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POSTER ABSTRACTS

627.AGGRESSIVE LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

A Phase 1, Open-Label, Dose Escalation and Dose Expansion Study of CLN-978 (CD19XCD3XHSA) in Patients with Relapsed/Refractory (R/R) B-Cell Non-Hodgkin Lymphoma (B-NHL)

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Background:
Patients with B-cell non-Hodgkin lymphoma (B-NHL) who are refractory to/or have relapsed (R/R) after treatment with anti-CD20 monoclonal antibodies, either alone or in combination with standard-of-care chemotherapy, have a poor prognosis. Response rates tend to decrease and duration of response shortens with each successive line.
CD19 represents a significant target for the development of novel immunotherapies for the treatment of patients with R/R B-NHL, many of whom develop disease that is refractory to CD20-containing regimens. CD19-directed therapies approved for B-NHL include an Fc-enhanced anti-CD19 monoclonal antibody, a CD19-directed antibody-drug conjugate, and several CD19-directed CAR-T cell products. While CAR-T approaches are an important alternative for some B-NHL subtypes, many patients still relapse, and challenges remain with toxicity and accessibility in the community setting. Consequently, substantial unmet needs remain for effective treatments with broad applicability across B-NHL subtypes and practice settings.
CLN-978 is a fully human, half-life extended, single-chain T cell engaging construct targeting CD19 and CD3, with a human serum albumin (HSA) binding moiety for half-life extension. Preclinically, CLN-978 effectively redirects T cells to kill CD19-expressing malignant cells and has demonstrated potent in vitro and in vivo efficacy against cancer cells expressing very low levels of human CD19.
Study Design and Methods:
This is a phase 1, open-label, multi-center, first-in-human, dose escalation, and dose expansion study of CLN-978 in patients with R/R B-NHL. Adult patients (≥ 18 years of age) with one of the following CD19+ B-cell histologies: diffuse large B-cell lymphoma - de novo or transformed, high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, follicular lymphoma, mantle cell lymphoma, or marginal zone lymphoma (nodal, extranodal, or mucosa-associated) for whom there is no available approved standard therapy will be recruited. Other key eligibility criteria include: ≥ 2 lines of prior chemotherapy, Eastern Cooperative Oncology Group Performance Status 0-2. Key exclusion criteria include prior treatment with allogeneic hematopoietic stem cell transplantation or any other investigational CD19 x CD3 T cell engager. Prior CAR-T therapy, unconjugated or radio-conjugated CD19 mAb, and CD19 antibody-drug conjugate are allowed.
The study consists of 2 parts: 1) a dose escalation phase commencing with accelerated titration in single-patient cohorts followed by a conventional 3+3 dose escalation design to identify the recommended phase 2 dose (RP2D) and 2) a dose expansion phase to further characterize the safety and preliminary efficacy of CLN-978 in disease-specific cohorts at the RP2D. CLN-978 will be subcutaneously (SC)-administered once weekly (QW) in 28-day cycles until progressive disease, intolerable toxicity, or a maximum of 24 cycles of treatment. Initial administration of CLN-978, inclusive of potential priming doses and the first target dose, will be administered on an inpatient basis. Subsequent doses may be given in the outpatient setting.
Based on emerging data, less frequent administration schedules may be implemented in Cycle 4 and beyond as approved by the Safety Review Committee. Safety, pharmacokinetic (PK), pharmacodynamic, and preliminary efficacy assessments will

guide the selection of the dose and schedule for further evaluation. The primary endpoint is safety. Key secondary endpoints include PK, anti-drug antibodies, overall response rate, duration of response, time to response, time to subsequent anti-lymphoma therapy, progression-free survival, and overall survival.
Approximately 90 patients (30 in dose escalation and 60 in dose expansion) will be enrolled at approximately 6 sites in the U.S., reflecting both community and academic centers.
The study is currently enrolling (NCT05879744).

