FUJIFILM Pharmaceuticals U.S.A., Inc.

FF1050201US101

A Phase 1/2a, dose-escalation study of FF-10502-01 for the treatment of advanced solid tumors

Statistical Analysis Plan

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Version 2.0

Prepared By:

Westat
5615 Kirby Drive, Suite 710
Houston, TX 77005

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1. Project Overview

1.1. Project Design

(Protocol Amendment #6). This is a Phase 1/2a, dose-escalation study of FF-10502-01. A total of up to N=161 patients with advanced solid tumors will be included in this study. In Phase 1 dose escalation, a total of up to 9 cohorts each will receive FF-10502-01 intravenously (IV) in 500 mL normal saline over a 1-hour period at doses of 8, 12, 18, 27, 40, 60, 90, 135 or 200 mg/m^2 weekly (Day 1, 8, 15) for three weeks, repeated every 28 days (= 1 cycle) until progression of disease. Once 6 patients are treated at the MTD in Phase 1, an additional 4 cohorts will be enrolled. Cohort 10 will enroll any patient with an advanced solid tumor who is otherwise eligible for this study (up to 20). Cohort 11 will enroll cholangiocarcinoma patients (up to 50). Cohort 12 will enroll gallbladder carcinoma patients (up to 10). Cohort 13 will enroll urothelial carcinoma patients (up to 27). Eligible patients enrolled in Phase 1 at the MTD may count towards the Phase 2a accrual.

Patients who demonstrate clinical benefit will be allowed to continue therapy with FF-1052-01 until progression of disease, observation of unacceptable adverse events (AEs), intercurrent illness or changes in the patient's condition that prevents further study participation.

During Phase 1 of the study, a Safety Review Committee (SRC) consisting of the actively recruiting investigators, the Medical Monitor, and FPHU, will review data from each cohort on an ongoing basis. Intermediate dose levels may be added if DLT is observed and it is recommended to do so by the SRC. During Phase 2a of the study, the SRC will review patient data at least quarterly and make recommendations to FPHU regarding the conduct of the trial.

The accrual for the Phase 1 dose escalation phase is expected to be 12 – 18 months. Accrual for the Phase 2a expansion phase is expected to be approximately 21 months, with the last patient followed every 3 months until death or patient's refusal to participate. The total study duration is expected to be approximately 57 months. The anticipated Phase 2a accrual rate is 3 – 5 patients per month for Cohort 10 and 1 – 2 patients with cholangiocarcinoma, gallbladder carcinoma and urothelial carcinoma (Cohorts 11, 12 and 13).

Safety will be assessed through the monitoring of AEs, clinical laboratory parameters (hematology, coagulation parameters, serum chemistry, and urinalysis), vital sign measurements, electrocardiograms (ECGs) and physical examinations.

Efficacy assessments will be determined on the basis of CT and/or MRI scans with best treatment response at any protocol-specified time point classified for solid tumors (RECIST v.1.1) and survival data (PFS and OS).

For Pharmacokinetics and Pharmacodynamics, the details of the analysis will be outlined in a separate PK/PD Report Analysis Plan.

1.2. Objectives

1.2.1. Primary Objective

To determine the safety profile, maximum tolerated dose (MTD), dose-limiting toxicities (DLT) and recommended Phase 2 dose (RP2D) in patients who receive FF-10502-01 for treatment of advanced solid tumors.

1.2.2. Secondary Objective

- To determine overall response rates
- To determine the duration of response and duration of stable disease (SD)
- To evaluate progression-free survival (PFS)
- To evaluate overall survival (OS)
- To evaluate the pharmacokinetics of FF-10502-01
- To evaluate FF-10502-01 incorporation into whole blood cellular DNA as a pharmacodynamic marker

1.3. Treatment(s)

1.3.1. Treatment Assignments

Phase 1: Following Screening, a total of up to 9 cohorts each will receive FF-10502-01 intravenously (IV) in 500 mL normal saline over a 1 hour period at doses of 8, 12, 18, 27, 40, 60, 90, 135 or 200 mg/m^2 weekly (Day 1, 8, 15) for three weeks, repeated every 28 days (= 1 cycle) until progression of disease.

