5. SUBJECT ELIGIBILITY

5.1. Inclusion Criteria

101) Relapsed or refractory B-precursor ALL defined as one of the following:
- Primary refractory disease
- First relapse if first remission ≤ 12 months
- Relapsed or refractory disease after two or more lines of systemic therapy
- Relapsed or refractory disease after allogeneic transplant provided subject is at least 100 days from stem cell transplant at the time of enrollment and off of immunosuppressive medications for at least 4 weeks prior to enrollment

102) Morphological disease in the bone marrow (> 5% blasts)

103) Subjects with Ph+ disease are eligible if they are intolerant to tyrosine kinase inhibitor (TKI) therapy, or if they have relapsed/refractory disease despite treatment with at least 2 different TKIs

104) Age 18 or older

105) Eastern cooperative oncology group (ECOG) performance status of 0 or 1

106) ANC ≥ 500/μL unless in the opinion of the PI cytopenia is due to underlying leukemia and is potentially reversible with leukemia therapy

107) Platelet count ≥ 50,000/μL unless in the opinion of the PI cytopenia is due to underlying leukemia and is potentially reversible with leukemia therapy

108) Absolute lymphocyte count ≥ 100/μL

109) Adequate renal, hepatic, pulmonary and cardiac function defined as:
- Creatinine clearance (as estimated by Cockcroft Gault) ≥ 60 cc/min
- Serum ALT/AST ≤ 2.5 x ULN (upper limit normal)
- Total bilirubin ≤ 1.5 mg/dl, except in subjects with Gilbert's syndrome.
- Left ventricular ejection fraction (LVEF) ≥ 50%, no evidence of pericardial effusion as determined by an ECHO, no NYHA class III or class IV functional classification, no clinically significant arrhythmias
- No clinically significant pleural effusion
- Baseline oxygen saturation > 92% on room air

110) Females of childbearing potential must have a negative serum or urine pregnancy test

111) In subjects previously treated with blinatumomab, CD19 tumor expression on blasts obtained from bone marrow or peripheral blood must be documented after completion of the most recent prior line of therapy. If CD19 expression is quantified, then blasts must be ≥ 90% CD19 positive.

5.2. Exclusion Criteria

201) Diagnosis of Burkitt's leukemia/lymphoma according to WHO classification or chronic myelogenous leukemia lymphoid blast crisis

202) History of malignancy other than non-melanoma skin cancer or carcinoma in situ (eg, cervix, bladder, breast) unless disease free for at least 3 years

203) History of severe hypersensitivity reaction to aminoglycosides or any of the agents used in this study

204) CNS abnormalities
- Presence of CNS-3 disease defined as detectable cerebrospinal blast cells in a sample of CSF with ≥ 5 WBCs per mm3 with or without neurological changes, and
- Presence of CNS-2 disease defined as detectable cerebrospinal blast cells in a sample of CSF with <5 WBCs per mm3 with neurological changes

Note: Subjects with CNS-1 (no detectable leukemia in the CSF) and those with CNS-2 without clinically evident neurological changes are eligible to participate in the study.
- History or presence of any CNS disorder such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, any autoimmune disease with CNS involvement, posterior reversible encephalopathy syndrome (PRES), or cerebral edema

205) History of concomitant genetic syndrome associated with bone marrow failure such as Fanconi anemia, Kostmann syndrome, Shwachman-Diamond syndrome

206) History of myocardial infarction, cardiac angioplasty or stenting, unstable angina, or other clinically significant cardiac disease within 12 months of enrollment

207) History of symptomatic deep vein thrombosis or pulmonary embolism within 6 months of enrollment.

208) Primary immunodeficiency

209) Known infection with HIV, hepatitis B or hepatitis C virus. A history of hepatitis B or hepatitis C is permitted if the viral load is undetectable per quantitative PCR and/or nucleic acid testing.

210) Presence of fungal, bacterial, viral, or other infection that is uncontrolled or requiring antimicrobials for management. Simple UTI and uncomplicated bacterial pharyngitis are permitted if responding to active treatment and after consultation with the Kite Medical Monitor

211) Prior medication:
- Salvage systemic therapy (including chemotherapy, TKIs for Ph+ ALL, and blinatumomab) within 1 week or 5 half-lives (whichever is shorter) prior to enrollment
- Prior CD19 directed therapy other than blinatumomab
- History of CTCAE grade 4 neurologic event or grade 4 CRS (Lee et al, 2014) with prior CD19-directed therapy
- Treatment with alemtuzumab within 6 months prior to enrollment, clofarabine or cladribine within 3 months prior to enrollment, or PEG-asparaginase within 3 weeks prior to enrollment
- Donor lymphocyte infusion (DLI) within 28 days prior to enrollment
- Any drug used for GVHD within 4 weeks prior to enrollment (eg, calcineurin inhibitors, methotrexate, mycophenolyate, rapamycin, thalidomide), or immunosuppressive antibody used within 4 weeks prior to enrollment (eg, anti-CD20,

anti-tumor necrosis factor, anti-interleukin 6 or anti-interleukin 6 receptor)
- At least 3 half-lives must have elapsed from any prior systemic inhibitory/stimulatory immune checkpoint molecule therapy prior to enrollment (eg, ipilimumab, nivolumab, pembrolizumab, atezolizumab, OX40 agonists, 4-1BB agonists etc)
- Corticosteroid therapy at a pharmacologic dose (> 5 mg/day of prednisone or equivalent doses of other corticosteroids) and other immunosuppressive drugs must be avoided for 7 days prior to enrollment

212) Presence of any indwelling line or drain (eg, percutaneous nephrostomy tube, indwelling Foley catheter, biliary drain, or pleural/peritoneal/pericardial catheter). Ommaya reservoirs and dedicated central venous access catheters such as a Port-a-Cath or Hickman catheter are permitted

213) Acute GVHD grade II-IV by Glucksberg criteria or severity B-D by IBMTR index; acute or chronic GVHD requiring systemic treatment within 4 weeks prior to enrollment

214) Live vaccine ≤ 4 weeks prior to enrollment

215) Women of child-bearing potential who are pregnant or breastfeeding because of the potentially dangerous effects of the preparative chemotherapy on the fetus or infant. Females who have undergone surgical sterilization or who have been postmenopausal for at least 2 years are not considered to be of childbearing potential

216) Subjects of both genders of child-bearing potential who are not willing to practice birth control from the time of consent through 6 months after the completion of KTE-X19

217) In the investigators judgment, the subject is unlikely to complete all protocol-required study visits or procedures, including follow-up visits, or comply with the study requirements for participation

218) History of autoimmune disease (eg, Crohns, rheumatoid arthritis, systemic lupus) resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years