Disclosures Shouse: *Beigene, Inc.:* Speakers Bureau; *Kite Pharmaceuticals:* Consultancy, Speakers Bureau. **Blum:** *BMS:* Research Funding; *Seattle Genetics:* Research Funding; *Cullinan Oncology, Inc.:* Research Funding. **Abramson:** *Kymera:* Consultancy; *Seagen Inc.:* Research Funding; *Regeneron:* Consultancy, Honoraria; *Ono Pharma:* Consultancy; *Mustang Bio:* Consultancy, Research Funding; *MorphoSys:* Consultancy; *Merck:* Research Funding; *Lilly:* Consultancy; *Epizyme:* Consultancy; *Genentech:* Consultancy; *Genmab:* Consultancy; *Kite Pharma:* Consultancy; *Janssen:* Consultancy, Honoraria; *Interius:* Consultancy; *Celgene:* Consultancy; *Takeda:* Consultancy; *Novartis:* Consultancy; *Incyte:* Consultancy; *Century Therapeutics:* Consultancy; *EMD Serono:* Consultancy; *Cellectar Biosciences:* Consultancy; *Caribou Biosciences:* Consultancy; *BMS:* Consultancy, Honoraria, Research Funding; *BeiGene:* Consultancy; *AstraZeneca:* Consultancy, Honoraria; *AbbVie:* Consultancy; *Alimera Sciences:* Consultancy; *Karyopharm Therapeutics:* Consultancy; *C4 Therapeutics:* Consultancy; *Bluebird Bio:* Consultancy; *AI Therapeutics:* Research Funding. **Narkhede:** *Genentech, Inc. / F. Hoffmann-La Roche Ltd:* Speakers Bureau; *Genentech, Inc. / F. Hoffmann-La Roche Ltd, ADC Therapeutics, KITE, Abbvie:* Honoraria; *Genentech, Inc. / F. Hoffmann-La Roche Ltd, Gilead, T.G Therapeutics, Kite, Beigene, EUSA, ADC Therapeutics, Adaptive:* Research Funding. **Michaelson:** *Cullinan Oncology, Inc.:* Current Employment, Current equity holder in publicly-traded company, Divested equity in a private or publicly-traded company in the past 24 months, Patents & Royalties: Inventor on multiple Cullinan patent applications; *Jounce Therapeutics:* Divested equity in a private or publicly-traded company in the past 24 months, Patents & Royalties: Inventor on multiple patent applications ; *Celsius Therapeutics:* Current equity holder in private company; *Biogen:* Patents & Royalties: Inventor on multiple patent applications . **Baeuerle:** *MPM Capital:* Consultancy; *Cullinan Oncology, Inc.:* Consultancy. **Meetze:** *Cullinan Oncology, Inc.:* Current Employment, Current equity holder in publicly-traded company, Patents & Royalties: Inventor on multiple Cullinan patent applications. **Shapiro:** *Cullinan Oncology, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Shearer:** *SpringWorks Therapeutics:* Current equity holder in publicly-traded company, Ended employment in the past 24 months; *Cullinan Oncology, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Inumerable:** *Cullinan Oncology, Inc.:* Current Employment, Current equity holder in publicly-traded company. **Jones:** *Cullinan Oncology, Inc.:* Current Employment, Current equity holder in publicly-traded company; *BMS:* Current equity holder in publicly-traded company. **Awan:** *Janssen, Gilead, Kite pharmaceuticals, Karyopharm, MEI Pharma, Verastem, Incyte, Johnson and Johnson, Merck, Epizyme, Loxo Oncology, Adaptive Biotechnologies, Genmab:* Other: Consulting Agreements; *Pharmacyclics LLC, an AbbVie Company.:* Other: Contracted Research; *AstraZeneca Pharmaceuticals LP:* Other: Advisory Committee; *AbbVie Inc, ADC Therapeutics, AstraZeneca Pharmaceuticals LP, BeiGene Ltd, Bristol-Myers Squibb Company, Cardinal Health, Caribou Biosciences Inc, Celgene Corporation, Cellectar Biosciences Inc, DAVA Oncology, Epizyme Inc, Genentech, a member of the Roche:* Other: Consulting Agreements.

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Figure 1