STATISTICAL ANALYSIS PLAN
Viracta Therapeutics, Inc.
VT3996-201

Protocol Title:	A Phase 1b/2 Open-Label, Dose Escalation and Expansion Study of Orally Administered VRx-3996 and Valganciclovir in Subjects with Epstein-Barr Virus-Associated Lymphoid Malignancies
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ABBREVIATIONS

Table 1 List of Abbreviations

Abbreviation	Definition
AE	Adverse event
ATC	Anatomical Therapeutic Chemical
AUC	Area under the curve
AR	Accumulation Ratio
BLQ	Below the limit of quantification
CR	Complete response
CSR	Clinical Study Report
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
DCR	Disease control rate
DILI	Drug-induced liver injury
DLT	Dose-limiting toxicity
DoR	Duration of response
EBV	Epstein-Barr Virus
ECG	Electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic case report form
EES	Efficacy Evaluable Set
ET	End of Treatment
FDG	Fluorodeoxyglucose
HDAC	Histone deacetylase
ICH	International Council for Harmonisation
IP	Investigational product
ITT	Intent-to-Treat
KPS	Karnofsky Performance Scale
KM	Kaplan-Meier
MedDRA	Medical Dictionary for Regulatory Activities
ORR	Overall response rate
OS	Overall survival
PET	Positron emission tomography
PBMC	Peripheral blood mononuclear cells
PFS	Progression-free survival
PK	Pharmacokinetic
PKS	Pharmacokinetic Set
PR	Partial response
PS	Performance status
qPCR	Quantitative polymerase chain reaction
RP2D	Recommended Phase 2 Dose

Abbreviation	Definition
SAE	Serious adverse event
SAP	Statistical Analysis Plan
SI	Système International
SRC	Safety Review Committee
SS	Safety Set
SUV	Standard uptake value
TEAE	Treatment-emergent adverse event
TTR	Time to response
WHODDE	World Health Organization Drug Dictionary Enhanced

1. INTRODUCTION

The purpose of this Statistical Analysis Plan (SAP) is to provide comprehensive and detailed descriptions of the methods and presentation of data analyses proposed for Viracta Therapeutics, Inc. Protocol VT3996-201 (A Phase 1b/2 Open-Label, Dose Escalation and Expansion Study of Orally Administered VRx-3996 and Valanciclovir in Subjects with Epstein-Barr Virus-Associated Lymphoid Malignancies). Descriptions of planned analyses for the clinical study report (CSR) are provided in order to avoid post hoc decisions that may affect the interpretation of the statistical analysis. Both the statistical methods applied to the study design and the planned analyses for this study are consistent with the International Council for Harmonisation (ICH) guideline *Statistical Principles for Clinical Trials (E9)* (1998). The final study analysis will be performed when the last patient with a partial response (PR) or complete response (CR) is followed for 12 months, and all enrolled subjects have completed efficacy, safety and other assessments.

This SAP will be finalized prior to data analysis and before database lock to provide comprehensive details of the tables, figures, and listings to be presented in the CSR. Any changes between the statistical methods provided in the clinical study protocol and this SAP will be explained herein; any changes or deviations from this SAP relative to the final analysis will be fully documented in the CSR. Minor changes or deviations from the templates for tables, figures, and listings need not be documented in the CSR.

2. STUDY OBJECTIVES

2.1 Primary Study Objectives

The primary objectives of this study are include the following:

- Determine the safety and tolerability of nanatinostat/valganciclovir
- Determine a recommended phase 2 dose (RP2D) of nanatinostat/valganciclovir
- Assess activity based on overall response rate (ORR)

2.2 Secondary Study Objectives

The secondary objectives of this study include the following:

- Evaluate pharmacokinetic (PK) profile of varying doses of nanatinostat in capsule form and in tablet form (at RP2D only for tablet form)
- Evaluate PK parameters of varying doses of valganciclovir
- Evaluate time to response (TTR)
- Evaluate duration of response (DoR)
- Determine progression-free survival (PFS) and overall survival (OS)

2.3 Exploratory Objectives

The exploratory objectives of this study include the following:

- Evaluate of changes in viral loads (cytomegalovirus [CMV], Epstein-Barr Virus [EBV]) by quantitative polymerase chain reaction (qPCR), where applicable
- Evaluate EBV latency/lytic profile
- Evaluate changes in histone acetylation in peripheral blood mononuclear cells (PBMCs)
- Evaluate immunophenotype and immune function in PBMCs

3. INVESTIGATIONAL PLAN

3.1 Overall Study Design

This is an open-label, 2-part, Phase 1b/2 study of nanatinostat and valganciclovir for the treatment of patients with relapsed/refractory, pathologically confirmed EBV–positive (EBV^+) lymphoid malignancies or lymphoproliferative diseases regardless of histologic subtype.

The study will be conducted at approximately 30 sites in the US and Brazil. Written informed consent in a language fully comprehensible to the prospective patient will be obtained from each patient prior to performing any study-related procedures.

The Phase 1b portion of the study will evaluate safety and define an RP2D using a modified 3+3 design for oncology studies in patients with EBV^+ lymphomas (Section 3.1.1). The Phase 2 portion of the study will evaluate the RP2D in patients with EBV-associated lymphomas or lymphoproliferative disease, using a Simon's 2-stage design to allow for early stopping for futility (Section 3.1.2). The study defines a cycle length as 28 days.

Safety assessments will make use of all available data including using adverse event, clinical laboratory parameters, vital signs, electrocardiograms (ECGs), physical exams, and performance status (PS) assessments.

Response will be assessed locally using a combination of physical exam and imaging (e.g. PET-CT scan, CT scan, MRI, bone marrow/aspirate) as appropriate for each patient. Response assessments will be performed at least every two cycles, with an initial assessment after Cycle 2, using imaging modalities appropriate for the patients' specific lymphoma based on the Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: the Lugano Classification (Cheson et al., 2014).

A PK assessment of both nanatinostat and valganciclovir will be performed predose, at various timepoints following the first administration of nanatinostat/valganciclovir, and at additional timepoints within the first two cycles for all patients. A detailed schedule

that describes the coordination of PK sampling and ECGs is provided in Table 14 of the clinical study protocol.

Survival and follow-up assessments will be conducted at least every 3 months for assessment of additional therapy, response status, and survival following the safety follow-up assessment.

