Inclusion Criteria

Individuals who meet all of the following criteria at screening are eligible for enrollment as study participants:

1. Participant or legally authorized representative must be able to understand and provide informed consent
2. Adult 18-70 years of age
3. Diagnosed with RA by fulfilling the ACR/EULAR 2010 Classification Criteria for RA ≥ 6 months prior to screening
4. Documented positive test for rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide antibody (ACPA)
5. SDAI ≥ 17
6. At least 4 tender and 4 swollen joints by a 44 joint count (Appendix 5)
7. TNFi therapy:
    a. Current treatment with etanercept 50 mg SC weekly or adalimumab 40 mg SC every other week for at least 12 weeks
    b. Willing to continue or discontinue treatment with their current TNFi at the same dose depending upon study arm assignment
8. If treated with leflunomide, sulfasalazine, or hydroxychloroquine, must be taking a stable dose for at least 12 weeks
9. If treated with methotrexate, must be taking a stable dose for at least 12 weeks. The following exceptions are permitted within the 12 weeks prior to screening:
    a. Holding methotrexate after SARS-CoV-2 vaccination as per American College of Rheumatology guidance
    b. Holding methotrexate for 1 or 2 weeks after influenza vaccination
10. COVID-19 vaccination:
    a. Completion of a primary COVID-19 vaccination series based on current CDC recommendations for individuals who are moderately to severely immunocompromised. The primary vaccination series should include at least 2 doses of an mRNA vaccine, one dose of an adenovirus-based vaccine, or the primary series for any other authorized or approved vaccine.
    b. Receipt of at least one booster dose of a COVID-19 vaccine after the primary vaccine series if recommended by the CDC for individuals who are moderately to severely immunocompromised
    c. The last COVID-19 vaccine dose must have been administered at least 14 days prior the initiation of the study drug (Visit 0)
11. All participants who engage in sexual activity that could lead to pregnancy must agree to use abstinence or an FDA-approved contraception for the duration of the study to prevent pregnancy (Section 7.5)

Individuals who meet any of these criteria at screening are not eligible for enrollment as study participants:

1. Inability or unwillingness to give written informed consent or comply with the study protocol
2. Prior or ongoing systemic inflammatory or autoimmune disease (other than RA and secondary Sjögren's syndrome) requiring or potentially requiring other systemic immunomodulatory therapy during the 40-week study period
3. Use of glucocorticoid and/or disease-modifying therapies as specified below:
    a. Prior treatment with any B cell depleting therapy (e.g., rituximab)
    b. History of treatment with more than two TNFi, including ongoing treatment with etanercept or adalimumab
    c. Treatment with other biologic therapy (i.e., not targeting TNF-α), including abatacept, tocilizumab, or sarilumab within the previous 12 weeks
    d. Treatment with a JAK inhibitor within the previous 12 weeks
    e. Concurrent use of methotrexate and leflunomide
    f. Prednisone > 10 mg a day or equivalent glucocorticoid use within the previous 4 weeks
    g. Intramuscular, intra-articular, or intravenous glucocorticoids within the previous 4 weeks
    h. Other immunomodulatory medications within the previous 12 weeks except for methotrexate, leflunomide, sulfasalazine, or hydroxychloroquine
4. Lack of any subjective or objective clinical response (i.e., complete non-responder) to current TNFi use, in the opinion of the study investigator based on information provided by the patient and referring rheumatologist
5. Use of an investigational agent including VIB4920 in the past 30 days or 5 half-lives, whichever is longer
6. History of a severe allergy, hypersensitivity reaction, or infusion reaction to any component of the VIB4920 formulation
7. History of Felty's syndrome
8. History of interstitial lung disease with FVC < 70% predicted, DLCO < 70% predicted, or requiring supplemental oxygen
9. Hypercoagulable state as specified below:
    a. Previous deep venous or arterial thrombosis or thromboembolism, or pulmonary embolism
    b. Known hypercoagulable state (e.g., inherited thrombin III deficiency, protein S deficiency, protein C deficiency, antiphospholipid antibody syndrome, MTHFR mutation)
    c. Risk factors for deep venous or arterial thromboembolism (e.g., immobilization or major surgery within 12 weeks prior to enrollment)
    d. Anti-phospholipid antibodies:
        1) Positive anti-cardiolipin IgG, IgM, or IgA antibodies at a moderate titer or higher (≥ 40 U)
        2) Positive anti-beta-2-glycoprotein I IgG, IgM, or IgA antibodies at a moderate titer or higher (≥ 40 U)
        3) Positive lupus anticoagulant test

