maximum grade by treatment will be provided for chemistry and hematology tests with CTCAE v 4.03 grading in the Safety Population.

Table 12 Laboratory Tests

Hematology Tests	Chemistry Tests
ALC	Albumin
Hemoglobin	Alkaline Phosphatase
Hematocrit	ALT
Basophils (Absolute)	AST
Basophils (%)	Blood Urea Nitrogen
Lymphocytes (Absolute)	Urea
Lymphocytes (%)	Calcium
Monocytes (Absolute)	Chloride
Monocytes (%)	CO2
Neutrophils (Absolute)	Creatinine
Neutrophils (%)	CRP
Eosinophils (Absolute)	Direct Bilirubin
Eosinophils (%)	Glucose
Platelets	Lactate Dehydrogenase
Red Blood Cells	Magnesium
White Blood Cells	Phosphate
	Potassium
	Sodium
	Total Bilirubin

	Total Cholesterol
	Total Protein
	Uric Acid
	TSH
	Free T4
	Adrenocorticotropic Hormone (ACTH)

All laboratory data will be listed by subject. Clinical laboratory values that are out of normal ranges will be flagged in the listing.

6.3.4 Vital Signs

Vital signs parameters including systolic blood pressure, diastolic blood pressure, pulse, respiration rate, and temperature will be summarized for absolute values and change from baseline by visit and time point for safety population. By-subject listing of vital signs and vital signs during infusion will be provided.

6.3.5 12-Lead ECG

A by-subject listing of 12-lead ECG abnormality (abnormal clinical significant, and abnormal not clinically significant) will be provided.

6.3.6 Other Safety Measures

By-subject listings for physical examinations and pregnancy tests will be provided.

6.4 Pharmacokinetic (PK), [redacted] and Immunogenicity Analyses

6.4.1 PK Analysis

The PK parameters calculation will be described in a separate analysis plan, this SAP only present the summary and plot of PK parameters.

The following PK parameters will be derived from concentration-time data for FPT155 when appropriate and applicable to characterize single-dose/multiple dose PK.

- Area under the concentration-time curve (AUC)
- Maximum observed concentration (C_{max})
- Trough observed serum concentration (C_{trough})
- Clearance (CL)
- Half-life (t1/2)
- Volume of distribution at steady state (Vss)

- C_{max} and C_{trough} as well as the accumulation ratio of C_{max} and C_{trough} for pembrolizumab may be calculated if data are available.

Other parameters, such as dose proportionality, accumulation ratio, attainment of steady state, will also be estimated if the data are available.

Individual and mean (± SD) serum FPT155 and pembrolizumab concentration-time data will be tabulated and plotted by dose level, respectively. PK parameters of FPT155 and pembrolizumab will be tabulated and summarized by dose level when appropriate and applicable, respectively.

PK analysis will be performed using PK-Evaluable population. PK parameters will be estimated using standard non-compartmental approaches and summarized by dose level using descriptive statistics including: means, standard deviations, geometric means, geometric CV (%), medians, minimums, and maximums.

[redacted]

6.4.3 Immunogenicity Analysis

The anti-drug antibodies (ADA) will be summarized in immunogenicity analysis for Safety Population. Number and percentage of baseline ADA-positive subjects for FPT155 and pembrolizumab will be summarized by treatment group. A baseline ADA-positive patient is defined as a patient who has an ADA positive sample at baseline.

Number and percentage of FPT155 and pembrolizumab treatment induced ADA-positive subjects after initiation of the treatment will be summarized by treatment group. A treatment induced ADA-positive patient is a patient with at least 1 ADA-positive sample relative to baseline after initiation of the treatment.

By-subject listings of FPT155 and pembrolizumab ADA will be provided

Reference

Agresti, A. and B. Coull (1998). "Approximate is Better than "Exact" for Interval Estimation of Binomial Proportions." The American Statistician 52(2): 119-126.

Eisenhauer, E. A., P. Bogaerts, L. H. Schwartz, et al. (2009). "New Response Evaluation Criteria in Solid Tumours: Revised RECIST Guideline (version 1.1)." European Journal of Cancer 45: 228-247.