DLT will be defined as the following drug-related events: Grade 4 thrombocytopenia of any duration; other Grade 4 hematologic toxicity lasting ≥ 7 days; ≥ Grade 3 non-hematologic toxicity (excluding Grade 3 nausea, vomiting or diarrhea that is adequately controlled with supportive care and resolves to ≤ Grade 2 within 48 hours); failure of Grade 3 platelets, absolute neutrophil count (ANC), or hemoglobin (Hb) to recover to Grade ≤ 1 within 4 weeks despite use of platelet and red blood cell (RBC) transfusions and/or growth factors; febrile neutropenia (defined as ANC < 1000/mm3 with a single temperature of > 38.3°C or sustained temperature of ≥ 38°C for over one hour); Grade 3 or 4 thrombocytopenia of any duration associated with bleeding; or other toxicity-related treatment interruption that does not resolve to ≤ Grade 1 by Day 28 when the toxicity has received appropriate medical treatment.

Phase 2a: Once 6 patients are treated at the MTD in Phase 1, an additional 4 cohorts will be enrolled. Cohort 10 will enroll any patient with an advanced solid tumor who is otherwise eligible for this study (up to 20 patients). Cohort 11 will enroll patients with cholangiocarcinoma (up to 50 patients). Cohort 12 will enroll patients with carcinoma of the gallbladder (up to 10 patients). Cohort 13 will enroll patients with urothelial carcinoma (up to 27 patients). Patients enrolled in Phase 1 at the MTD will count towards the Phase 2a accrual.

1.3.2. Selection and Timing of Doses

Phase 1: A single-patient dose escalation schema will be followed until the observation of ≥ Grade 2 toxicity. One patient per cohort will be dosed and followed for 28 days through Cycle 1 for DLT. If no ≥ Grade 2 toxicity is seen, the next patient will be enrolled at the next dose level. Dose escalation will proceed in this manner until Grade 2 or greater toxicity is observed in at least one patient per cohort during the first 28 days. At that point, the current dose cohort will be expanded to 3 patients before proceeding in standard 3+3 manner. The dose escalation in subsequent cohorts will proceed in standard 3+3 manner. For all patient cohorts, if 1 of 3 patients per cohort experiences DLT, the cohort will be expanded to 6. If 2 or more of 6 patients per cohort experience DLT, all further dose escalation will stop. If the next lowest dose has only 3 patients, 3 more patients will be treated at that dose to verify it as the MTD. If that dose turns out to be too toxic, then this process will be repeated until the MTD is found through dose de-escalation. If 0 of 3 or ≤ 1 of 6 patients per cohort experience DLT by Day 28 following dosing of FF-10502-01, dose escalation will proceed to the next cohort. The highest dose level below the dose level eliciting DLT in ≥ 2 patients will be declared the MTD. A total of 6 patients will be treated at the MTD. The MTD will be declared the RP2D. No intra-patient dose escalation will be allowed from previous dose levels until at least one patient has completed Cycle 1 at the higher dose level, with no Grade 2 or greater toxicities observed.

Dose level adjustments for DLT will be made. Patients who experience DLT at the first dose level, 8 mg/m^2, will not be dose-reduced, and will be discontinued.

Phase 2a: Patients in Cohorts 1 to 12 will receive FF-10502-01 on a weekly schedule for 3 weeks (Days 1, 8, and 15), repeated every 28 days. The Phase 2a dose regimen is FF-10502-01 90 mg/m2, administered on Days 1, 8, and 15 of a 28-day cycle. Patients in Cohort 13 (urothelial carcinoma) will receive FF-10502-01 on a weekly schedule for 2 weeks (Days 1 and 8), repeated every 21 days.

