body size metrics and cellular kinetics/pharmacokinetics, safety, or effectiveness. In addition, cellular kinetic modeling from CAR-Ts such as tisagenlecleucel and lisocabtagene maraleucel have demonstrated that body weight does not have a significant relationship with CAR-T cell expansion/contraction (Awasthi 2020; Ogasawara 2021; He 2022).

4.4. End of Study Definition

Data Cut-off, Participant Completion, End of Study Definition

The Sponsor will communicate to the study sites a clinical data cutoff for CSR analysis, which may occur before the end of study. Participants who are in the follow-up phase after the data cutoff will be encouraged to take part in an extension of the follow-up period.

A participant will be considered to have completed the study unless their participation ends prior to the clinical data cutoff for any reason other than death.

The end of the study is defined as 2 years after the last participant has been administered JNJ-90014496, or after all participants have died or discontinued the study, whichever is earlier. The final data from the study site will be sent to the Sponsor (or designee) after completion of the final participant assessment at that study site, in the time frame specified in the Clinical Trial Agreement.

5. STUDY POPULATION

Screening for eligible participants will be performed within 28 days before apheresis. Refer to Section 5.4, Screen Failures for conditions under which the repeat of any screening procedures are allowed.

The inclusion and exclusion criteria for enrolling participants in this study are described below. If there is a question about these criteria, the investigator must consult with the appropriate Sponsor representative and resolve any issues before enrolling a participant in the study. Waivers are not allowed. For a discussion of the statistical considerations of participant selection, refer to Section 9.5, Sample Size Determination.

5.1. Inclusion Criteria

Each potential participant must satisfy all of the following criteria to be enrolled in the study:

Age

1. Be ≥18 years of age (or the legal age of majority in the jurisdiction in which the study is taking place, whichever is greater) at the time of informed consent.

Disease Characteristics

2. Criterion modified per Amendment 3.

   2.1 Diagnosis of mature aggressive large B cell non-Hodgkin lymphoma and follicular lymphoma, as defined by the 2016 WHO classification of lymphoid neoplasms (Swerdlow 2016).

3. Criterion modified per Amendment 3.

   3.1 Histologically confirmed CD19 and/or CD20 positive disease by flow cytometry or immunohistochemistry test result and corresponding pathology report from:

   - an archived biopsy collected from the last relapse, or
   - most recent biopsy collected (if participant has never achieved a complete response), or
   - fresh biopsy collected at Screening

4. Criterion modified per Amendment 3.

   4.1. All participants must have relapsed or refractory disease with the following indications for each histologic subtype:

   - **Mature aggressive large B cell NHL and Follicular Lymphoma Grade 3b**: Participants must have ≥2 lines of systemic therapy or ≥1 line of systemic therapy in case of participants ineligible for high-dose chemotherapy and autologous HSCT. Participants also must have had exposure to an anthracycline and an anti-CD20 targeted agent.

   - **Follicular lymphoma Grade 1-3a and Marginal Zone Lymphoma**: Participants must have ≥2 prior lines of anti-neoplastic systemic therapy. Participants also must have prior exposure to an anti-CD20 monoclonal antibody.

5. Measurable disease per the Lugano 2014 Classification (Cheson 2014) (Appendix 10.13), having at least one lesion defined as:

   - Nodal lesion with longest diameter ≥ 1.5 cm, or
   - Extranodal lesion with longest diameter ≥ 1.0 cm by CT, or
   - Focal FDG uptake in nodal or extranodal sites consistent with lymphoma by PET-CT

Performance Status

6. Have an ECOG performance status of 0 to 1 (Appendix 10.14).

Renal Function

7. Defined as:

- A serum creatinine of ≤ 1.5 x ULN or
- Creatinine clearance (as estimated by Cockcroft Gault) ≥ 50 mL/min

Hepatic Function

8. Defined as:

- AST ≤3 x ULN
- ALT ≤3 x ULN
- Bilirubin ≤2.0 x ULN (except in participants with Gilbert's syndrome; participants with Gilbert's syndrome may be included if their total bilirubin is ≤ 3.0 × ULN and direct bilirubin ≤ 1.5 × ULN).