3.1.1 Phase 1b (Dose Escalation)

During the dose escalation portion of the study, dosing will be based on assigned cohort. Approximately 25 patients are expected to enroll in this phase. Cohort size will be up to 7 patients using a conventional modified 3+3 design for dose escalation studies in oncology.

On Cycle 1 Day 1, in an effort to ensure that patients tolerate oral valganciclovir prior to receiving nanatinostat, valganciclovir will be taken first, followed by nanatinostat approximately 1 hour later. For all subsequent administrations, the sequence of nanatinostat and valganciclovir can be dictated by patient convenience (e.g., both drugs may be taken together if tolerated by the patient). With the implementation of Protocol Amendment 4.0, nanatinostat and valganciclovir will be taken together at all timepoints, including Cycle 1 Day 1.

The first cycle is defined as the dose-limiting toxicity (DLT) assessment period. Grading of DLTs will be according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) version 5 and detailed in Section 3.1.5 of the protocol as well as Section 3.4.1 of the SAP. Patients who are unable to complete the DLT assessment period for reasons other than study drug-related toxicity may be replaced if needed to achieve at least 3 patients evaluable for DLTs.

A Safety Review Committee (SRC) comprised of study investigators, the study medical monitor and a Sponsor representative will govern the conduct of the study,and will have the option of defining additional cohorts and doses either below, above, or intermediate to the planned doses as needed based on data generated from prior cohorts. The SRC may also modify the dosing schedule for either nanatinostat or valganciclovir as required to accommodate different dosage strengths and patient convenience. However, when the schedule is adjusted, the total daily dose will remain unchanged. The Phase 1b planned doses for each cohort are provided in Table 2.

Table 2 Phase 1b Dose Levels by Cohort

Cohort Number	Dose Nanatinostat	Dose Valganciclovir
1	10 mg BID (20 mg daily dose)	900 mg BID
2a	5 mg BID (10 mg daily dose)	450 mg BID
2b	10 mg QD (10 mg daily dose)	450 mg BID

Cohort Number	Dose Nanatinostat	Dose Valganciclovir
2c	10 mg QD (10 mg daily dose)	900 mg QD
3	20 mg QD (20 mg daily dose), 4 days on and 3 days off in a 7-day regimen	900 mg QD

BID, twice daily; QD, once daily.

3.1.2 Phase 2 (Dose Expansion)

The phase 2 dose expansion portion of the study will evaluate the RP2D in 30 patients with relapsed/refractory EBV^+ lymphomas. This sample size is based on a Simon's 2-stage design where the Phase 2 portion of the study may be stopped if none of the first 10 treated patients have a response.

The dose and schedule of nanatinostat and valganciclovir used during the Phase 2 portion of the study will be the RP2D for nanatinostat and valganciclovir as determined by the SRC at the conclusion of the Phase 1b portion of the study. A Core SRC consisting of 2 investigators and 1 clinical expert appointed by the Sponsor will assess the toxicity during the phase 2 dose expansion and modify the dosing schedule of nanatinostat and/or valganciclovir as appropriate. Changes to the schedule will be enacted with minimal or no change to the total daily dose. Patients who are unable to complete at least one disease assessment to evaluate efficacy during the Phase 2 portion of the study may be replaced.

In both phases, patients will continue to receive nanatinostat/valganciclovir if, in the opinion of the Investigator, the patient is still receiving clinical benefit, the patient does not demonstrate progressive disease (in the absence of clinical deterioration, patients may continue on study drug until a repeat scan confirms progression), and in the absence of unacceptable toxicity.

3.1.3 Tablet Cohort

Once the Phase 2 arm has completed enrollment, approximately 10 patients will be enrolled into a cohort to receive nanatinostat tablets instead of capsules. The dose and schedule of nanatinostat and valganciclovir administered to patients in the tablet cohort will be the RP2D. With exceptions as described in the protocol, patients will follow the protocol/assessments as detailed for the Phase 2 expansion cohort patients.

3.1.4 Other Aspects of the Study Design

Exploratory biomarkers will be evaluated in this study as indicated in the schedule of events (Table 15) in the clinical study protocol. Archived blood, PBMCs, plasma, and/or tissue samples may be used for assessment of other exploratory biomarkers (if identified).

The End of Treatment (ET) Visit is the visit at the time of study treatment discontinuation. If the decision is made to discontinue study treatment outside of a

scheduled visit, an attempt will be made to have the patient return for an ET visit. Safety will be assessed at the Safety Follow-Up Visit, approximately 28 days following the final administration of nanatinostat/valganciclovir.

Survival and follow-up assessment will be conducted at least every 3 months for assessment of new antitumor therapy, disease progression status, and survival following the safety follow-up assessment. This assessment may be conducted by review of the patient records or by patient contact (e.g., telephone, email). Patients who are unable to be contacted following at least three attempts (one of which is contact by registered mail) will be considered lost to follow-up.

3.2 Schedule of Assessments

For the complete schedule of assessments, refer to Section 7 (Table 15, Schedule of Events) in the clinical study protocol.

3.3 Treatments

3.3.1 Treatments Administered

3.3.1.1 Nanatinostat

Nanatinostat is a hydroxamic acid-based histone deacetylase (HDAC) inhibitor. Nanatinostat drug product is currently supplied as 5 mg strength capsules and 10 mg film-coated immediate-release tablets were introduced in this study with amendment 5. The comparability between the tablets and capsules has been established via in vitro dissolution studies and in vivo dog pharmacokinetic studies.

Nanatinostat capsules will be administered in the Phase 1b portion of the study at a dose and schedule determined by the assigned cohort. In the Phase 2 portion of the study, patients will receive nanatinostat at the RP2D (nanatinostat 20 mg daily, Days 1 through 4/7 per week and valganciclovir 900 mg daily) and schedule determined in the Phase 1b portion of the study.

For the approximately 10 patients in the tablet cohort, patients will receive nanatinostat tablets rather than capsules. The dose and schedule of nanatinostat administered in the tablet cohort will be the same used with capsules in the Phase 2 portion of the study.

3.3.1.2 Valganciclovir

Valganciclovir (VALCYTE®), an oral prodrug of valganciclovir, is a cytomegalovirus (CMV) nucleoside analogue DNA polymerase inhibitor. In the Phase 1b portion of the study, the starting dose of valganciclovir will be determined by assigned cohort. In the Phase 2 portion of the study (including the tablet cohort), the starting dose and schedule of valganciclovir will be at the RP2D determined by the SRC at the conclusion of the Phase 1b portion.

