

## TRANSFORM JCAR017-BCM-003

### 4.2. Inclusion Criteria

Subjects must satisfy the following criteria to be enrolled in the study:

1. Subject is  $\geq 18$  years and  $\leq 75$  years of age at the time of signing the informed consent form (ICF).
2. Subject must understand and voluntarily sign an ICF prior to any study-related assessments/procedures being conducted.
3. Subject is willing and able to adhere to the study visit schedule and other protocol requirements.
4. ECOG performance status  $\leq 1$ .
5. Histologically proven diffuse large B-cell lymphoma (DLBCL) NOS (de novo or transformed indolent NHL), high grade B-cell lymphoma with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple-hit lymphoma [DHL/THL]), primary mediastinal (thymic) large B-cell lymphoma (PMBCL), T cell/histiocyte-rich large B-cell lymphoma (THRBCL) or follicular lymphoma grade 3B (FL3B). Enough tumor material must be available for confirmation by central pathology. If archival sample is before most recent relapse or no or insufficient archival sample is available, a new tumor biopsy is mandated to confirm diagnosis. Note: Subjects with secondary CNS involvement are eligible. Subject selection must consider clinical risk factors for severe adverse events (AEs) and alternative treatment options. Subjects should only be enrolled if the Investigator assesses that the potential benefit outweighs the risk for the subject.
6. Refractory (SD, PD, PR or CR with relapse before 3 months) or relapsed (CR with relapse on or after 3 months) within 12 months from CD20 antibody and anthracycline containing first-line therapy. Note: The time of relapse is calculated from the date of the first disease assessment confirming a CR obtained with first-line treatment for disease under study, to the date of first assessment demonstrating a relapse.
7. [18F] fluorodeoxyglucose (FDG) positron emission tomography (PET) positive lesion per Lugano criteria at screening.
8. Adequate organ function, defined as:
  - Adequate bone marrow function defined as: absolute neutrophil count (ANC)  $\geq 1.0 \times 10^9$  cells/L and platelets  $\geq 50 \times 10^9$  cells/L in absence of bone marrow involvement
  - Serum creatinine  $< 1.5 \times$  upper limit of normal (ULN) or creatinine clearance  $> 45$  mL/min (estimated by Cockcroft Gault; see Appendix D for calculation)

- Alanine aminotransferase (ALT)  $\leq 5 \times$  ULN and total bilirubin  $< 2.0$  mg/dL (or  $< 3.0$  mg/dL for subjects with Gilbert's syndrome or lymphomatous infiltration of the liver)
  - Adequate pulmonary function, defined as  $\leq$  Grade 1 dyspnea according to Common Terminology Criteria for Adverse Events (CTCAE) and oxygen saturation (SaO<sub>2</sub>)  $\geq 92\%$  on room air and FEV<sub>1</sub>  $\geq 50\%$
  - Adequate cardiac function, defined as left ventricular ejection fraction (LVEF)  $\geq 40\%$  as assessed by echocardiogram (ECHO) or multi-gated acquisition scan (MUGA) performed within 4 weeks of randomization
9. Adequate vascular access for leukapheresis.

### 4.3. Exclusion Criteria

The presence of any of the following will exclude a subject from enrollment:

1. Subject has any significant medical condition, laboratory abnormality, or psychiatric illness that would prevent the subject from participating in the study based on investigator's judgment.
2. Subject has any condition including the presence of laboratory abnormalities, which places the subject at unacceptable risk if he/she were to participate in the study based on investigator's judgment.
3. Subject has any condition that confounds the ability to interpret data from the study based on investigator's judgment.
4. Subjects not eligible for hematopoietic stem cell transplantation (HSCT).
5. Subjects planned to undergo allogeneic stem cell transplantation.
6. Subjects with primary cutaneous large B-cell lymphoma, EBV (Epstein-Barr virus) positive DLBCL of the elderly and Burkitt lymphoma.
7. Subjects with prior history of malignancies, other than aggressive R/R NHL, unless the subject has been free of the disease for  $\geq 2$  years with the exception of the following noninvasive malignancies:
  - Basal cell carcinoma of the skin
  - Squamous cell carcinoma of the skin
  - Carcinoma in situ of the cervix
  - Carcinoma in situ of the breast
  - Incidental histologic finding of prostate cancer (T1a or T1b using the TNM [tumor, nodes, metastasis] clinical staging system) or prostate cancer that is curative.
  - Other completely resected stage 1 solid tumor with low risk for recurrence
8. Treatment with any prior gene therapy product.
9. Subjects who have received previous CD19-targeted therapy.
10. History of or active hepatitis B, hepatitis C, or human immunodeficiency virus (HIV) infection.

11. Subjects with uncontrolled systemic fungal, bacterial, viral or other infection (including tuberculosis) despite appropriate antibiotics or other treatment.

12. Active autoimmune disease requiring immunosuppressive therapy.

13. History of any one of the following cardiovascular conditions within the past 6 months prior to signing the ICF: Class III or IV heart failure as defined by the New York Heart Association (NYHA), cardiac angioplasty or stenting, myocardial infarction, unstable angina, or other clinically significant cardiac disease.

14. History or presence of clinically relevant central nervous system (CNS) pathology such as epilepsy, seizure, aphasia, stroke, cerebral edema, severe brain injuries, dementia, Parkinson's disease, cerebellar disease, organic brain syndrome, or psychosis.

15. Tumor invasion of venous or arterial vessels.

16. Deep venous thrombosis (DVT)/ Pulmonary embolism (PE) within 3 months prior to leukapheresis, and/or DVT/ PE that requires ongoing therapeutic levels of anticoagulation.

17. Pregnant or nursing (lactating) women.

18. Use of the following (see Section 8.2 for full details):

- Therapeutic doses of corticosteroids (defined as > 20 mg/day prednisone or equivalent) within 7 days prior to unstimulated leukapheresis. Physiologic replacement, topical, and inhaled steroids are permitted.

- Cytotoxic chemotherapeutic agents that are not considered lymphotoxic (see below) and intrathecal (IT) chemotherapy must be stopped  $\geq 7$  days prior to unstimulated leukapheresis.

- Lymphotoxic chemotherapeutic agents (eg, cyclophosphamide, ifosfamide, bendamustine) 2 weeks prior to unstimulated leukapheresis.

- Experimental agents within 4 weeks prior to signing the ICF unless no response or progressive disease (PD) is documented on the experimental therapy and at least 3 half-lives have elapsed prior to unstimulated leukapheresis.

- Immunosuppressive therapies within 4 weeks prior to unstimulated leukapheresis (eg, calcineurin inhibitors, methotrexate or other chemotherapeutics, mycophenolate, rapamycin, thalidomide, immunosuppressive antibodies such as anti-tumor necrosis factor [TNF], anti-IL-6, or anti-IL-6R).

- Radiation within 4 weeks prior to signing the ICF. Subjects must have progressive disease in irradiated lesions or have additional non-irradiated, PET-positive lesions to be eligible. Radiation to a single lesion, if additional non-irradiated, measurable PET-positive lesions are present, is allowed up to 2 weeks prior to unstimulated leukapheresis.

- Systemic immunostimulatory agents (including but not limited to interferon and IL-2) within 6 weeks or 5 half-lives of the drug, whichever is shorter, prior to JCAR017 infusion.