Blood for hematology, coagulation parameters and serum chemistry determinations for Cohorts 1 to 12 will be collected within 28 days of Cycle 1 Day 1, on Days 1, 8, 15 and 22 of Cycle 1, on Day 1 of each subsequent cycle and at the End of Study Visit. Blood for hematology and coagulation parameters will be collected pre-dose on Days 8 and 15 of each cycle. Urine will be collected for urinalysis within 28 days of Cycle 1 Day 1, on Day 1 of each subsequent cycle and at the End of Study Visit. Blood for hematology and serum chemistry determinations for Cohort 13 will be collected within 28 days before Cycle 1 Day 1, on Days 1, 8, and 15 of Cycle 1, on Day 1 of each subsequent cycle, and at End of Treatment. After Cycle 1, blood for hematology also will be collected pre-dose on Day 8 of each cycle. Urine will be collected for urinalysis within 28 days before Cycle 1 Day 1, on Day 1 of each cycle, and at the End-of-Treatment Visit.

Disease assessments, based on computed tomography (CT) or magnetic resonance image (MRI) will be obtained at Week 8 and every 8 weeks thereafter until documented progression of disease (PD) for Cohorts 1 to 12; and at Week 6 and every 6 weeks thereafter until

documented PD for Cohort 13. Patients who demonstrate clinical benefit will be allowed to continue therapy with FF-10502-01 until progression of disease, observation of unacceptable AEs, intercurrent illness or changes in the patient's condition that prevents further study participation.

1.4. Procedures

1.4.1. Patient Identification

Once study eligibility has been determined, a patient will be enrolled into the study and will be assigned a sequential Patient Identification number within each participating site. The identification number will consist of a 1-digit site number, a 2-digit cohort number, and a 2 digit Patient number. The Patient identification number will be assigned sequentially within the cohort. The cohort number will remain the same if a patient's dose is increased or decreased. If a patient is replaced, the identification number will not be reassigned.

1.4.2. Randomization

Not Applicable

1.4.3. Blinding/Unblinding

This is an unblinded study.

1.4.4. Replacement

Patients who are screened, but do not receive FF-10502-01, will be replaced.

1.4.5. Data Monitoring

During the study, an SRC consisting of the actively recruiting investigators, the Medical Monitor, and FUJIFILM Pharmaceuticals (FPHU), will review data from each cohort on an ongoing basis.

The sponsor is responsible for ensuring the proper conduct of the study with regard to ethics, protocol adherence, site procedures, integrity of the data, and applicable laws and/or regulations. At regular intervals during the study and following completion of the study, the sponsor's study monitors will contact the study site via visits to the site, telephone calls, and letters in order to review study progress, CRF completion, and address any concerns or questions regarding the study conduct. During monitoring visits, the following aspects of study conduct will be carefully reviewed: informed consent of patients, patient recruitment, and patient compliance with the study procedures, source data verification, drug accountability, use of concomitant therapy by patients, AE and SAE documentation and reporting, and quality of data. Records pertaining to these aspects are expected to be kept current.

2. Statistical Analysis Considerations

2.1. Sample Size and Power

A total of up to N=161 patients with advanced solid tumors are planned in this study.

Phase 1: The sample size reflects requirements associated with a single patient dose escalation until ≥ Grade 2 toxicity is observed, thereafter a 3+3 design. A total of 3 to 54 patients are planned (1 to 6 patients in each of 9 dose cohorts).

Phase 2a: The sample size reflects four additional cohorts: Cohort 10 (advanced solid tumors) will enroll up to 20 patients, Cohort 11 (cholangiocarcinoma) will enroll up to 50 patients, Cohort 12 (gallbladder carcinoma) will enroll up to 10 patients, and Cohort 13 (urothelial carcinoma) will enroll up to 27 patients for a total of up to 107 patients.

2.2. Analysis Populations

2.2.1. Full Analysis Set (FAS) Population

The FAS includes all patients who have a valid baseline and one or more post-treatment assessments. All efficacy endpoints will be based on the FAS population.