3.3.2 Method of Assigning Patients to Treatment Groups

This is an open-label study that consists of a dose-escalation phase, followed by a dose-expansion phase. There will be no blinding. Patients in the dose-escalation phase will

be enrolled in cohorts based on recommendations by the SRC. Patients in the dose expansion phase and tablet cohort will receive the RP2D determined at the conclusion of the Phase 1b portion.

3.4 Safety and Efficacy and Safety Variables

3.4.1 Safety Variables

Safety assessments consist of monitoring and recording all AEs, regular laboratory evaluation for hematology, blood chemistry, coagulation and urinalysis, periodic measurement of vital signs, electrocardiograms (ECGs), performance status and physical examinations.

3.4.1.1 Primary Safety Endpoints

An AE is any untoward medical event that occurs in a patient following the start of investigational product (IP) administration, whether the event is considered IP-related or not. Pre-existing conditions are not considered an AE unless the condition worsens by at least 1 grade following the start of IP administration. Adverse events will be captured with the first dose of study drugs (on Cycle 1 Day 1) and continue until 28 days after the last dose of study drugs or until a new anticancer treatment is started whichever is first.

Dose-limiting toxicity AEs must meet all of the following criteria:

- Occurs during the first cycle (28 days) of study drug administration in Phase 1b only
- Is not incontrovertibly related to underlying disease
- In addition, to be considered a DLT, the AE will meet at least one of the criteria listed below:
    - Grade 4 anemia unexplained by underlying disease
    - Grade 4 febrile neutropenia
    - Grade 4 neutropenia lasting >5 days
    - Any other Grade 4 hematologic toxicity (thrombocytopenia, neutropenia, febrile neutropenia, anemia) of any duration
    - Grade 4 or higher tumor lysis syndrome
    - Grade 3 or higher thrombocytopenia (with or without bleeding)
    - Any requirement for platelet transfusion
    - Grade 3 or higher non-hematologic toxicity despite adequate supportive care
    - Results in a dose hold of >7 consecutive days

AEs that persist <72 hours and are able to be managed with supportive care may be excluded.

3.4.1.2 Secondary Safety Endpoints

Laboratory Parameters

Clinical laboratory evaluations will follow those outlined in the clinical study protocol and will be performed using a central or local laboratory. Evaluations include hematology, chemistry, urinalysis, coagulation, and pregnancy tests (for women of childbearing-potential only). Specific parameters to be collected are listed below:

- Hematology (blood): Complete blood count with differential to include white blood cells and differential, red blood cells, hemoglobin, hematocrit, platelets, mean corpuscular hemoglobin, mean corpuscular volume

- Chemistry (blood): Sodium, potassium, chloride, bicarbonate, blood urea nitrogen, creatinine, glucose, calcium, phosphate, magnesium, aspartate aminotransferase (AST),aminotransferase, alanine aminotransferase (ALT), total bilirubin, alkaline phosphatase, total protein, albumin, uric acid, and lactate dehydrogenase

- Coagulation (blood): prothrombin time, partial thromboplastin time, and international normalized ratio

- Urinalysis (urine): color, appearance, glucose, bilirubin, ketone, specific gravity, blood pH, protein, urobilinogen, nitrite, leukocyte esterase, red blood cells, white blood cells, epithelial cells

Electrocardiograms

Electrocardiograms will be performed as outlined in the clinical study protocol. When performed on days that include PK draws, ECGs will be performed prior to or as close as possible to the PK draw. For days when there are no scheduled PK draws, the ECG will be performed at any time during the clinic visit, irrespective of the time of study drug dosing. Prior to each ECG, the patient will lie in a supine position in a calm environment for at least five minutes. For patients enrolled under protocol amendment 5.0, triplicate assessments no more than five minutes apart are required for the following times:

- Screening
- Cycle 1 Day 1 pre-dose
- Cycle 1 Day 2 pre-dose and post-dose at 2 hours
- Cycle 1 Day 15 pre-dose and post-dose at 2 hours
- Cycle 2 Day 1 pre-dose and post-dose at 0.5, 1, 2, 4, and 6 hours
- Cycle 2 Day 15 pre-dose and post-dose at 2 hours

At times not listed above, single ECGs will be performed. On study days requiring a single ECG, if ECG indicates an increased QTcF interval, two additional ECGs will be performed at least two minutes apart.

Vital Signs

Vital signs, including weight, heart rate, respiratory rate, blood pressure, temperature, and oxygen saturation by pulse oximeter, will be collected as outlined in the clinical study protocol. On Cycle 1 Day 1, measurements will be collected prior to first dose of valganciclovir and nanatinostat and PK draws. For all other regularly scheduled visits, measurements will be collected prior to administration of study drugs.

Other Safety Variables

Physical exams will be performed at the screening visit only; symptom-directed physical exams will be conducted at each visit through Safety Follow-up as outlined in the clinical study protocol. Performance status will be measured by either the Eastern Cooperative Oncology Group (ECOG) or Karnofsky Performance Scale (KPS) and will be regularly evaluated as outlined in the clinical study protocol.

Plasma CMV DNA levels were monitored for 12 months by qPCR.

3.4.2 Efficacy Variables

3.4.2.1 Primary Efficacy Variable

The primary efficacy endpoint is the ORR, defined as the proportion of patients with a best overall response of complete response (CR) or partial response (PR) according to the Lugano criteria (Cheson 2014).

3.4.2.2 Secondary Efficacy Variables

Secondary efficacy endpoints include the following:

- Duration of response: defined as the interval from date of first observed complete or partial response per Lugano criteria (Cheson 2014) to the date of documented disease progression or death due to any cause. Dates of progression and censoring will be determined as described in Section 4.4.6.2.

- Disease control rate: defined as the proportion of patients with CRs, PRs, or stable disease (SD) per Lugano criteria (Cheson 2014).

- Time to response: defined as the interval from the start of study drug treatment to the first documentation of CR or PR per Lugano criteria (Cheson 2014). Patients who do not achieve a response will be censored at the date of their last tumor assessment.

- Progression-free survival: defined as the interval from the start of study treatment to the first documented date of disease progression or death from any cause, whichever occurs first. Dates of progression and censoring will be determined as described in Section 4.4.6.2.

- Overall survival: defined as the time from date of first study drug treatment to date of death, for any reason. Patients without documentation of death at the time of analysis will be censored at the date the patient was last known to be alive.

