A phase 1b/2, open-label, multinational, interventional trial to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics/biomarkers, immunogenicity, and preliminary efficacy of epcoritamab in combination with other standard of care (SOC) agents in subjects with B-cell Non-Hodgkin Lymphoma (B-NHL).

GCT3013-02 - Subject Eligibility

Detailed Description:

All participants in the trial will receive epcoritamab, as monotherapy or in combination. The following regimens will be investigated:

- Arm 1: epcoritamab + rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP) in subjects with previously untreated diffuse large B-cell lymphoma (DLBCL)
- Arm 2: epcoritamab + rituximab and lenalidomide (R2) in subjects with relapsed/refractory (R/R) follicular lymphoma (FL)
- Arm 3: epcoritamab + rituximab and bendamustine (BR) in subjects with previously untreated FL
- Arm 4: epcoritamab + rituximab, cytarabine, dexamethasone, and oxaliplatin/ carboplatin (R-DHAX/C) in subjects with R/R DLBCL eligible for autologous stem cell transplant (ASCT)
- Arm 5: epcoritamab + gemcitabine and oxaliplatin (GemOx) in subjects with R/R DLBCL ineligible for ASCT due to age, performance status (PS), or comorbidity
- Arm 6: epcoritamab + R2 in subjects with previously untreated FL
- Arm 7: epcoritamab maintenance in subjects with FL who achieve a complete response (CR) or a partial response (PR) with SOC treatment
- Arm 8: epcoritamab + reduced dose of R-CHOP (R mini-CHOP) in subjects with previously untreated DLBCL who are ineligible to receive full-dose anthracycline

The trial consists of two parts: Part 1 ('Dose Escalation') and Part 2 ('Dose Expansion'). The primary objective of Part 1 is safety, and it includes Arm 1-5. Part 2 includes all 8 arms (Arm 1-8) and the primary goal of all arms, except Arm 7, is preliminary efficacy. For Arm 7, the primary goal is safety. Patients in Arm 1-5 can only participate in either Part 1 or Part 2. Dose Limiting Toxicities (DLTs) will be assessed in Part 1 and for a selected number of patients in Arm 8 during a 28-day period ('safety-run phase'). The arms are conducted in parallel.

Arms and Interventions

Arm	Intervention/treatment
Experimental: Arm 1 - Epcoritamab + R-CHOP **In subjects with previously untreated DLBCL**	Drug: rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone 21-day cycles Other Name: R-CHOP Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 2 - Epcoritamab + R2 **In subjects with R/R FL**	Drug: rituximab and lenalidomide 28-day cycles Other Name: R2

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Arm	Intervention/treatment
	Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 3 - Epcoritamab + BR **In subjects with previously untreated FL**	Drug: rituximab and bendamustine 28-day cycles Other Name: BR Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 4 - Epcoritamab + R-DHAX/C **In subjects with R/R DLBCL Eligible for ASCT**	Drug: rituximab, cytarabine, dexamethasone, and oxaliplatin/carboplatin 21-day cycles Other Name: R-DHAX/C Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 5 - Epcoritamab + GemOx **In subjects with R/R DLBCL Ineligible ASCT**	Drug: gemcitabine and oxaliplatin28-day cycles Other Name: GemOx Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 6 - Epcoritamab + R2 **In subjects with previously untreated FL**	Drug: rituximab and lenalidomide 28-day cycles Other Name: R2 Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 7 - Epcoritamab maintenance **In subjects with FL who achieved a CR or PR after receiving SOC treatment in 1L or 2L**	Biological: Epcoritamab Maintenance 28-day cycle for Cycle 1 and then 56-day cycle from Cycle 2 through 13 Other Name: GEN3013; DuoBody®-CD3xCD20
Experimental: Arm 8 - Epcoritamab + R mini-CHOP **In subjects with previously untreated DLBCL who are ineligible to receive full-dose anthracycline**	Biological: Epcoritamab Epcoritamab will be administered in combination with the respective standard of care chemotherapy. Other Name: GEN3013; DuoBody®-CD3xCD20 Drug: rituximab, cyclophosphamide, reduced dose of doxorubicin, vincristine, and prednisone 21-day cycle Other Name: R mini-CHOP

Criteria:

Key Inclusion Criteria

1. Subject must sign an Informed Consent Form (ICF)
2. At least 18 years of age
3. Measurable disease defined as ≥1 measurable nodal lesion (long axis >1.5 cm and short axis >1.0 cm) or ≥1 measurable extra-nodal lesion (long axis >1.0 cm) on computed tomography (CT) or magnetic resonance imaging (MRI)
4. Eastern Cooperative Oncology Group (ECOG) PS score of 0, 1 or 2
5. Acceptable organ function at screening
6. CD20-positive non-Hodgkin lymphoma (NHL) at most recent representative tumor biopsy
7. If of childbearing potential subject must practicing a highly effective method of birth control
8. A man who is sexually active with a woman of childbearing potential must agree to use a barrier method of birth control

Arm 1:

- Newly Diagnosed Documented diffuse large B-cell lymphoma (DLBCL)
- DLBCL, NOS
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B

Arm 2: R/R FL

Arm 3: Newly diagnosed, previously untreated FL grade 1-3A

Arm 4:

- Documented DLBCL and eligible for HDT-ASCT
- DLBCL, NOS
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B

Arm 5:

- Relapsed or refractory documented DLBCL and ineligible for HDT-ASCT
- DLBCL, NOS
- "double-hit" or "triple-hit" DLBCL

- FL Grade 3B

Arm 6: Newly diagnosed, previously untreated FL grade 1-3A

Arm 7:

- FL Grade 1-3A
- If PR or CR per Lugano criteria following first-line or second-line treatment with SOC regimen, and last dose of SOC within 6 months prior to enrollment.

Arm 8:

- DLBCL, NOS
- T-cell/histiocyte rich DLBCL
- "double-hit" or "triple-hit" DLBCL
- FL Grade 3B

Key Exclusion Criteria

1. Chemotherapy, radiation therapy, or major surgery within 4 weeks prior to the first dose of epcoritamab
2. Any prior treatment with a bispecific antibody targeting CD3 and CD20.
3. Treatment with CAR-T therapy within 30 days prior to first dose of epcoritamab
4. Clinically significant cardiovascular disease
5. Evidence of significant, uncontrolled concomitant diseases that could affect compliance with the protocol or interpretation of results
6. CNS lymphoma or known CNS involvement by lymphoma at screening as confirmed by MRI/CT scan of the brain and, if clinically indicated, by lumbar puncture
7. Active positive tests for hepatitis B virus or hepatitis C virus indicating acute or chronic infection
8. Known history of seropositivity of human immunodeficiency virus (HIV)
9. Active tuberculosis or history of completed treatment for active tuberculosis within the past 12 months
10. Neuropathy > grade 1
11. Receiving immunostimulatory agent
12. Prior allogeneic HSCT
13. Current seizure disorder requiring anti-epileptic therapy

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NOTE: Other protocol defined Inclusion/Exclusion criteria may apply.