Appendix 1: Schedule of Assessments – Dose Escalation (monotherapy and FPT155 + pembrolizumab)

Phase 1a									
Study Phase	**Screening**	**Cycle 1 (21 Days)**					**Subsequent Cycles* (21 Days)**	**EOT Follow-Up**	**Notes**
Cycle Day	**Screening**	**D1**	**D2**	**D4**	**D8**	**D15**	**D1**	**28 and 100 Days Post Last Dose**	
Window (Days)	**-28**			**± 1**	**± 1**	**± 1**	**± 3**	**± 7**	
Study Assessments: Unless specified, procedure is to be performed prior to administration of study treatment. Any clinical assessment, laboratory test, or additional non-specified test may be obtained at any time if clinically indicated. If all study treatment is permanently discontinued for any reason other than withdrawal of consent, EOT follow-up visits should take place at the specified time points. The EOT follow-up visit at approximately 100 days after the last dose of study drug will be considered the end of study in Phase 1a.									
Review/Confirm Eligibility Criteria	X	X							
Informed Consent	X								
Medical History/ Demographics	X	X							Medical history includes significant past medical events including surgeries or hospitalizations, a review of the disease under study, prior anti-cancer therapies, and any concurrent medical illnesses.
Physical Examination	X	X			X	X	X	X	A complete physical examination including height and weight will be performed at screening. A limited physical examination (e.g., symptomdirected examination of specific organ systems/body area) should be conducted at the specified time points after screening. Additional physical examinations may be performed as clinically indicated for patients in the first dose cohort that are hospitalized for the initial infusion or for any patients showing evidence of ≥ Grade 2 CRS.
Height and Weight	X	X			X	X	X	X	Height (without shoes) should be measured at screening only and recorded in centimeters. Weight (without shoes) should be measured at each physical examination and reported in kilograms.
Vital Signs	X	X	X	X	X	X	X	X	Vital signs include blood pressure, respiratory rate, pulse and temperature. For the first and second infusions of FPT155, measure vital signs prior to dosing, every 15 minutes during the infusion, and after completion of each FPT155 IV infusion at the following time points: 5 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 3, hours, 4, hours, 5 hours, and 6 hours post-dose. Additional vital signs may be performed as clinically indicated for patients in the first dose cohort that are hospitalized for the initial infusion or for any patients showing evidence of ≥ Grade 2 CRS. For all subsequent infusions, measure vital signs prior to dosing, every 15 minutes during the infusion, and after completion of each FPT155 IV infusion.
12-Lead ECG	X	X					X	X	ECG is required at screening, pre-dose on Day 1 of every cycle, and at the EOT visits.
ECOG Performance status	X	X					X	X	
Prior/Concomitant Medications		←					→		
Adverse Events Review		←					→		AEs will be assessed before and after study drug dosing on