2.2.2. Randomized Population

Since this is not a randomized study, there is no randomized population.

2.2.3. Safety Population

The safety analysis population includes all patients who are administered any fraction of a dose of study drug.

2.2.4. PK/PD population

The PK population consists of all patients in the FAS who complete all PK assessments. The PD population consists of all patients in the FAS who complete a baseline and at least one follow-up PD assessment.

2.3. Data Handling

2.3.1. Measurement Times

2.3.1.1. Visit Windows

Visit windows will not be used. The visit time point entered on the case report forms will be used. Unscheduled assessments, if any, will be listed, but will not be included in tabulations by visit.

2.3.1.2. Baseline Values

The screening assessments are performed within 28 days of Cycle 1, Day 1, before the first dose of study medication. Unless otherwise mentioned, baseline will be the last observation before patients receive initially assigned dose. Generally, this will be Cycle 1 Day 1 pre-dose measurements. If a pre-dose assessment is not performed on Cycle 1 Day 1, the immediate previous non-missing value, including screening, will be treated as baseline. If there are multiple baseline assessments, the most recent one will be flagged as the baseline value and will be used for statistical analysis (evaluations may occur on the same day as Study Day 1, prior to dosing).

2.3.2. Missing Data Conventions

Unless otherwise specified, missing data will be considered missing and will not be imputed.

2.3.3. Imputation of Incomplete Dates

Imputation of partial dates may be performed during the data analysis and will be documented. For start date of AE or Concomitant Medication (CM) with a missing day, the imputed date is the first day of the month. For stop date of AE or CM with a missing day, the imputed date is the last day of the month. For start date with both missing day and missing month, the imputed date is the patient start study date if AE or CM start year is the same as study start year. Otherwise, the imputed start date is the first day of the year. For stop date with both missing day and missing month, the imputed date is the patient end of study date if AE or CM stop year is the same as the study end year. Otherwise, the imputed stop date is the last day of the year.

2.4. Statistical Methods

2.4.1. General Overview and Plan of Analysis

All data will be analyzed using Statistical Analysis System (SAS Version 9.4 or higher for Windows, SAS Institute, Cary, NC). Continuous variables will be summarized using number, mean, standard deviation, median, minimum, and maximum. Categorical variables will be summarized using frequencies and percentages.

2.4.2. Hypothesis Testing

No formal hypothesis tests are planned.

2.4.3. Modeling

Not Applicable in this study.

2.4.4. Multiplicity Issues/Multiple Comparisons

There is no planned Multiplicity Issues/Multiple Comparisons analysis for this study.

2.4.5. Project Center Effects

The study will be conducted at The University of Texas M.D. Anderson Cancer Center, Filip Janku, M.D., Principal Investigator (PI) and Sarah Cannon Research Institute, Denver, CO, Gerald Falchook, M.D., PI. Drs. Janku and Falchook will serve as Co-PIs for the study. Once experience is gained at these institutions, up to 2-4 additional sites may be added to complete study enrollment in a timely manner.

2.4.6. Interim Analysis

No formal interim analysis is planned. AE listings and appropriate summary tables will be generated for Scientific Review Committee meetings and Development Safety Update Reports (DSURs).

2.4.7. Pharmacokinetic and Pharmacodynamic Analyses

Pharmacokinetic and Pharmacodynamic data will be summarized in a separate report.

3. Statistical Analysis

Data will be presented for clinical review and interpretation. Categorical variables will be summarized using frequency counts and percentages. Continuous variables will be summarized using descriptive statistics (n, mean, SD, median, minimum, and maximum). All listings will be presented for the safety analysis population except for PK and PD data.

3.1. Enrollment and Disposition of Patients

Patients with advanced solid tumors will be included.

Major selection criteria are: age ≥ 18 years, histologically confirmed solid tumor with documented disease progression following previous therapy. Patients must be ≥ 4 weeks beyond chemotherapy (or ≥ 5 half-lives for targeted agents, whichever is shorter), radiotherapy, major surgery, or other experimental treatments, and recovered from all acute toxicities (≤ Grade 1), have adequate renal and hepatic function, and no known history of significant cardiac disease.