Cardiovascular Dysfunction

9. No requirement for supplemental oxygen to maintain adequate oxygenation

10. Hemodynamically stable and cardiac LVEF ≥ 45%

Hematologic Values

11. Participants should have:

- Hemoglobin ≥ 8.0 g/dL without transfusion within 7 days of laboratory test
- Neutrophils ≥ 1.0 x 10^3/μL
- Absolute lymphocyte count ≥ 300/μl
- Platelets ≥50 x 10^3/μL without transfusion within 7 days of laboratory test

Sex and Contraceptive/Barrier Requirements

12. Criterion modified per Amendment 3/EEA-1.

12.1 A female participant of childbearing potential must have a negative highly sensitive serum or urine pregnancy test (β-human chorionic gonadotropin) at screening and commit to avoid breastfeeding for a period of 1 year following JNJ-90014496 CAR-T therapy. See Appendix 10.11 for the definition of female participants who are not of reproductive potential.

13. A female participant of childbearing potential must commit either to abstaining continuously from heterosexual intercourse or agree to use 2 methods of reliable birth control simultaneously. One of them a highly effective method of contraception (failure rate of <1% per year when used consistently and correctly; see examples below) and one other effective method (ie, male latex or synthetic condom, diaphragm, or cervical cap) and agree to remain on both methods from the time of signing the informed consent form until at least 1 year after receiving JNJ-90014496 (Appendix 10.11). Examples of highly effective contraceptives include:

    - user-independent methods: 1) implantable progestogen-only hormone contraception associated with inhibition of ovulation; 2) intrauterine device; intrauterine hormone-releasing system; 3) vasectomized partner;
    - user-dependent methods: 1) combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation: oral or intravaginal or transdermal; 2) progestogen-only hormone contraception associated with inhibition of ovulation (oral or injectable).

    Reliable contraception is indicated even where there has been a history of infertility, unless it is due to hysterectomy. Female participants of childbearing potential should be referred to a qualified provider of contraceptive methods, if needed.

    Note: Hormonal contraception may be susceptible to interaction with the study treatment, which may reduce the efficacy of the contraceptive method.

14. Male and female participants must agree not to donate gametes (ie, eggs or sperm) or freeze for future use for the purposes of assisted reproduction during the study and for a period 1 year following JNJ-90014496 CAR-T therapy. Participants should consider preservation of gametes prior to study treatment as anti-cancer treatments may impair fertility.

15. A male participant must commit either to abstaining continuously from heterosexual intercourse or if sexually active with a WOCBP or a pregnant woman, must agree to use a barrier method of contraception (eg, latex or synthetic condom with spermicidal foam/gel/film/cream/suppository), from the time of signing the ICF until at least 1 year after receiving JNJ-90014496 infusion, even if they have undergone a successful vasectomy.

Informed Consent

16. Must sign an ICF indicating that the participant understands the purpose of, and procedures required for, the study and is willing to participate in the study.

Other

17. Be willing and able to adhere to the lifestyle restrictions specified in this protocol.

5.2. Exclusion Criteria

Any potential participant who meets any of the following criteria will be excluded from participating in the study:

Medical Conditions

1. Medical history of deep vein thrombosis or pulmonary embolism within 6 months of infusion (line associated DVT is allowed).

2. Criterion modified per Amendment 3/EEA-1.

   2.1 Any known allergies or contraindications to fludarabine or cyclophosphamide (refer to the approved local label).

3. Known allergies, hypersensitivity, or intolerance to excipients of JNJ-90014496 cell product (refer to the IB).

4. History of stroke, unstable angina, myocardial infarction, congestive heart failure (NYHA Class III or IV; Appendix 10.17), severe cardiomyopathy or ventricular arrhythmia requiring medication or mechanical control within 6 months of screening

5. History of a seizure disorder, cerebrovascular ischemia/hemorrhage, cerebellar disease, dementia, or neurodegenerative disorder.