Phase 1a									
Study Phase	**Screening**	**Cycle 1 (21 Days)**					**Subsequent Cycles* (21 Days)**	**EOT Follow-Up**	**Notes**
Cycle Day	**Screening**	**D1**	**D2**	**D4**	**D8**	**D15**	**D1**	**28 and 100 Days Post Last Dose**	
Window (Days)	**-28**			**± 1**	**± 1**	**± 1**	**± 3**	**± 7**	
									applicable visits. AEs ascribed to study drug and SAEs should be assessed through the Day 100 EOT visit.
CT or MRI	X						X	X	Tumor evaluation by CT or MRI should be conducted according to RECIST v1.1 at screening, every 6 (± 1) weeks from the first dose for 24 weeks, and then every 12 (± 2) weeks thereafter. Imaging performed as standard of care may be used if it has been performed within 28 days of treatment. Once an initial CR or PR is noted, confirmatory scans must be performed 4-6 weeks later. Patients who terminate treatment prior to the next scheduled CT or MRI assessment should have a scan performed at the EOT visits (if not conducted in the previous 8 weeks or if tumor progression was previously determined). After discontinuation of study treatment for reasons other than progressive disease, withdrawal of consent, or initiation of additional anti-cancer therapy, tumor assessments will continue approximately every 12 (± 1) weeks until disease progression, withdrawal of consent or start of new anti-cancer therapy.
Archival Tumor Tissue (or Fresh Biopsy if Archival Not Available)	X								In dose escalation cohorts, archival tumor tissue is required. If archival tumor tissue is not available, a fresh biopsy is required prior to treatment. Blocks are preferred, if not available, a minimum of 15 slides are acceptable.
Sample Collection									
Chemistry	X	X	X		X	X	X**	X	All samples are assessed locally. Labs may be drawn up to 24 hours in advance of treatment. Additional labs may be performed as clinically indicated for patients in the first dose cohort that are hospitalized for the initial infusion or for any patients showing evidence of ≥ Grade 2 CRS. ** During dose escalation, chemistry and hematology panel will be drawn on Day 2, 8 and 15 of Cycles 2 and 3.
Hematology	X	X	X		X	X	X**	X	
Coagulation	X	X					X	X	
Urinalysis	X	X					X	X	
HBsAg and HCV RNA	X								
Pregnancy Test	X	X					X		For WOCBP, a serum pregnancy test will be performed at screening (within 7 days of Cycle 1 Day 1) and pregnancy testing will be performed at each subsequent cycle of treatment prior to dosing. All samples are assessed locally.
PK Sampling	Refer to Protocol Table 3								Blood samples will be collected for PK analyses at the time points specified and submitted to the central laboratory
PD Sampling	Refer to Protocol Table 3								Blood samples will be collected for PD analyses at the time points specified and submitted to the central laboratory
ADA Sampling	Refer to Protocol Table 3								Blood samples will be collected for ADA analyses at the time points specified and submitted to the central laboratory
Tumor Tissue Biopsy	X						X	X	In dose escalation cohorts, optional pre- and on-treatment fresh biopsies will be requested from the primary tumor or metastatic tumor site at screening (prior to treatment) and prior to the Cycle 3 Day 1 dose (± 1 week), from the same lesion where feasible. An additional optional biopsy will be requested at the Day 28 EOT visit from patients who have documented disease progression.
Study Drug Dosing									

Phase 1a									
Study Phase	**Screening**	**Cycle 1 (21 Days)**					**Subsequent Cycles* (21 Days)**	**EOT Follow-Up**	**Notes**
Cycle Day	**Screening**	**D1**	**D2**	**D4**	**D8**	**D15**	**D1**	**28 and 100 Days Post Last Dose**	
Window (Days)	**-28**			**± 1**	**± 1**	**± 1**	**± 3**	**± 7**	
Study Drug Dosing		X					X		FPT155 will be administered over approximately 60 minutes by IV infusion Q3W. Patients may continue receiving study treatment Q3W at the investigator's discretion until any of the protocol-specified treatment discontinuation criteria are met. For FPT155 + pembrolizumab cohorts, pembrolizumab will be administered 30 minutes after completion of the FPT155 IV infusion at a dose of 200 mg by 30 min IV infusion. If one study drug is discontinued, the other may be administered for up to 12 months or until protocol-specified discontinuation criteria are met. The DLT evaluation period consists of 21 days. Upon completion of the DLT evaluation period, patients may continue receiving study treatment per the parameters above.

Abbreviations: ADA = anti-drug antibody; CR = complete response; CRS = cytokine release syndrome; CT = computed tomography; DLT = dose limiting toxicity; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; EOT = end of treatment; IV = intravenous; HBsAG = hepatitis B surface antigen; HCV RNA = hepatitis C virus ribonucleic acid; MRI = magnetic resonance imaging; PD = pharmacodynamic; PK = pharmacokinetic; PR = partial response; Q3W = every 3 weeks; RECIST = Response Evaluation Criteria in Solid Tumors; WOCBP = women of childbearing potential

*There is a ± 3-day window for subsequent cycles after Cycle 1

Appendix 2: Schedule of Assessments – Dose Exploration/Expansion (monotherapy and FPT155 + pembrolizumab)