3.4.2.3 Exploratory Efficacy Variables

Plasma EBV DNA levels were monitored for 12 months by qPCR.

3.4.3 Pharmacokinetics

Pharmacokinetic endpoints include observed plasma concentrations and estimated PK parameters for nanotinostat and ganciclovir. For details of PK parameters, please refer Section 4.7.3.

3.5 Data Quality Assurance

Report summaries will be generated using validated Base SAS® software, version 9.4 or higher, on a PC or server-based platform. Additional validated software may be used to generate analyses, as needed.

All SAS programs that create outputs or supporting analysis datasets will be validated by a second statistical programmer or biostatistician. At a minimum, validation of programs will consist of a review of the program log, review of output or dataset format and structure, and independent confirmatory programming to verify output results or dataset content. Additionally, all outputs will undergo a review by a senior level team member before finalization.

The content of the source data will be reviewed on an ongoing basis by project statistical programmers and statisticians. Data will be checked for missing values, invalid records, and extreme outliers through defensive programming applications, analysis-based edit checks, and other programmatic testing procedures. All findings will be forwarded to the project data manager for appropriate action and resolution.

4. STATISTICAL METHODS

4.1 General Methodology

Data will be analyzed by Emanate biostatistics personnel. Statistical analyses will be reported with tables, figures, and listings, presented in rich text format, and using recommended ICH numbering. Output specifications for all tables, figures, and listings will be in conformance with guidelines specified by the ICH in Appendix 7 of the Electronic Common Technical Document Specification (Apr 2003).

4.1.1 Reporting Conventions

Tables and figures will be summarized by cohort and study phase. Tables will also include a column for all patients who receive the capsule formulation. In general, all data collected, and any derived data will be presented in patient data listings, for all enrolled patients. Listings will be ordered by site, study phase, patient number, cohort,

and assessment or event date. The cohort presented in listings will be based on the planned assignment, unless otherwise noted.

Summaries will be based on patient data from both the dose escalation and dose expansion phases up until the time when the final dose escalation patient has completed at least 12 months of follow-up from their first disease response assessment after two cycles of therapy, or until all patients have discontinued the study, died, withdrawn consent, discontinued, or are lost to follow-up, whichever occurs first.

In general, continuous variables will be summarized to indicate the study population sample size (N), number of patients with available data (n), mean, SD, median, minimum, and maximum values. Categorical variables will be summarized by the population size (N), number of patients with available data (n), number of patients in each category, and the percentage of patients in each category. Unless otherwise noted, the denominator to determine the percentage of patients in each category will be based on the number of patients with available data. Select ordinal data may be summarized using both descriptive statistics and counts and percentages of patients in each category, as appropriate.

Non-zero percentages will be rounded to one decimal place. Rounding conventions for presentation of summary statistics will be based on the precision of the variable of summarization, as it is collected in its rawest form (i.e., on the electronic case report form [eCRF] or as provided within an external file) and are outlined as follows:

- The mean and median will be rounded to one more decimal place than the precision of the variable of summarization.
- Measures of variability (e.g., SD, SE) will be rounded to two more decimal places than the precision of the variable of summarization.
- Minimum and maximum values will be presented using the same precision as the variable of summarization.

Other statistics (e.g., CIs) will be presented using the same general rules outlined above or assessed for the most appropriate presentation based on the underlying data.

No formal statistical analysis will be performed to compare cohorts. This study is exploratory in nature; descriptive statistics will be tabulated by study phase and cohort and reviewed to evaluate all study endpoints.

4.1.2 Summarization by Visit

In general, data summarized by study visit will be based on the nominal, scheduled visit label as reported on the eCRF. Data collected for the last patient visit will be summarized separately and this summary will be labeled as “End of Treatment” in the analysis.

For laboratory data summaries, data summarized by study visit will be based on the nominal, scheduled visit label as reported on the eCRF when available. If the scheduled visit is not available, then all data collection, including unscheduled and early

termination visits, will be reassigned a study visit based on the actual days relative to baseline using the visit windows identified in Table 3 below.

Table 3 Visit Windows for Analysis

Scheduled Visit	Target Study Day	Study Day Interval
Baseline	0	≤ 0
Cycle 1 Day 1	1	1
Cycle 1 Day 2*	2	2
Cycle 1 Day 8	8	3 – 11
Cycle 1 Day 15	15	12 – 18
Cycle 1 Day 22	22	19 – *XX***
Cycle 2 Day 1	*XX* + 1	*XX* + 1
Cycle 2 Day 8	*XX* + 8	(*XX* + 2) – (*XX* + 11)
…		

*Note Cycle 1 is the only cycle with a schedule Day 2 visit

** Day 22 is the last scheduled visit within each cycle, and the end of the study interval (*XX*) is calculated as the day before the start of the subsequent cycle.

If more than one value is mapped to the same visit, the value collected closest to the target study day will be considered for summarization. If two values collected on different days are mapped to the same scheduled visit and are equidistant from the target study day, the earlier of the values will be considered. The visit displayed on subject data listings will be reflective of the scheduled visit label as reported on the eCRF. Study days relative to baseline will be displayed for each visit to indicate to which visit the assessment may have been reassigned, if any.

Otherwise, data collected at unscheduled visits will not be included in by-visit summaries but will be considered when endpoint derivations potentially include multiple visits (e.g., determination of baseline value, determination of worst post-baseline value, etc.). All data will be included in patient listings.

4.1.3 Data Handling Rules

Unless otherwise noted, values reported as greater than or less than some quantifiable limit (e.g., "< 1.0") will be summarized with the sign suppressed in summary tables and figures, using the numeric value reported. Data will display on patient listings to include the sign.

4.1.4 Baseline Value

Unless otherwise noted, the baseline value will be defined as the last value reported prior to first dose of study drug.

4.1.5 Standard Calculations

Where appropriate, the calculated study day of each assessment or event will be presented with the assessment or event date on patient data listings, where study day will be determined as:

- The assessment/event date minus the date of first dose of study drug, if the assessment/event date is prior to the date of first dose; and
- The assessment/event date minus the date of first dose of study drug, plus one, if the assessment/event date is on or after the date of first dose.

