5.1.1. Inclusion Criteria

Subjects must meet all of the following criteria to be eligible for enrollment into the study:

1. Sign and date the ICF, prior to the start of any study-specific qualification procedures.
2. Subjects ≥18 years of age or the minimum legal adult age (whichever is greater) at the time the ICF is signed.
3. Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0, 1, or 2
4. Cohort 1 (R/R PTCL): Should be pathologically confirmed by the local pathologist/investigators; local histological diagnosis will be used for eligibility determination. Subjects with the following subtypes of PTCL are eligible, according to 2016 World Health Organization classification prior to the initiation of study drug.[5] Any T-cell lymphoid malignancies not listed below are excluded. Below is the complete list of eligible subtypes:
    - Enteropathy-associated T-cell lymphoma
    - Monomorphic epitheliotropic intestinal T-cell lymphoma
    - Hepatosplenic T-cell lymphoma
    - Primary cutaneous γδ T-cell lymphoma
    - Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma
    - Peripheral T-cell lymphoma, NOS
    - Angioimmunoblastic T-cell lymphoma
    - Follicular T-cell lymphoma
    - Nodal PTCL with TFH phenotype
    - Anaplastic large cell lymphoma, ALK positive
    - Anaplastic large cell lymphoma, ALK negative
5. Cohort 2 (R/R ATL): Acute, lymphoma, or unfavorable chronic type (Section 10.3.7). R/R ATL should be pathologically or hematocytologically confirmed by the local pathologist/investigators; local histological/ hematocytologically diagnosis will be used for eligibility determination. The positivity of anti-HTLV-1 antibody will be locally determined for eligibility (Section 10.3.7).
6. Must have at least 1 of the following lesions which are measurable in 2 perpendicular dimensions on CT (or MRI) based on local radiological read:

- Longest diameter (LDi) ≥2.0 cm for a nodal lesion
- LDi >1.0 cm for an extranodal lesion

  For Cohort 2 (ATL), subjects who had disease only in peripheral blood or/and skin lesions are eligible, as defined below.

  - An abnormal lymphocyte count (actual number) is ≥1.0 × 10^9/L and the abnormal lymphocyte-to-leucocyte ratio is ≥5%.
  - Skin lesion(s) measured by modified severity weighted assessment tool (mSWAT) score.

7. Documented refractory, relapsed, or progressive disease after at least 1 prior line of systemic therapy.

   Refractory is defined as

   - Failure to achieve CR (or uncertified CR [CRu] for ATL) after first-line therapy
   - Failure to reach at least PR following second-line therapy or beyond

8. Must have at least 1 prior line of systemic therapy for PTCL or ATL.
   - Subjects must also be considered as HCT-ineligible during Screening due to disease status (active disease), comorbidities, or other factors; the reason for HCT ineligibility must be clearly documented.
   - In Cohort 1, subjects with ALCL must have prior brentuximab vedotin treatment.

9. Screening local laboratory data must meet the following criteria to confirm relatively preserved organ function:

   a. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤3.0 × upper limit of normal (ULN)
   b. Total bilirubin ≤1.5 × ULN, except for subjects with Gilbert's syndrome (eg, a gene mutation in UGT1A1), who can have total bilirubin <3.0 mg/dL
   c. Absolute neutrophil count (ANC) ≥1.0 × 10^9/L
   d. Hemoglobin ≥8.0 g/dL
   e. Platelet count ≥75 × 10^9/L
   f. Creatinine clearance ≥30 mL/min (measured by the Cockcroft-Gault equation) (Section 10.3.1)

10. Acute non-hematologic toxic effects (as evaluated by National Cancer Institute [NCI] Common Terminology Criteria for Adverse Events [CTCAE], Version 5.0) of any prior therapy (except alopecia) resolved as shown below:
    - Peripheral neuropathy: Grade ≤2
    - Fatigue: Grade ≤2
    - All others: Grade ≤1

11. Is willing to provide tumor tissue (obtained during Screening or previously collected as a standard of care). In Cohort 2, subjects with ATL disease should also be willing to submit peripheral blood samples.
12. If the subject is a female of childbearing potential, she must have a negative serum pregnancy test at Screening and must be willing to use highly effective birth control, as detailed in Section 10.3.6, upon enrollment, during the Treatment Period, and for 3 months, following the last dose of study drug. A female is considered of childbearing potential following menarche and until becoming postmenopausal (no menstrual period for a minimum of 12 months) unless permanently sterile (undergone a hysterectomy, bilateral salpingectomy or bilateral oophorectomy) with surgery at least 1 month before the first dose of study drug or confirmed by follicle-stimulating hormone (FSH) test >40 mIU/mL and estradiol <40 pg/mL (<140 pmol/L).
13. If male, the subject must be surgically sterile or willing to use highly effective birth control (Section 10.3.6) upon enrollment, during the Treatment Period, and for 3 months following the last dose of study drug.
14. Female subjects must not donate, or retrieve for their own use, ova from the time of screening and throughout the study treatment period, and for at least 3 months after the final study drug administration.
15. Male subjects must not freeze or donate sperm starting at Screening and throughout the study period, and for at least 3 months after the final study drug administration.
16. Is willing and able to comply with scheduled visits, drug administration plan, laboratory tests, other study procedures, and study restrictions.