Phase 1b										
Study Phase	**Screening**	**Cycle 1 (21 Days)**					**Subsequent Cycles* (21 Days)**	**EOT Follow-Up**	**LTFU**	**Notes**
Cycle Day	**Screening**	**D1**	**D2**	**D4**	**D8**	**D15**	**D1**	**28 and 100 Days Post Last Dose**		
Window (Days)	**-28**			**± 1**	**± 1**	**± 1**	**± 3**	**± 7**	**± 14**	
Study Assessments: Unless specified, procedure is to be performed prior to administration of study treatment. Any clinical assessment, laboratory test, or additional non-specified test may be obtained at any time if clinically indicated. If FPT155 is permanently discontinued for any reason other than withdrawal of consent, EOT follow-up visits should take place at the specified time points. In the Phase 1b portion of the study, patients will also undergo LTFU for survival by clinic visit or by telephone approximately every 3 months after the Day 28 EOT visit, or until death, loss to follow-up, withdrawal of consent, or study termination by the Sponsor (whichever occurs first), which will be considered the end of the study in Phase 1b.										
Review/Confirm Eligibility Criteria	X	X								
Informed Consent	X									
Medical History/ Demographics	X	X								Medical history includes significant past medical events including surgeries or hospitalizations, a review of the disease under study, prior anti-cancer therapies, and any concurrent medical illnesses.
Physical Examination	X	X			X	X	X	X		A complete physical examination including height and weight will be performed at screening. A limited physical examination (e.g., symptom-directed examination of specific organ systems/body area) should be conducted at the specified time points after screening. Additional physical examinations may be performed as clinically indicated.
Height and Weight	X	X			X	X	X	X		Height (without shoes) should be measured at screening only and recorded in centimeters. Weight (without shoes) should be measured at each physical examination and reported in kilograms.
Vital Signs	X	X	X	X	X	X	X	X		Vital signs include blood pressure, respiratory rate, pulse and temperature.For the first and second infusions of FPT155, measure vital signs prior to dosing, every 15 minutes during the infusion, and after completion of each FPT155 IV infusion at the following time points: 5 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 3, hours, 4, hours, 5 hours, and 6 hours post-dose. For all subsequent infusions, measure vital signs prior to dosing, every 15 minutes during the infusion, and after completion of each FPT155 IV infusion. Additional vital signs may be performed as clinically indicated.
12-Lead ECG	X	X						X		ECG is required at screening, pre-dose on Cycle 1 Day 1, and at the EOT visits. Additional ECGs may be obtained at any time if clinically indicated.
ECOG Performance status	X	X					X	X		
Prior/Concomitant Medications		←							→	
Adverse Events Review		←							→	AEs will be assessed before and after FPT155 dosing on applicable visits. AEs ascribed to study drug and SAEs should be assessed through the Day 100 EOT visit.

