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Trial in Progress: Open-Label Phase 1 Study to Evaluate Safety of SGN-35C in Adults With Select Relapsed/ Refractory Lymphomas (SGN35C-001)

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Objective

To describe a phase 1 study that is evaluating the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of SGN-35C in patients with R/R CD30-expressing lymphoid malignancies.

Conclusions

Enrollment for dose escalation is ongoing in the US, EU, and UK.

References:

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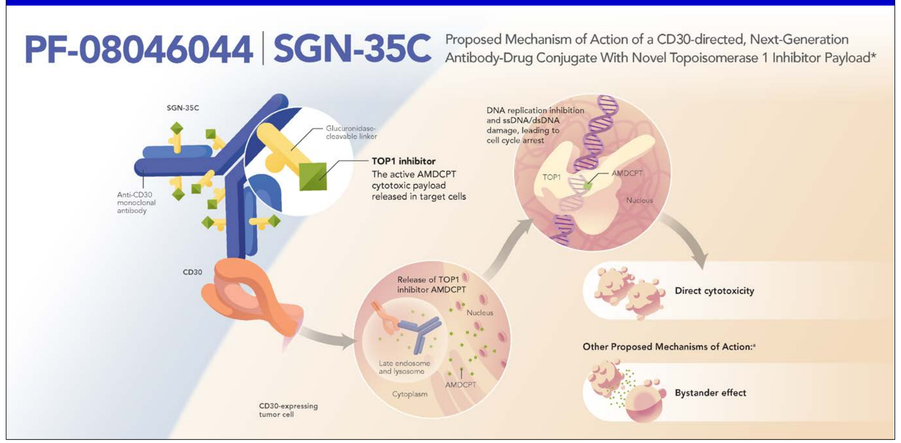
Background

- Patients with relapsed/refractory (R/R) lymphomas have limited treatment options and poor mortality rates versus patients with non-R/R disease.[1-3]
- CD30 is an established therapeutic target in R/R lymphoid malignancies.[4]
  - Brentuximab vedotin (BV) is a CD30-directed antibody-drug conjugate (ADC) with demonstrated clinical benefit in classical Hodgkin lymphoma and peripheral T-cell lymphoma.[5]
- SGN-35C is an investigational ADC comprised of the same CD30-directed mAb as BV, conjugated to a novel topoisomerase I inhibitor via a protease-cleavable glucuronide linker.[6] (**Figure 1**).
  - ADCs utilizing topoisomerase 1 inhibitors are anticipated to have a distinct tolerability profile compared to vedotin ADCs.[6]
  - Preclinically, SGN-35C elicits efficient binding, internalization, and cytotoxicity in CD30+ tumor cells, and induces antitumor activity via direct cytotoxicity and bystander effect including in BV-resistant lymphoma models, providing rationale to clinically develop SGN-35C.[6]
- SGN-35C is currently being investigated in the phase 1 study SGN35C-001 (NCT06254495).

Figure 1: Proposed mechanism of action for SGN-35C



AMDCPT = 7-aminomenthyl-10, 11-methendioxycamptothecin; CD30 = cluster of differentiation 30; dsDNA = double-stranded DNA; ssDNA = single-stranded DNA; OP1 = topoisomerase 1

[a]Additional mechanisms of action and their potential to complement the direct cytoxicity of some camptothecin-based antibody-drug conjugates are currently under investigation

*SGN-35C is an investigational agent, and its safety and efficacy have not been established.

Eligibility Criteria

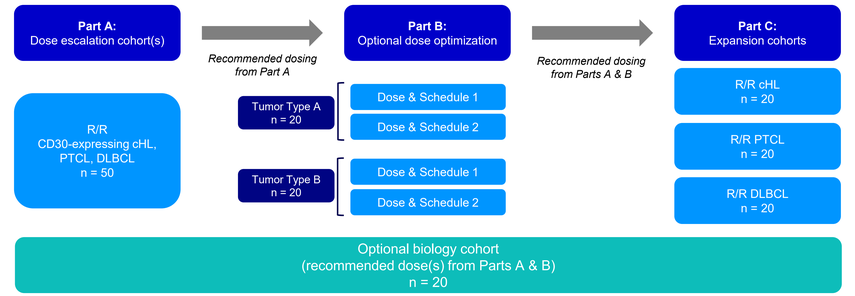
Key inclusion criteria

- Enrolled patients must be ≥18 years of age, have measurable disease per Lugano, and an Eastern Cooperative Oncology Group Performance Status score ≤1.
- Patients must have histologically confirmed R/R lymphoid malignancy as per the 2016 World Health Organization (WHO) classification, with no standard therapy available.
  - Eligible lymphoma subtypes include:
    - Classical Hodgkin lymphoma (cHL)
    - Peripheral T cell lymphoma (PTCL)
    - Diffuse large B-cell lymphoma (DLBCL)
- For Parts A and B, in patients with PTCL or DLBCL, CD30 expression must be ≥1% in tumor tissue from the most recent biopsy or obtained at or after relapse, as determined by local pathology except in diagnoses where CD30 is universally expressed.
- For Part C, patients are eligible irrespective of CD30 expression and must provide tumor tissue for evaluation; the number of prior therapies permitted is dependent on histologic subtype.

Study Design

- SGN35C-001 is a first-in-human, open-label, multicenter, global, phase 1 dose-escalation and dose-expansion study to assess the safety, tolerability, pharmacokinetics (PK), pharmacodynamics, and antitumor activity of SGN-35C in patients with select relapsed/refractory (R/R) lymphomas (**Table 1**).
- Patients will be enrolled into dose-escalation (Part A), optional dose-optimization (Part B), dose-expansion (Part C), and optional biology cohorts (**Figure 2**).

Figure 2: Study Design



cHL = chronic Hodgkin lymphoma; DLBCL = diffuse large B-cell lymphoma; PTCL = peripheral T-cell lymphoma; R/R=relapsed/refractory

Table 1. Study objectives and endpoints

Objectives	Endpoint
Primary	
Characterize safety and tolerability	• Incidence and severity of adverse events and laboratory abnormalities • Frequency of dose modifications due to AEs
Identify MTD	• Incidence of DLTs
Identify recommended dose (Parts A and B)	• Incidence of DLTs and cumulative safety by dose level
Secondary	
Characterize PK	• Estimates of selected PK parameters
Characterize immunogenicity	• Incidence of ADA
Assess antitumor activity (response-based)	• ORR and CR rate, as assessed by the investigator • DOR

ADA = antidrug antibodies; AE = adverse event; CR = complete response; DLT = dose-limiting toxicity; DOR = duration of response; MTD = maximum tolerated dose; ORR = objective response rate; PK = pharmacokinetic

Key exclusion criteria

- Estimated life expectancy <12 weeks
- History of another malignancy within 3 years before first dose of study drug or any evidence of residual disease from a previously diagnosed malignancy
- Active cerebral/meningeal disease related to underlying malignancy
- Autologous stem cell transplant (SCT) <12 weeks prior to the first dose
- Allogenic SCT in <100 days or active acute or chronic graft vs host disease or receiving immunosuppressive therapy for graft vs host disease
- Significant cytomegalovirus infection
- Grade ≥2 pulmonary or interstitial lung disease
- Clinically significant lung disease requiring treatment with systemic corticosteroids within 6 months prior to enrollment
- History of clinically significant GI disease or complications