Other variables requiring calculations will be derived using the following formulas:

- **Days:** A duration between two dates expressed in days will be calculated using the following conventions:
    - Later date – earlier date + 1, if the earlier date is on or after the date of first dose of study drug; or
    - Later date – earlier date, if the earlier date is prior to the date of first dose of study drug.
- **Months:** A duration expressed in months will be calculated by dividing the duration in days by 30.44.
- **Years:** A duration expressed in years will be calculated by dividing the duration in days by 365.25.
- **Change from Baseline:** Change from baseline will be calculated as the post baseline value minus the baseline value.
- **Percentage Change from Baseline:** Percentage change from baseline will be calculated as the change from baseline divided by the baseline value, multiplied by 100.

4.2 Analysis Sets

The analysis sets are defined as follows:

- Intent-to-Treat (ITT) Set: The ITT includes all enrolled patients.
- Safety Analysis Set: includes all enrolled patients who receive at least one dose of nanatinostat.
- Efficacy Evaluable Set: includes all patients with measurable/evaluable disease at screening who have met all eligibility criteria and have at least one evaluable post-baseline efficacy tumor assessment.
- Pharmacokinetic Analysis Set: includes all patients in the ITT who have receive at least one post-dose PK sample obtained and analyzed (i.e. valid result being

available). The PK Analysis Set is used for tabulation of nanatinostat and ganciclovir concentrations from PK plasma samples.

4.3 Study Patients

4.3.1 Disposition of Patients

Patient disposition will be summarized for the ITT by study phase and cohort and over all patients combined. Summaries will include the number and percentage of patients in each analysis set, completing treatment, completing the study, and discontinuing treatment or study early by the primary reason for discontinuation, and status at last contact.

4.3.2 Protocol Deviations

Deviations from the protocol and relevant details will be tracked throughout the study. All protocol deviations will be listed by subject.

4.4 Demographic and Baseline Characteristics

Demographic variables including country of participation, age (<65, ≥65, ≥75), sex, ethnicity, and race will be summarized by study phase and cohort and over all patients combined for the intent-to-treat set. Age as collected on the eCRF will be summarized using descriptive statistics. County of participation, sex, ethnicity, race, and disease stage will also be summarized with the number and percentage of patients in each parameter category.

Medical history verbatim terms on case report forms will be mapped and tabulated to/by system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA, version 25.0). Frequency counts and percentages to summarize patients reporting abnormal medical history by system organ class and preferred term will be presented. Lymphoma and non-lymphoma medical history will be summarized separately. For lymphoma medical history, the number of patients diagnosed with lymphoma in their lifetime, number refractory to last therapy received prior to entering study, and the number of patients who exhausted all prior therapies will also be summarized with the number and percentage of patients in each category. Listing will include start and stop dates or notation of ongoing for conditions continuing into treatment.

4.5 Safety Evaluation

Safety analysis will be carried out for the safety analysis set, to include all patients who receive at least one dose of study drug. Patients who do not complete the study, for whatever reason, will have all available data up until the time of termination included in the analysis.

4.5.1 Exposure to Study Treatment

Extent of exposure to both study treatments will be summarized for the safety analysis set by study phase and cohort. The duration of exposure to each treatment will be presented in days and calculated as the date of last dose of study drug minus the date of

first dose of study drug, plus one. Duration of exposure, number of patients treated (by duration), and total dose received (mg) will be summarized using descriptive statistics.

4.5.2 Adverse Events

Treatment-emergent adverse events (TEAEs) are defined as those adverse events (AEs) with onset after the first dose of study drug or pre-existing events that worsened by at least one grade after the first dose during the study. Treatment-emergent AEs will be summarized by study phase and cohort. Events reported with a partial onset date (e.g., month and year are reported but the day is missing) will be considered to be treatment-emergent if it cannot be confirmed that the event onset was prior to the first dose of study drug based on the available date entries.

Verbatim terms on case report forms will be mapped to preferred terms and system organ classes using the Medical Dictionary for Regulatory Activities (MedDRA, version 25.0). As an additional safety analysis, certain hematological AEs will be programmatically re-mapped to preferred terms and system organ classes consistent with CTCAE v5.0 categories. Select AE summaries will be repeated using this alternative mapping.

Summaries that are displayed by system organ class and preferred terms will be ordered by descending incidence of system organ class and preferred term within each system organ class. Summaries displayed by preferred term only will be ordered by descending incidence of preferred term. Summaries of the following types will be presented:

- Overall summary of number of unique TEAEs and patient incidence of TEAEs meeting various criteria.
- Overall summary of number of unique SAEs and patient incidence of SAEs meeting various criteria
- Patient incidence of TEAEs by MedDRA system organ class and preferred term
- Patient incidence of TEAEs by CTCAE toxicity grade, MedDRA system organ class, and preferred term.
- Patient incidence of dose-limiting toxicity AEs by MedDRA system organ class and preferred term.
- Patient incidence of TEAEs leading to dose interruption, reduction or discontinuation of valganciclovir by MedDRA system organ class and preferred term.
- Patient incidence of TEAEs leading to reduction or interruption of nanatinostat and valganciclovir by system organ class and preferred term
- Patient incidence of TEAEs leading to discontinuation of nanatinostat and valganciclovir by system organ class and preferred term

- Patient incidence of SAEs by MedDRA system organ class and preferred term.
- Patient incidence of SAEs by CTCAE toxicity grade, MedDRA system organ class, and preferred term.
- Patient incidence of TEAEs leading to study withdrawal by MedDRA system organ class and preferred term;
- Patient incidence of TEAEs leading to death by MedDRA system organ class and preferred term

Select AE summaries will also be repeated for different age subgroups (<65 years old, ≥65 years old, ≥65 years old and <75 years old, and ≥75 years old).

At each level of summarization (e.g., any AE, system organ class, and preferred term), patients experiencing more than one TEAE will be counted only once. In the summary of TEAEs by CTCAE grade, patients will be counted once at the highest severity reported at each level of summarization; in the summary of TEAEs by relationship, patients will be counted once at the closest relationship to study drug. Related events include those reported as "Possibly Related" or "Definitely Related" to study drug; events considered not related are those reported as "Unrelated" to study drug.

Adverse event data will be presented in data listings by study part, patient, cohort, and event. Serious AEs and AEs leading to discontinuation of the study drugs will be also be presented in separate data listings.

4.5.3 Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

All deaths during the study, including the post treatment follow-up period, will be listed by patient, to include the primary cause of death. Serious AEs and other significant AEs, including those that led to withdrawal, interruption, or dose reduction of either study drug, will be provided in separate patient data listings.