Phase 1b										
Study Phase	**Screening**	**Cycle 1 (21 Days)**					**Subsequent Cycles* (21 Days)**	**EOT Follow-Up**	**LTFU**	**Notes**
Cycle Day	**Screening**	**D1**	**D2**	**D4**	**D8**	**D15**	**D1**	**28 and 100 Days Post Last Dose**		
Window (Days)	**-28**			**± 1**	**± 1**	**± 1**	**± 3**	**± 7**	**± 14**	
CT or MRI	X						X	X	X	Tumor evaluation by CT or MRI should be conducted according to RECIST v1.1 at screening, every 6 (± 1) weeks from the first dose for 24 weeks, and then every 12 (± 2) weeks thereafter. Imaging performed as standard of care may be used if it has been performed within 28 days of treatment. Once an initial CR or PR is noted, confirmatory scans must be performed 4-6 weeks later. Patients who terminate treatment prior to the next scheduled CT or MRI assessment should have a scan performed at the EOT visits (if not conducted in the previous 8 weeks or if tumor progression was previously determined). After discontinuation of study treatment for reasons other than progressive disease, withdrawal of consent, or initiation of additional anti-cancer therapy, tumor assessments will continue approximately every 12 (± 1) weeks until disease progression, withdrawal of consent or start of new anti-cancer therapy. Patients in LTFU for survival must have tumor scans every 12 (±2) weeks if tumor progression was not previously determined and/or use of alternative anti-cancer therapy has not been initiated. Any new anti-cancer therapy should be documented.
Archival Tumor Tissue (or Fresh Biopsy if Archival Not Available)	X									Archival tumor tissue is required. The fresh biopsy required at screening will be accepted in lieu of archival tumor tissue if archival tissue is not available. Blocks are preferred, if not available, a minimum of 15 slides are acceptable.
Sample Collection										
Chemistry	X	X	X		X	X	X	X		All samples are assessed locally. Labs may be drawn up to 24 hours in advance of treatment. Additional labs may be performed as clinically indicated.
Hematology	X	X	X		X	X	X	X		
Coagulation	X	X					X	X		
Urinalysis	X	X					X	X		
HBsAg and HCV RNA	X									
Pregnancy Test	X	X					X			For WOCBP, a serum pregnancy test will be performed at screening (within 7 days of Cycle 1 Day 1) and pregnancy testing will be performed at each subsequent cycle of treatment prior to dosing. All samples are assessed locally.
PK Sampling		Refer to Protocol Table 4								Blood samples will be collected for PK analyses at the time points specified and submitted to the central laboratory
PD Sampling		Refer to Protocol Table 4								Blood samples will be collected for PD analyses at the time points specified and submitted to the central laboratory
ADA Sampling		Refer to Protocol Table 4								Blood samples will be collected for ADA analyses at the time points specified and submitted to the central laboratory

Phase 1b										
Study Phase	**Screening**	**Cycle 1 (21 Days)**					**Subsequent Cycles* (21 Days)**	**EOT Follow-Up**	**LTFU**	**Notes**
Cycle Day	**Screening**	**D1**	**D2**	**D4**	**D8**	**D15**	**D1**	**28 and 100 Days Post Last Dose**		
Window (Days)	**-28**			**± 1**	**± 1**	**± 1**	**± 3**	**± 7**	**± 14**	
Tumor Tissue Biopsy	X						X	X		In dose exploration and expansion, pre- and on-treatment fresh biopsies will be mandatory at screening (prior to treatment) and prior to the Cycle 3 Day 1 dose, from the same lesion where feasible. An additional optional biopsy will be requested at the Day 28 EOT visit from patients who have ocumented disease progression.
Study Drug Dosing										
Study Drug Dosing		X					X			FPT155 will be administered over approximately 60 minutes by IV infusion Q3W. Patients may continue receiving study treatment Q3W at the investigator's discretion until any of the protocol-specified treatment discontinuation criteria are met. For FPT155 + pembrolizumab cohorts, pembrolizumab will be administered 30 minutes after completion of the FPT155 IV infusion at a dose of 200 mg by IV infusion. If one study drug is discontinued, the other may be administered for up to 12 months or until protocol-specified discontinuation criteria are met.
Survival Assessment										
Survival Assessment									X	Patients will undergo LTFU for survival by clinic visit or by telephone approximately every 3 months ± 14 days after the Day 28 EOT visit, or until death, loss to follow-up, withdrawal of consent, or study termination by the Sponsor (whichever occurs first).

Abbreviations: ADA = anti-drug antibody; AE = adverse event; CR = complete response; CRS = cytokine release syndrome; CT = computed tomography; DLT = dose limiting toxicity; ECG = electrocardiogram; ECOG = Eastern Cooperative Oncology Group; EOT = end of treatment; IV = intravenous; HBsAG = hepatitis B surface antigen; HCV RNA = hepatitis C virus ribonucleic acid; LTFU = long-term follow-up; MRI = magnetic resonance imaging; PD = pharmacodynamic; PK = pharmacokinetic; PR = partial response; Q3W = every 3 weeks; RECIST = Response Evaluation Criteria in Solid Tumors; WOCBP = women of childbearing potential.

* There is a ± 3-day window for subsequent cycles after Cycle 1