5.1.2. Exclusion Criteria

Unless otherwise specified, the below criteria will be evaluated during Screening.

Subjects who meet any of the following criteria will be disqualified from entering the study:

1. Diagnosis of mycosis fungoides, Sézary syndrome, and primary cutaneous ALCL and systemic dissemination of primary cutaneous ALCL
2. Diagnosis of precursor T-cell leukemia and lymphoma (T-cell acute lymphoblastic leukemia and T-cell lymphoblastic leukemia), T-cell prolymphocytic leukemia, or T-cell large granular lymphocytic leukemia
3. Prior malignancy active within the previous 2 years except for locally curable cancer that is currently considered as cured, such as cutaneous basal or squamous cell carcinoma, superficial bladder cancer, or cervical carcinoma in situ, or an incidental histological finding of prostate cancer
4. Presence of active central nervous system (CNS) involvement of lymphoma
5. History of autologous HCT within 60 days prior to first dose of study drug
6. History of allogeneic HCT within 90 days prior to the first dose of study drug
7. Clinically significant graft-versus-host disease (GVHD) or GVHD requiring systemic immunosuppressive prophylaxis or treatment

8. Inadequate washout period from prior lymphoma-directed therapy before enrollment, defined as follows:
    - Prior systemic therapy (eg, chemotherapy, immunomodulatory therapy, or monoclonal antibody therapy) within 3 weeks prior to the first dose of study drug
    - Had curative radiation therapy or major surgery within 4 weeks or palliative radiation therapy within 2 weeks prior to the first dose of study drug
9. Uncontrolled or significant cardiovascular disease, including the following:
    - Evidence of prolongation of QT/QTc interval (eg, repeated episodes of QT corrected for heart rate using Fridericia's method [QTcF] >450 ms) (average of triplicate determinations)
    - Diagnosed or suspected long QT syndrome, or known family history of long QT syndrome
    - History of clinically relevant ventricular arrhythmias, such as ventricular tachycardia, ventricular fibrillation, or Torsade de Pointes
    - Uncontrolled arrhythmia (subjects with asymptomatic, controllable atrial fibrillation may be enrolled), or asymptomatic persistent ventricular tachycardia
    - Subject has clinically relevant bradycardia of <50 bpm unless the subject has a pacemaker
    - History of second- or third-degree heart block. Candidates with a history of heart block may be eligible if they currently have pacemakers, and have no history of fainting or clinically relevant arrhythmia with pacemakers, within 6 months prior to Screening
    - Myocardial infarction within 6 months prior to Screening
    - Angioplasty or stent graft implantation within 6 months prior to Screening
    - Uncontrolled angina pectoris within 6 months prior to Screening
    - New York Heart Association (NYHA) Class 3 or 4 congestive heart failure (see Section 10.3.2)
    - Coronary/peripheral artery bypass graft within 6 months prior to Screening
    - Uncontrolled hypertension (resting systolic blood pressure >180 mmHg or diastolic blood pressure >110 mmHg)
    - Complete left or right bundle branch block
10. History of treatment with other EZH inhibitors
11. Current use of moderate or strong cytochrome P450 (CYP)3A inducers (Table 10.4)
12. Systemic treatment with corticosteroids (>10 mg daily prednisone equivalents). Note: Short-course systemic corticosteroids (eg, prevention/treatment for transfusion reaction) or use for a non-cancer indication (eg, adrenal replacement) is permissible.

13. Female who is pregnant or breast-feeding or intends to become pregnant during the study
14. Any positive test for hepatitis B virus or hepatitis C virus indicating acute or chronic infection within 28 days prior to the first dose of study drug
15. Known history of testing positive for human immunodeficiency virus (HIV) or known acquired immunodeficiency syndrome
16. Evidence of ongoing uncontrolled systemic bacterial, fungal, or viral infection requiring treatment with intravenous antibiotics, antivirals, or antifungals. Note: Subjects with localized fungal infections of skin or nails are eligible.
17. Any active uncontrolled systemic diseases or other medical conditions considered to be poorly controlled by the investigator, including, but not limited to, bleeding diatheses
18. A medical history or complication considered inappropriate for participation in the study, or a serious physical or psychiatric disease, the risk of which may be increased by participation in the study in the investigator's opinion
19. Psychological, social, familial, or geographical factors or substance abuse that would prevent regular follow-up to be compliant with the protocol