Open-Label Phase 1 Study to Evaluate the Safety of SGN-35T in Patients With Relapsed/Refractory CD30-Expressing Lymphoid Malignancies

Tatyana Feldman[1], Radhakrishnan Ramchandren[2], Hun Ju Lee[3], Gizelle Popradi[4], Graham P Collins[5], Daniel Morillo[6], Mingjin Yan[7], Tara L. Chen[7], Youn H Kim[8]

[1]Hackensack University Medical Center, Hackensack, NJ, USA; [2]University of Tennessee Medical Center, Knoxville, TN, USA; [3]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [4]McGill University Health Centre, Montreal, Quebec, Canada; [5]Oxford University Hospitals, Oxford, UK; [6]START Madrid - Fundacion Jimenez Diaz, Madrid, Spain; [7]Pfizer Inc, Bothell, WA, USA; [8]Stanford Cancer Center, Stanford, CA, USA

Objective

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

Conclusion

- Enrollment is ongoing in the United States, Europe, and planned globally.

Background

- Patients with relapsed/refractory (R/R) lymphomas have limited treatment options and poor mortality rates vs 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 (cHL) and peripheral T-cell lymphoma.[5]
- SGN-35T is an investigational ADC comprising an anti-CD30 monoclonal antibody conjugated to monomethyl auristatin E (MMAE) via a novel protease-cleavable tripeptide linker with a drug-to-antibody ratio of ~4 (**Figure 1**).
  - SGN-35T has the same antibody backbone as BV, but the tripeptide linker is designed to preferentially release MMAE in target cells to improve tolerability.
  - Preclinically, SGN-35T elicits antitumor activity through MMAE-mediated direct cytotoxicity, CD30+ regulatory T-cell depletion, bystander effect, and immunogenic cell death, providing rationale to clinically develop SGN-35T.
- SGN-35T is currently being investigated in the phase 1 study SGN35T-001 (NCT06120504).

Study Design

- SGN35T-001 is a phase 1, open-label, multicenter dose escalation and dose expansion study designed to characterize the safety, tolerability, pharmacokinetics, pharmacodynamics, and preliminary antitumor activity of SGN-35T in adults with select 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**).

Eligibility Criteria

KEY INCLUSION CRITERIA

- Enrolled patients must be ≥18 years of age, have measurable disease per Lugano (as applicable), and an Eastern Cooperative Oncology Group performance status score ≤1.

PARTS A AND B

- Patients must have histologically confirmed R/R lymphoid malignancy as per the World Health Organization (WHO) classification, with no standard therapy available.
  - 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.
  - Eligible lymphoma subtypes include:
    - cHL
    - Peripheral T-cell lymphoma
    - Mature B-cell lymphoma
    - Primary cutaneous lymphoma.

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.

KEY EXCLUSION CRITERIA

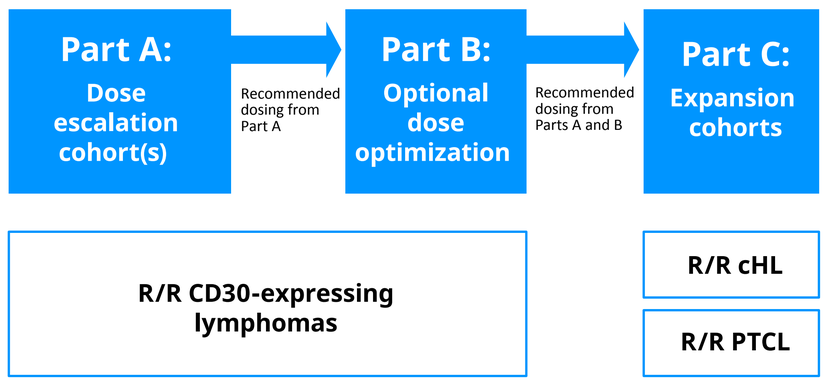
- Estimated life expectancy <12 weeks.
- History of another malignancy within 3 years before the first dose of study drug or any evidence of residual disease from a previously diagnosed malignancy.
- Active cerebral/meningeal disease related to underlying malignancy.
- Autologous stem cell transplant (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.