4.5.4 Clinical Laboratory Evaluation

All descriptive summaries of laboratory results will be based on data analyzed by the central or local laboratory and presented in Système International (SI) units, as suggested by the Center for Biologics Evaluation and Research and the Center for Drug Evaluation and Research *Position on Use of SI Units for Lab Tests* (Oct 2013). All data will be included in by-patient data listings. Laboratory measurements identified as abnormal (i.e., outside the normal range and ≥ Grade 3) will also be listed separately by patient, laboratory test, and unit. In addition, normal ranges provided by the central and local laboratories will be presented in a separate listing.

Clinical laboratory measurements, including serum chemistry, hematology, and coagulation will be summarized by study phase and cohort. Descriptive statistics will be presented for observed values and changes from baseline at each visit where parameters were scheduled to be collected per the clinical study protocol.

The cumulative number and percentage of patients with liver function test abnormalities meeting drug-induced liver injury (DILI) criteria will be summarized by treatment group. Patients meeting DILI criteria will also be presented in a patient data listing.

In addition, creatinine clearance will be calculated by the Cockcroft-Gault formula. For males, the creatinine clearance in mL/min will be calculated as [(140 - age) × weight (kg)]/[72 ×serum creatinine (mg/dL)]. For females, the creatinine clearance in mL/min will be calculated as 0.85 × the male value. The mean change from baseline over time for creatinine and creatinine clearance will be presented graphically over time by cohort and over all patients combined.

Where applicable, hematology and chemistry results will be classified as "low," "normal," or "high" with respect to the parameter-specific reference ranges (i.e., below the lower limit of the normal range, within the normal range, or above the upper limit of the normal range). Three-by-three contingency tables will be presented for each parameter to summarize the shift from the baseline category to the worst post-baseline measurement, defined as the value numerically farthest outside of the normal range across all post-baseline visits through the end of the study. Summary results will include the count and percentage of patients within each shift category and cohort.

Where applicable, hematology and chemistry results for select parameters will be assigned a toxicity grade based on the U.S. Department of Health and Human Services *Common Terminology Criteria for Adverse Events (CTCAE)*, version 5.0 (27 Nov 2017). If the quantitative criteria for grading are equivalent for two grades and the differentiation is described by clinical interventions, the clinical intervention component will not be considered and the highest CTCAE grade will be assigned. Similarly, death related to AE (i.e., Grade 5) cannot be determined with available laboratory-based data collection and, thus, will not be summarized as a category. Laboratory parameters that include multiple sets of criteria for each direction (e.g., separate criteria for potassium measures to assess hyperkalemia and hypokalemia) will be summarized separately to reflect each set of criteria.

Five-by-five contingency tables will be presented for lab tests where toxicity grading can be applied, to summarize the shift from the baseline grade to the worst post-baseline grade. Grades will be presented as none (Grade 0; i.e., measurements did not meet any CTCAE criteria for Grades 1 through 4), mild (Grade 1), moderate (Grade 2), severe (Grade 3), or life-threatening (Grade 4). Summary results will include the count and percentage of patients within each shift category.

4.5.5 Vital Signs, Physical Findings, and Other Observations Related to Safety

4.5.5.1 Vital Signs

Vital sign parameter measurements will be summarized by study phase and cohort. Descriptive statistics will be presented for results and change from baseline at each visit where parameters were scheduled to be collected.

4.5.5.2 12-Lead Electrocardiogram

Twelve-Lead ECG interval parameters will be summarized by study phase and cohort. Descriptive statistics will be presented for observed values and changes from baseline

at each visit where parameters were scheduled to be collected. For select visits, the ECGs will be performed in triplicate and the mean of these triplicate measurements at each timepoint will be used for summarization.

Twelve-lead ECG will be classified by the investigator as "normal," "abnormal, not clinically significant," or "abnormal, clinically significant." Three-by-three contingency tables will be presented to summarize the shift from the baseline category to the worst post-baseline value. Summary results will include the count and percentage of patients within each shift category and cohort.

Prolonged QTc intervals will be summarized as QTc measurements (msec) that are >450, >480, and >500 at each visit where ECG is routinely collected per the clinical study protocol. Change from baseline categories will also be summarized for measurements that represent a change >30 or >60 relative to the baseline value. Summary results will include the percentage of patients within each category and cohort.

Clinically significant abnormalities occurring at any point in the study post-baseline will be presented in patient-data listings.

4.5.5.3 Physical Examination

Results of the physical examination will be presented in patient data listings by patient, study visit, and body system. Any findings during symptom-directed exams will be reported as AEs.

4.5.5.4 Performance Status Assessments

Performance status will be assessed using either the ECOG or KPS. Karnofsky grades will be converted to the equivalent ECOG grade using the conversion table provided in Table 16 of the clinical study protocol. Performance status will be summarized by study phase and cohort. Descriptive statistics will be presented for observed values and changes from baseline at each visit where assessments were scheduled to be collected per the clinical study protocol. Results will be presented in patient data listings.

4.5.5.5 CMV Viral Loads

Patient's CMV viral loads will be presented in patient data listings only.

4.5.5.6 Prior and Concomitant Medications

Medications will be coded using the World Health Organization Drug Dictionary Enhanced (WHODDE), version September 1, 2017. Medications entered on the eCRF will be mapped to Anatomical Therapeutic Chemical (ATC) drug class (level 4) and drug name.

Prior and concomitant medications will be summarized separately, and the categorization of each medication will be determined programmatically based on medication start and end dates. A prior medication is defined as any medication administered prior to the date of the first dose of study drug with an end date prior to date of first dose of study drug. A concomitant medication is defined as any medication

administered on or after the date of the first dose of study drug through 28 days after the last dose of study medication. Any medication whose start date/time cannot be determined due to partial or missing medication start and/or end dates, will be considered a concomitant medication.

For both prior and concomitant medications summaries, the number and percentage of patients receiving any medication will be summarized by cohort, as will the number and percentage receiving any medication by ATC drug class and generic drug name. Prior medications will also be summarized over all patients combined. Patients reporting use of more than one medication at each level of summarization (any medication received, ATC class, and generic drug name) will be counted only once. ATC class terms will be displayed by descending order of incidence, as will generic drug names within each ATC class. The study phase during which each medication was received (e.g., prior, concomitant, or both) will be presented on the listing of prior and concomitant medications.