The analyses of patient disposition will be performed on the safety analysis population for patients in Phase 1 dose escalation and for patients in Phase 2a expansion phase by disease cohort treated at MTD. The number of patients screened, treated, completed study, and terminated early from the study, along with their reasons for early termination, will be presented.

3.2. Baseline Characteristics

3.2.1. Demographic

Summary statistics for demographic characteristics will be presented for patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase by disease cohort treated at MTD using the safety analysis population. Tabulations will be performed for age, sex

(male or female), ethnicity (Hispanic/Latino or other), and race (American Indian or Alaska Native, Black or African American, White, Asian, Native Hawaiian or Other Pacific Islander, Unknown, or other). Age will be calculated as the number of complete years between a patient's date of birth and the date of screening visit.

3.2.2. Physical Characteristics

Summary statistics will be presented for height (cm) and weight (kg) at screening for patients in dose escalation phase and for patients in expansion phase by disease cohort treated at MTD using the safety analysis population. ECOG performance status at screening will be summarized.

3.2.3. Disease Characteristics

Summary statistics will be presented for primary diagnosis at screening for patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase by disease cohort treated at MTD using the safety analysis population. Tabulations will be presented for primary tumor type, primary tumor location, sites of extension/metastases, and stage of disease. Medical history findings will be listed but not summarized.

3.2.4. Concomitant Medications at Entry

Concomitant medications coded using WHO Drug Dictionary will be listed but not summarized for patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase. Medication start and stop dates will be compared to the date of first dose of medication to allow medications to be classified as either prior or concomitant. Medications that start and stop prior to the date of first dose of study medication will be classified as prior medications. If a medication starts before the date of first dose of study medication or starts on or after the first dose of study medication, and stops on or after the date of first dose of study medication, then the medication will be classified as a concomitant medication.

3.3. Analysis of Efficacy

All efficacy analyses will be conducted for patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase by disease cohort treated at MTD using the FAS population.

3.3.1. Primary Endpoints

The primary efficacy endpoint is the proportion of patients in each disease cohort (cholangiocarcinoma, gallbladder carcinoma, urothelial carcinoma, or other solid tumor) with objective response (OR) within 4 cycles of study drug. Thus, this is the proportion of patients in Cohorts 1-12 with an OR within 16 weeks of their first dose of study drug and the proportion of patients in Cohort 13 with an OR within 12 weeks of their first dose of study drug. The OR rate is defined as the proportion of patients with a confirmed complete or partial response. Ninety percent confidence intervals for the OR rate will be estimated. See Appendix A for the schedule of study procedures.

Target Lesions in patients with measurable disease is evaluated by the PI as follows:

- **Complete Response (CR):** Disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to < 10mm.
- **Partial Response (PR):** At least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters.
- **Progressive Disease (PD):** At least a 20% increase in the sum of the diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that is the smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. (Note: the appearance of one or more new lesions is also considered progression).
- **Stable Disease (SD):** Neither sufficient decrease to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.
- **Not Evaluable:** One or more Target Lesions could not be assessed.

Non-Target Lesions (for all other lesions, or in patients with non-measurable disease only) is evaluated by the PI as follows:

- **Complete Response (CR):** Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (< 10 mm short axis).
- **Non-CR/Non-PD:** Persistence of one or more non-target lesion(s) and/or maintenance of tumor marker level above the normal limits.
- **Progressive Disease (PD):** Unequivocal progression of existing non-target lesions, or appearance of one or more new lesions. When the patient also has measurable disease, to achieve 'unequivocal progression' on the basis of non-target disease, there must be an overall level of substantial worsening in non-target disease such that, even in the presence of SD or PR in target disease, the overall tumor burden has increased sufficiently to merit discontinuation of therapy.
- **Not Evaluable:** One or more Non-Target Lesions could not be assessed.