Table 1: Study objectives and endpoints

Objectives	Endpoints
Primary	
Characterize safety and tolerability	• Incidence and severity of AEs 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 ADAs
Assess antitumor activity (response-based)	• ORR and CR rate, as assessed by the investigator • DOR
Exploratory	
Characterize potential biomarkers associated with response, toxicity, and resistance	• Actual and change from baseline values in immune subsets and cytokines in peripheral blood
Assess antitumor activity (time-to-event based)	• PFS and OS

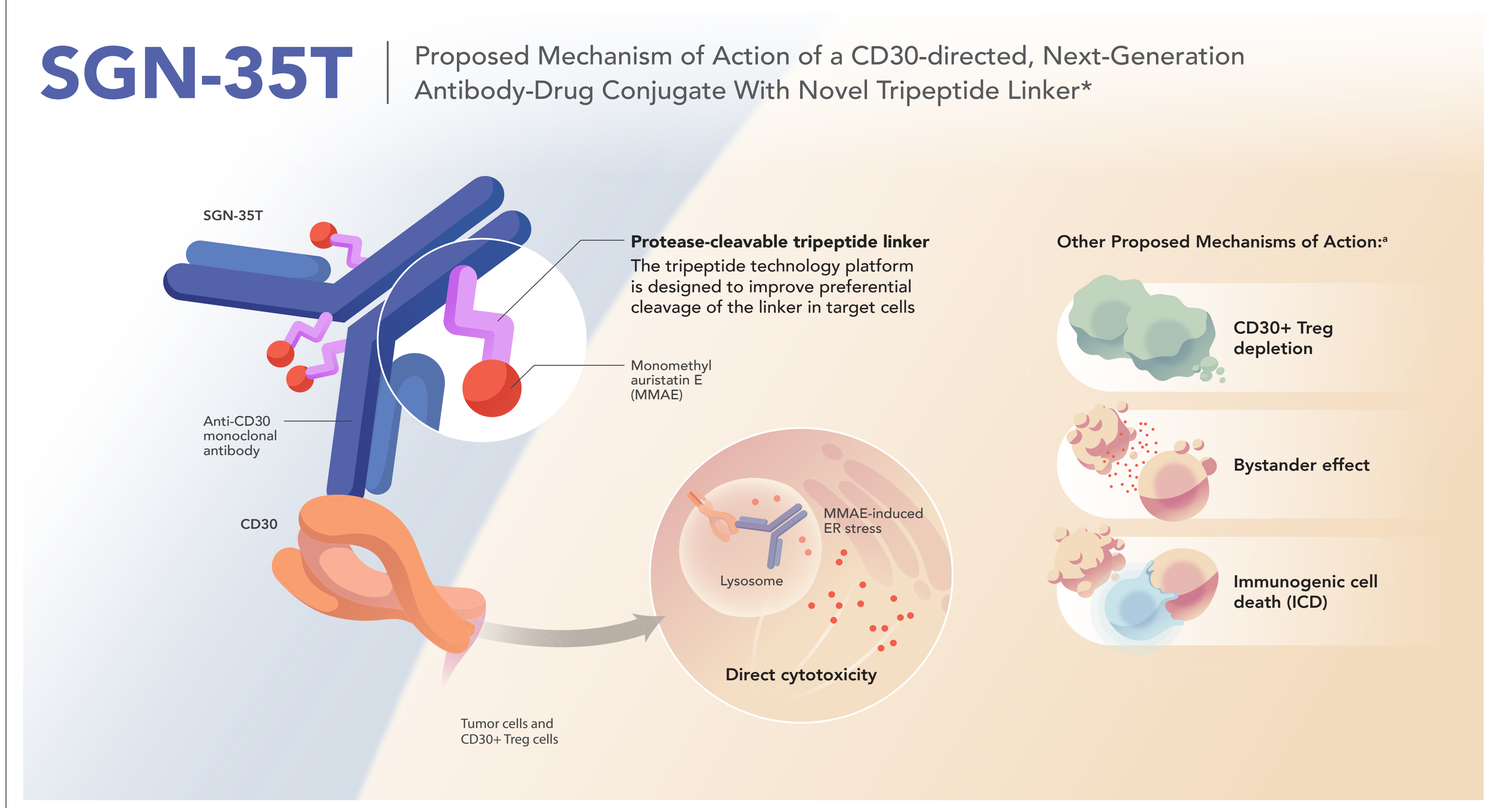
ADA=antidrug antibody; AE=adverse event; CR=complete response; DLT=dose-limiting toxicity; DOR=duration of response; MTD=maximum tolerated dose; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; PK=pharmacokinetics