4.6 Efficacy Evaluation

4.6.1 Datasets Analyzed

All efficacy summaries will be based on the EES. A data listing of patients excluded from the EES, to include the reason for exclusion, will be presented.

4.6.2 Primary Efficacy Endpoint Analysis Methods

Counts and percentages for each tumor response category per investigator assessment will be presented by study phase and cohort. This analysis will also be presented by lymphoma subtype. The best overall response, as well as the ORR with corresponding exact binomial 95% confidence interval using the Clopper-Pearson Method, will also be presented.

Results from tumor assessments will be provided in separate listings.

4.6.3 Secondary Endpoint Analysis Methods

Disease control rate will be analyzed using the same statistical methodologies as applied to the primary efficacy endpoint in Section 4.6.2.

Time to response, DoR, PFS, and OS will be summarized in days using Kaplan-Meier (KM) methodology. The number of patients who experienced the event of interest and the number of patients censored will be presented; as will KM product limit estimates of the median with associated CIs (where estimable) using Greenwood's formula. The range for all patients, as well as those who experience the event of interest will also be summarized. Kaplan-Meier estimates of the survival distribution function for DoR, PFS, and OS over time will be generated for all patients receiving study treatment. All derived efficacy measures will also be provided in a separate listing. A swimmer plot of each patient's overall tumor response assessment by EBV+ lymphoma subtype will also be presented. A listing will be provided that lists each patient's lymphoma subtype, response category, and percentage of EBER-ISH positive tumor cells.

4.6.4 Exploratory Endpoint Analysis Methods

Each patient's EBV viral load will be plotted over time by lymphoma subtype and displayed on logarithmic scales.

4.6.5 Statistical/Analytical Issues

4.6.5.1 Adjustments for Covariates

There are no planned applications of covariate adjustments; all statistical results are descriptive in nature.

4.6.5.2 Handling of Dropouts or Missing Data

Best overall response is based on those patients with available data (baseline and post-baseline response assessment). Non-evaluable patients are considered non-responders and will be included in the denominator. Progression-free survival and DoR will be right-censored for patients who met one of the following conditions: 1) non-protocol systemic anti-cancer treatment started before documentation of disease progression or death, 2) death or disease progression after more than one missed disease assessment visit, or 3) alive and does not have documentation of disease progression before a data analysis cutoff date. These conventions are based on the FDA Guidance for Industry, *Clinical Trial Endpoints for the Approval of Cancer Drugs and Biologics* (2018). The analysis of PFS and DoR will be right-censored according to the conventions described in Table 4.

Table 4 Conventions for Censoring for PFS and DoR

Situation	Date of Progression or Censoring	Outcome
New anti-cancer therapy started before documentation of PD or death	Date of last disease assessment prior to start of new anti-cancer therapy	Censored
Death or PD immediately after more than one consecutively missed disease assessment visit	Date of last disease assessment visit without documentation of PD that is before the first missed visit	Censored
Alive and without PD documentation	Date of last disease assessment	Censored
Death or PD between planned disease assessments	Date of death or first disease assessment showing PD, whichever occurs first	Progressed
Death before first disease assessment	Date of death	Progressed

4.6.5.3 Interim Analyses and Data Monitoring

An SRC will govern the conduct of the study. The SRC will consist of the following individuals appointed by Viracta:

- Study Investigators
- Study Medical Monitor
- A Viracta Representative

Responsibilities of the SRC will include the following:

- Reviewing study safety data throughout conduct of the study
- Confirming or modifying the specific dose escalations between cohorts
- Defining intermediate dose levels as appropriate
- Declaring the maximum tolerated dose (if reached)
- Determining the RP2D
- Providing guidance on treatment-related issues raised by an Investigator

The SRC will meet at the end of each cohort during the Phase 1b portion and approximately quarterly during the Phase 2 portion, or as needed based on the rate of enrollment. A core SRC consisting of two investigators and one clinical expert appointed by the sponsor will assess the toxicity during Phase 2 dose expansion.

4.6.5.4 Multicenter Studies

This is a multicenter study, with approximately 30 sites expected to participate. Efficacy data collected from all study sites will be pooled for data analysis. The effect of study site on the efficacy analysis results may be explored post-hoc, as needed.

4.6.5.5 Multiple Comparisons/Multiplicity

There will be no adjustments for multiple comparisons in the efficacy analysis for this study. Results are descriptive in nature and no statistical hypothesis testing is planned.

4.6.5.6 Use of an "Efficacy Subset" of Patients

The efficacy analysis will be performed on the Efficacy Evaluable Set, which is a subset of the ITT Set.

4.6.5.7 Active-Control Studies Intended to Show Equivalence

This study does not include an active-control product and is not intended to demonstrate equivalence between any two drug products.

4.6.5.8 Examination of Subgroups

The primary efficacy endpoint will be summarized by various subgroups of interest based on baseline and demographic categories including age (e.g., < 65 years of age and ≥ 65 years of age) and number of prior therapies (e.g., ≥1 prior therapies and ≥2 prior therapies). Summaries by subgroup will only be produced if there are at least 6 subjects in the category of interest.

Additional subgroup analyses may be performed post-hoc, as appropriate.

4.7 Pharmacokinetics

The PK Analysis Set will be used for individual plasma concentration listings and summaries of plasma concentrations. The PK Population will also be used for individual and mean figures for plasma concentrations.

The PK Analysis Set will be used for noncompartmental analyses (NCA), inferential statistics, PK parameter listings, and parameter summaries.

4.7.1 Data Handling

Plasma concentrations that are below the limit of quantification (BLQ) will be treated as zero for the calculation of descriptive statistics. If the calculated mean concentration is BLQ, the mean value will be reported as BLQ, and the SD and CV% will be reported as not applicable. For PK analysis, all predose BLQ values will be treated as zero and all postdose BLQ values will be treated as missing. If consecutive BLQ concentrations are followed by quantifiable concentrations in the terminal phase, those quantified concentrations after BLQ concentrations will be treated as missing. Missing concentrations will be treated as missing from the PK parameter calculations.

For Cycle 1 Day 1 only, if the pre-dose value is > 5% of C_{max}, the subject will be flagged in all associated data listings and the affected profile will be excluded from all PK summaries and statistical evaluations.

4.7.2 Plasma Concentrations

The PK sampling schedule with the allowable time window for all patients is displayed in Table 14 in all versions of study protocol. Serial blood samples for the determination of nanatinostat and ganciclovir will be collected on Cycle 1 Day 1 for all patients, and Cycle 2 Day 1 for some patients in Phase 2 capsule cohort and all patients in Phase 2 tablet cohort.