6. Known history or prior diagnosis of optic neuritis or other immunologic or inflammatory disease affecting the central nervous system

7. Active autoimmune disease (without any immunosuppressive medications) within 2 years prior to signing informed consent:

   - Participants with well-controlled sarcoidosis, and who are not on immunosuppressants, may be allowed to enroll after discussion with the Sponsor
   - Participants with vitiligo or resolved childhood asthma/atopy are an exception to this exclusion criterion.
   - Additionally, participants with the following conditions would not be excluded from the study: require intermittent use of bronchodilators or local steroid injections, have hypothyroidism stable on hormone replacement, or have a history of transient autoimmune manifestations of an acute infectious disease that resolved upon treatment of the infectious agent (eg, acute Lyme arthritis).

8. Criterion modified per Amendment 3.

   8.1 Active CNS involvement by malignancy. Lymphoma with CNS involvement may be allowed in separate cohorts if approved by SET.

9. Current active liver or biliary disease (except for Gilbert's syndrome or asymptomatic gallstones, liver metastases or otherwise stable chronic liver disease per Investigator assessment).

10. Previous or concurrent malignancy with the following exceptions:
    - Adequately treated basal cell or squamous cell carcinoma (adequate wound healing is required prior to apheresis)
    - In situ carcinoma of the cervix or breast, treated curatively and without evidence of recurrence for at least 3 years prior to apheresis
    - A primary malignancy which has been completely resected and in complete remission for ≥ 5 years
11. Uncontrolled active infection.
12. Following chronic viral infections:
    - HIV positive.
    - Active hepatitis B infection. Hepatitis B infection as defined according to Appendix 10.16. In the event the infection status is unclear, quantitative levels are necessary to determine the infection status (Hwang 2015).
    - Active hepatitis C infection. Hepatitis C infection defined as anti-HCV antibody positive or detectable HCV-RNA or known to have a history of hepatitis C. NOTE: Participants with a positive hepatitis C antibody due to prior treated disease can be enrolled, but only with a confirmatory HCV RNA test that is undetectable at screening. For participants with known history of HCV infection, confirmation of sustained virologic response (defined as ≥24 weeks after completion of antiviral therapy) is required for study eligibility.
13. Major surgery within 2 weeks prior to apheresis, or has surgery planned during the study or within 2 weeks after study treatment administration. (Note: participants with planned surgical procedures to be conducted under local anesthesia may participate.)

Disease Characteristics

14. Criterion modified per Amendment 3.

    14.1 HHV8-positive DLBCL
15. Burkitt and Burkitt-like lymphoma

Prior/Concomitant Therapy or Clinical Study Experience

16. Any prior solid organ or allogeneic stem cell transplantation
17. Autologous stem cell transplant within 12 weeks of CAR T cell infusion

18. Criterion modified per Amendment 3.

    18.1 Received any of the following therapies:

    Corticosteroids: Therapeutic doses are not allowed < 72 hours prior to apheresis. The following physiological replacement doses of steroids is permitted: prednisone ≤ 5 mg/day or equivalent.

    Immunosuppressive therapy: Any systemic immunosuppressive medication is not allowed ≤ 2 weeks prior to apheresis.

    Chemotherapy: Any chemotherapy is not allowed ≤2 weeks or 5 half-lives, whichever is shorter, prior to apheresis

    Antibody use ≤2 weeks prior to apheresis or 5 half-lives of the respective antibody, whichever is shorter

    Investigational medicinal products: Any investigational therapies are not allowed ≤28 days or 5 half-lives, whichever is shorter, prior to apheresis

    Prior systemic radiation therapy ≤2 weeks of apheresis

    Prior CAR-T therapy: ≤ 12 weeks prior to apheresis

19. Received or plans to receive any live vaccine within 4 weeks prior to apheresis.

Other Exclusions

20. Any condition for which, in the opinion of the investigator, participation would not be in the best interest of the participant (eg, compromise the well-being) or that could prevent, limit, or confound the protocol-specified assessments.

5.3. Lifestyle Considerations

Potential participants must be willing and able to adhere to the following lifestyle restrictions during the study to be eligible for participation:

1. Carry a “wallet study card” with pertinent information about the study for the duration of study participation.

2. Agree to self-monitor for signs and symptoms of CRS (such as fever) and neurotoxicity and to seek immediate medical intervention.

3. Any blood donation is not allowed at any time during and after the study following the rules of local blood donation organizations.