Figure 2: Study design



cHL=classical Hodgkin lymphoma; PTCL=peripheral T-cell lymphoma; R/R=relapsed/refractory

Figure 1: Mechanism of action for SGN-35T



CD30=cluster of differentiation 30; ER=endoplasmic reticullum; Treg=regulatory T cell
[a]Additional mechanisms of action and their potential to complement the direct cytoxicity of some MMAE-based antibody-drug conjugates are currently under investigation
***SGN-35T is an investigational agent, and its safety and efficacy have not been established.**

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Disclosures: TF has received consultancy fees from ADCT, AstraZeneca, BMS, Epizyme, Genmab, Seagen, and Pharmacyclics; has received honoraria from ADCT, AstraZeneca, Epizyme, Genmab, Seagen, Takeda, and Pharmacyclics; has participated in the Speakers Bureau for Takeda, Seagen, and Genmab; has received research funding from ADCT, AstraZeneca, BMS, Corvus, Daiichi, Genmab, Kymera, Merck, Seagen, TESSA, Trillium, Alexion, and Portola; and holds equity in Genomic Testing Cooperative and OMI. **HJL** has received consultancy fees from Pfizer, AstraZeneca, and Oncternal; has received honoraria from Pfizer, AstraZeneca, MJH Life Sciences, and Onviv; has received research funding from Pfizer, AstraZeneca, Oncternal, BMS, and Takeda; and is employed by MD Anderson Cancer Center. **GP** has received consultancy fees and honoraria from and has participated in the Speakers Bureau for Pfizer. **GPC** has received consultancy fees from Roche, Abbvie, Takeda, AstraZeneca, Sobi, and Beigene; has received honoraria from Roche, Kite, AbbVie, Takeda, AstraZeneca, Sobi, and Beigene; has participated in the Speakers Bureau for Roche, Kite, AbbVie, Takeda, and Beigene; and has received research funding from Beigene, Pfizer, Amgen, and BMS. **DM** has received honoraria from Roche, Takeda, and GSK; and has received travel funds from Roche and Kite. **YHK** has received research funding from Corvus, CRISPR Therapeutics, DrenBio, Eisai, Elorac, Galderma, Innate Pharma, Kyowa-Kirin-Pharma, Pfizer/Seattle Genetics, Portola/Alexion Pharma, Soligenix, and Trillium; has received honoraria from Galderma, Kyowa-Kirin-Pharma, Regeneron, Sanofi, and Secura Bio; and has membership on a board or advisory committee for Corvus, Galderma, Innate Pharma, Kyowa-Kirin-Pharma, Mundipharma, Regeneron, Sanofi, and Secura Bio. **MY** and **TL** are employed by Pfizer. **RR** was an employee of Pfizer.

Acknowledgments: This study was sponsored by Seagen Inc., Bothell, WA, USA, which was acquired by Pfizer in December 2023. The authors thank all the patients and families for their participation in the study and research personnel for their support of this trial. Medical writing support was provided by Haniya Javaid of Engage Scientific Solutions and was funded by Pfizer.

Presented at the International Symposium on Hodgkin Lymphoma (ISHL13), October 26–28, 2024, Cologne, Germany