Overall Response

At each protocol-specified time point (Day 28 of every 2nd cycle for Cohorts 1-12:and day 21 of every 2nd cycle for Cohort 13), an overall response assessment is made by the PI. Criteria for overall response for target and non-target disease are summarized in the table below:

Overall Response for Target and Non-Target Disease

	Target Lesion	Non-Target Lesion	New Lesions
Complete Response (CR)	CR	CR or NA	No
Partial Response (PR)	CR	Non-CR/Non-PD	No
	CR	Not evaluated	No
	PR	Non-PD or not all evaluated	No
Stable Disease (SD)	SD	Non-PD or not all evaluated	No
Progressive Disease (PD)	PD	Any	Yes or No
	Any	PD	Yes or No
	Any	Any	Yes
Not Evaluable (NE)	Not all evaluated	Non-PD	No

Best Overall Response
The Best Overall Response is the best response across all protocol time points.

3.3.2. Secondary Endpoints

Duration of Objective Response: length of time from the date of first evidence of response (CR or PR) to date of first evidence of PD or death. Patients who did not experience progression or death will be censored at the time of last contact (on the long-term follow-up date or the end of study date, whichever is later).

Duration of Stable Disease: length of time from the date of first evidence of response (CR, PR or SD) to date of first evidence of PD or death. Patients who did not experience progression or death will be censored at the time of last contact (on the long-term follow-up date or the end of study date, whichever is later).

Progression-Free Survival: length of time from the date of first administration of study drug to the date of first evidence of disease progression or death. Patients who did not experience progression or death will be censored at the time of last contact (on the long-term follow-up date or the end of study date, whichever is later).

Overall Survival: length of time from the date of first administration of study drug to the date of death from any cause. Patients who did not experience death will be censored at time of last contact (on the long-term follow-up date or the end of study date, whichever is later).

Duration of response, duration of stable disease, progression-free survival, and overall survival will be estimated using Kaplan-Meier product limit estimates and the estimated median and 90% confidence interval of the time-to-event.

3.3.3. Exploratory/Other Analyses

Pharmacokinetic and pharmacodynamic analyses will be provided by the outside laboratory.

3.4. Analysis of Safety and Tolerability

All safety endpoints will be summarized using descriptive statistics and will be based on the safety analysis for all patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase by disease cohort.

3.4.1. Study Drug Administration

Total duration of study drug exposure will be summarized using descriptive statistics for patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase by disease cohort at the MTD. Total duration of exposure to study drug in weeks will be calculated as the date of last dose minus the date of first dose plus one divided by 7, if there are no drug interruptions. If there are drug interruptions, the total duration will be determined minus the time of all drug interruptions. The number of weeks in all such cycles will be added within each dose cohort to calculate Total Duration of Exposure. Dose intensity (mg/m2/week) will be calculated as the total dose received per week during the cycle. The

total mg of drug received/week is calculated from the Volume Administered collected on the Study Drug Administration CRF page as follows: Total mg dose received = total mg dose prepared (mg/m2 dose x BSA in m2) x (Volume Administered divided by total volume (mL) in which the drug dose was prepared), cumulative over Days 1, 8 and 15 of each cycle divided by 4 weeks (=1 cycle) for all Phase 1 patients, Phase 2a Cohort 10 (other cancer), 11 (cholangiocarcinoma), and 12 (gallbladder) patients. For Cohort 13 patients, the calculation will be based on cumulative doses over Days 1 and 8 of each cycle divided by 3 weeks (=1 cycle). Relative dose intensity will be calculated by dividing the Mean Dose Intensity per week by Total Dose Prescribed (in mg/week). For 'all other cycles', the Duration of Exposure, Dose Intensity, Relative Dose Intensity and Proportion of Patients <80% will be captured on a 'per cycle' basis (averaged across all subsequent cycles) and not as a cumulative sum of all subsequent cycles.

The details of study drug administration will be presented in a listing.