10. Infection:
    a. Evidence of current or prior infection with hepatitis B, as indicated by a positive test for the hepatitis B surface antigen (HBsAg) or a positive test for the hepatitis B core antibody (HBcAb)
    b. Positive HCV serology unless treated with an anti-viral regimen resulting in a sustained virologic response (undetectable viral load 24 weeks after cessation of therapy)
    c. Evidence of HIV infection
    d. Evidence of active tuberculosis, untreated or incompletely treated latent tuberculosis, or recent close contact with a person who has active tuberculosis
    e. Positive QuantiFERON-TB Gold, QuantiFERON-TB Gold Plus, or T-SPOT-TB test without history of previous treatment for active or latent TB
    f. Indeterminate QuantiFERON-TB Gold, QuantiFERON-TB Gold Plus, or T-SPOT. TB test which remains indeterminate on repeat testing, and any of the following additional required screening which indicates an increased risk of TB infection:
        1) History of tuberculosis exposure
        2) History of travel to an area where tuberculosis is endemic
        3) Findings on chest radiograph suggestive of prior exposure to tuberculosis (e.g., granulomas or apical scarring) obtained at screening or within the past 3 months
        4) Positive purified protein derivative (PPD) skin test for tuberculosis obtained in the past 3 months, either obtained at screening or within the past 3 months
        5) Prior history of a positive QuantiFERON-TB Gold, QuantiFERON-TB Gold Plus, T-SPOT.TB, or purified protein derivative (PPD) test without history of previous treatment for latent TB
    g. Positive test for acute COVID-19 infection (e.g., PCR test for SARS-CoV-2 or alternative viral test according to CDC guidance)
    h. Symptoms of presumed or documented COVID-19 infection in the past 30 days
    i. More than one episode of herpes zoster in the past 12 months
    j. An opportunistic infection in the past 12 months
    k. Acute or chronic infection, including current use of suppressive systemic anti-microbial therapy for chronic or recurrent bacterial or fungal infection, hospitalization for treatment of infection in the past 60 days, or parenteral anti-microbial (including anti-bacterial, anti-viral, or anti-fungal agents) use in the past 60 days for infection
    l. History of bronchiectasis with recurrent pulmonary infections
11. History of a primary immunodeficiency disorder
12. Vaccination with a live vaccine within the past 30 days
13. Women who are pregnant or breast-feeding
14. WBC count $< 3.0 \times 10^3/\mu l$
15. Absolute neutrophil count $< 1.5 \times 10^3/\mu l$
16. Hemoglobin < 9 g/dL
17. Platelet count $< 100 \times 10^3/\mu l$

18. Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥ 2x the upper limit of normal (ULN)
19. History of malignant neoplasm within the last 5 years, except for basal cell or squamous cell carcinoma of the skin treated with local resection only or carcinoma in situ of the uterine cervix treated locally
20. Current, diagnosed mental illness or current, diagnosed or self-reported drug or alcohol abuse that, in the opinion of the investigator, would interfere with the participant's ability to comply with study requirements
21. Any new or uncontrolled condition occurring within the past 12 weeks which, in the judgment of the investigator, could interfere with participation in the trial (e.g., diabetes mellitus with HbA1c ≥ 9.0%, myocardial infarction, or stroke)
22. Past or current medical problems or findings from physical examination or laboratory testing that are not listed above, which, in the opinion of the investigator, may pose additional risks from participation in the study, may interfere with the participant's ability to comply with study requirements, or that may impact the quality or interpretation of the data obtained from the study
23. Inability to comply with study and follow-up procedures