PK collections that have an actual sampling time that is out of time window and deviates by more than 20% of the nominal sampling time will be flagged in the data listings and excluded from the calculation of concentration summary statistics. If an actual blood collection time or a dosing time is missing, the nominal time may be used. Individual plasma concentrations will be presented in data listings and summarized separately using descriptive statistics (number of subjects (N), number of observations (n), arithmetic mean, SD, CV%, median, minimum, and maximum) by nominal time point for each treatment.

Individual plasma concentrations will be plotted by actual time on both linear and semi logarithmic scales. Mean plasma concentrations will be plotted by treatment and nominal time on both linear and semi-logarithmic scales with all treatments overlaid on the same plots.

Plasma PK concentrations will be reported to 3 significant figures in summary statistics except n (and N), and CV%, which will be reported to integer and 1 decimal place, respectively.

4.7.3 Plasma Pharmacokinetic Parameters

Plasma concentration-time data will be analyzed by non-compartmental analysis using Base SAS® software, version 9.4 or higher. The following PK parameters will be calculated for nanatinostat and ganciclovir, where data permit:

Table 5 Pharmacokinetic Parameters

C_{max}	Maximum observed concentration.
T_{max}	Time of maximum observed concentration.
T_{last}	Time of last measurable concentration
AUC_{0-t}	Area under the concentration-time curve from time 0 to the last measurable observed concentration (C_t), calculated using the linear trapezoidal rule.
AUC_{0-inf}	Area under the concentration-time curve from time 0 extrapolated to infinity, calculated as $[AUC_{0-t} + (C_{last} / \lambda_z)]$ where Clast is the last observed measurable concentration (for Cycle 1 Day 1 only) (if applicable)
AUC_{0-6h}	Area under the concentration-time curve from time 0 to 6 hours (if applicable for nanotinostat)
AUC_{0-7h}	Area under the concentration-time curve from time 0 to 7 hours (if applicable for ganciclovir)
AUC_{0-8h}	Area under the concentration-time curve from time 0 to 8 hours (if applicable for nanotinostat and ganciclovir)
AUC_{0-24h}	Area under the concentration-time curve from time 0 to 24 hours (if applicable)
λz	Apparent terminal elimination rate constant, where λ_z is the magnitude of the slope of the linear regression of the log concentration versus time profile during the terminal phase.
$t_{1/2}$	Apparent terminal elimination half-life, calculated as: ln (2) / λ_z.
CL/F	Apparent total body clearance, calculated as: Dose / AUC_{0-inf} for C1D1, and Dose / AUC_{0-24h} for Cycle 2 Day 1.
V_z/F	Apparent volume of distribution during the terminal phase, calculated as: Dose / [λ_z * AUC_{0-inf}] for C1D1, and Dose / [λ_z * AUC_{0-24h}] for Cycle 2 Day 1.
$\%AUC_{ext}$	Percentage of AUC_{0-inf} due to extrapolation; AUC_{0-inf}, CL/F and V_z/F values on C1D1 will be flagged and excluded from summary statistics where $\%AUC_{ext} > 20\%$.
AR_{Cmax}	Accumulation ratio based on C_{max} between Cycle 2 Day 1 and Cycle 1 Day 1
$AR_{AUC0-24h}$	Accumulation ratio based on AUC_{0-24h} between Cycle 2 Day 1 and Cycle 1 Day 1

Actual sampling times will be used for the estimation of all plasma PK parameters, and all concentrations will be included in the analysis (including concentrations collected outside predefined collection windows).

Plasma PK parameters will be presented in data listings and summarized separately using descriptive statistics (number of subjects (N), number of observations (n), arithmetic mean, SD, CV%, geometric mean, geometric CV%, median, minimum, and maximum) by treatment. T_{max} will be summarized using number of observations, median, minimum, and maximum only.

Plasma PK parameters will be displayed to 3 significant figures in all data listings and summary tables except for CV%, which will be reported to 1 decimal place. Time variables (t_{max}, λ_z lower, and λ_z upper) will be displayed to 2 decimal places.

4.7.4 Pharmacokinetic Inferential Statistics

The dose proportionality of the key nanatinostat PK parameters C_{max}, $AUC_{0-\infty}$ and AUC_{0-6h}, if appropriate over the administered dose range, will be assessed using the following model using all dose groups:

log (parameter) = a + b * log (dose)

where 'a' is the intercept and 'b' is the slope. The model will be fit to the pooled, individual group patient data. Parameter estimates of b, including the standard error and 90% CIs will be summarized in a table. If the 90% CI for b includes 1.0, then linearity will be concluded.

4.8 Determination of Sample Size

The Phase 2 portion of the study will accrue 30 patients. Any patients in screening at the time that the 30th patient is enrolled will be permitted to enroll, should they be eligible. This sample size is based on a Simon's 2-stage design where the Phase 2 portion of the study may be stopped if none of the first 10 treated patients have a response. The hypothesized response rate of a poor drug is 5%, while the hypothesized response rate of a good drug would be at least 20%. Using a 1-sided alpha of 0.05 and power of 80%, if at least 1 of the first 10 patients has a response, the Simon's design recommends accruing up to at least 29 total patients to test the null hypothesis. The probability of stopping early is 59.9% with a type I error rate of 0.0468.

4.9 Changes in the Conduct of the Study or Planned Analyses

The following changes to planned analyses identified within the development of this SAP, relative to the descriptions provided within the clinical study protocol are listed below:

- Section 3.1.3 of the protocol includes a table for intended Phase 1b Cohort Doses.
    - The original intended Valganciclovir dose for Cohort 1 was 900 mg BID, but this was modified per the SRC recommendation after the first

4 patients. The actual Valganciclovir dosing was 900 mg BID for the first 4 patients and then 450 mg BID for the last 3 patients.

- The original intended Nanatinostat dose for Cohort 3 was 20 mg QD. The SRC later recommended to revise this dose to 20 mg QD 4 days per week following review of Cohort 1 safety data.

- Section 3.8 of the protocol states that a central review of patient scans will be performed and may include an assessment based on both Lugano and RECIL criteria. This central review was not performed.

- Section 6.4.1 of the protocol describes urine PK sample collection and, but this was not collected and will not be analyzed.

5. REFERENCE LIST

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