3.4.2. Adverse Events

AEs reported from the date of the first dose of study drug to 28 days following the last dose of study drug will be presented. All AEs will be coded based on the Medical Dictionary for Regulatory Affairs (MedDRA; Version 17.0 or higher). An AE will be considered a treatment emergent adverse event (TEAE) if the onset is after the first dose of study drug or if the condition was present at baseline but worsened after the first dose.

All AEs for each patient will be listed, including intensity grading, relationship to study drug, action taken and outcome. Table summaries and patient listings of deaths, serious TEAEs, and TEAEs leading to treatment discontinuation will be provided.

TEAE summaries will be presented for patients in Phase 1 dose escalation phase and for patients in Phase 2a expansion phase by disease cohort. All TEAE summaries will show the number and percentage of patients experiencing at least 1 TEAE for each preferred term, arranged by system organ class, and the number of unique occurrences of the event. Separate summaries will be produced by relationship to study medication, and by severity, and for those events with an incidence of at least 2% in any group or overall. Patients with multiple events will be counted only once per SOC and preferred term. For each level of summarization, the event with the highest level of severity, or strongest drug relationship will be presented. TEAEs with Grade 3 or Grade 4 and drug-related TEAES with Grade 3 or Grade 4 will be summarized. TEAEs leading to study drug interruption or discontinuation, Grade 3 and 4 TEAEs, Serious TEAEs will be summarized and also provided in a separate listing. In addition, a summary of TEAEs for the total occurrences of the events will be provided.

3.4.3. Clinical Laboratory Results

The Hematology results that are collected include: Red blood cell count, Hemoglobin, Hematocrit, White blood cell count, Platelets, and differentials for Neutrophils, ANC, Lymphocytes, Monocytes, Eosinophils, and Basophils. Also CD4, CD8, and B-cells counts are being collected. The Serum Chemistry results that are collected include: Serum creatinine, BUN, Glucose (non-fasting,) Albumin, AST, ALT, LDH, Total bilirubin, Total

protein, Alkaline phosphatase, Calcium, Phosphorus, Magnesium, Sodium, Potassium, Chloride, and Bicarbonate. The Urinalysis results that are collected include: pH, Blood, Nitrates, Glucose, Ketones, Leukocytes, Protein, and Microscopic examination. Coagulation parameters include: Fibrinogen, aPTT, and PT (INR).

All laboratory data will be listed by patient. Values above and below normal ranges will be indicated, and whether statistically significant. All laboratory values will be graded according to the NCI-CTCAE version 4.03 criteria. Laboratory data for hematology and serum chemistry will be summarized by actual value and change from baseline using number of non-missing observations, mean standard deviation, median, minimum and maximum. In addition, grade shift tables from Baseline to most extreme post-Baseline grade will be presented for hematology and serum chemistry.

3.4.4. Vital Signs

Vital sign measurements include body temperature, blood pressure and pulse rate. Vital signs will be listed by patient. Values above and below normal ranges will be indicated as will clinical significance. Vital sign data will be summarized by actual value and change from baseline using number of non-missing observations, mean, standard deviation, median, minimum and maximum.

3.4.5. Physical/Other Examinations

Complete physical examinations include the following body system evaluations: General Appearance, Skin, Musculoskeletal, Eyes, Ears, Nose, Throat, Cardiovascular, Chest, Abdomen, Lymph Nodes, and Neurological. Data collected for physical examinations, ECGs and related measures will be listed. ECG changes from baseline will be summarized.

3.4.6. Treatment Discontinuation, Study Discontinuation, and Death

The participants who discontinued from treatment and/or study (with reasons) and deaths will be listed. A summary of the number and percentage of patients discontinuing the study due to AEs and due to death will be presented.

4. Proposed Summary Tables, Figures and Listings

4.1. Mock Tables

The following tables will be presented for patients in the Phase 1 dose escalation phase and by disease cohort at MTD for patients in the Phase 2a expansion phase.

4.1.1. Patient Disposition

- Patient Disposition

4.1.2. Demographics and Baseline Characteristics

- Demographics and Baseline Characteristics (Ethnic, Race, Sex, Age at Study Entry, Weight, Height and ECOG)
- Baseline Primary Diagnosis

4.1.3. Prior and Concomitant Medication

- Summary of Prior Medications
- Summary of Concomitant Medications

4.1.4. Primary Efficacy Summaries

- Proportion of Patients with Objective Response (OR) within 4 Cycles and 90% Confidence Intervals
- Disease Response for Non-Lymphoma Solid Tumor

4.1.5. Secondary Efficacy Summaries

- Kaplan-Meier Summary of Duration of Objective Response (OR)
- Kaplan-Meier Summary of Stable Disease (SD)
- Kaplan-Meier Summary of Progression-Free Survival (PFS)
- Kaplan-Meier Summary of Overall Survival

4.1.6.Safety Summaries

4.1.6.1. Study Drug Administration

- Summary of Study Drug Exposure

4.1.6.2. Adverse Event Summaries

- Summary of Treatment Emergent Adverse Events
- Treatment Emergent Adverse Events by System Organ Class and Preferred Term
- Treatment Emergent Adverse Events by Relationship to Study Drug
- Treatment Emergent Adverse Events by Severity
- Grade 3 and 4 Treatment Emergent Adverse Events
- Drug-related Grade 3 and Grade 4 Treatment Emergent Adverse Events
- Treatment Emergent Adverse Events with at least 2% Incidence in Any Group or Overall
- Serious Treatment Emergent Adverse Events

4.1.6.3. Laboratory Assessments

- Summary of Laboratory Assessments by Visit

- Change From Baseline in Laboratory Assessments by Visit
- Shift Table from Baseline to Most Extreme Post-Baseline Result by CTC Grade

4.1.6.4. Other Safety Summaries

- Summary of Vital Sign Results
- Change From Baseline in Vital Sign Results
- Change From Baseline in 12-Lead Electrocardiogram Results

4.2. Mock Figures

- Kaplan-Meier Curve for Duration of Object Response (OR)
- Kaplan-Meier Curve for Stable Disease (SD)
- Kaplan-Meier Curve for Progression-Free Survival (PFS)
- Kaplan-Meier Curve for Overall Survival

4.3. Mock Listings

The following listings will be presented in Phase 1 dose escalation phase and patients in Phase 2a expansion phase.

- Inclusion Criteria Not Met
- Exclusion Criteria Not Met
- Protocol Violations/Deviations/Exemptions
- Demographics
- End of Treatment
- End of Study
- Medical History
- Prior Cancer Therapy
- Radiation Therapy History
- Physical Examination
- Prior Medications
- Concomitant Medications
- Primary Diagnosis
- Study Drug Administration
- Pharmacokinetic (PK) Blood Sample Collection
- Pharmacodynamic (PD) Blood Sample Collection
- Screening Target Lesion Assessment (Non-Lymphoma Solid Tumor)
- Target Lesion Assessment (Non-Lymphoma Solid Tumor)
- Screening Non-Target Lesion Assessment (Non-Lymphoma Solid Tumor)
- Non-Target Lesion Assessment (Non-Lymphoma Solid Tumor)
- Tumor Biopsy Collection
- Disease Response Assessment (Non-Lymphoma Solid Tumor)
- Best Overall Disease Response Assessment
- Treatment Emergent Adverse Events (TEAEs)

- Serious Treatment Emergent Adverse Events
- Treatment Emergent Adverse Events Leading to Dose Adjustment, Temporary Interruption, or Permanent Discontinuation of Study Drug
- Treatment Emergent Adverse Events Leading to Permanent Discontinuation from Study
- Dose Limiting Toxicities
- Deaths
- Hematology
- Coagulation Parameters
- T Lymphocytes and B Lymphocytes
- Chemistry
- Urinalysis
- Vital Signs
- 12-lead Electrocardiogram
- Other Procedures
- Long Term Follow-up