A PHASE 1/2, FIRST-IN-HUMAN, MULTICENTER, OPEN-LABEL TRIAL EVALUATING THE SAFETY, TOLERABILITY, AND ANTILEUKEMIC ACTIVITY OF DEBIO1562M IN PATIENTS WITH RECURRENT REFRACTORY ACUTE MYELOID LEUKEMIA (AML)

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BACKGROUND

Unmet Medical Need

- Acute myeloid leukemia (AML) is the most common acute leukemia, an aggressive malignancy characterized by the abnormal proliferation of myeloid progenitor cells, often resulting in poor outcomes and high relapse rates.
- Patients with relapsed or refractory (R/R) AML face a particularly poor prognosis with currently available therapies, with low complete remission (CR) rates (~10%) (Stahl 2018).
- Despite advances in treatment, AML remains challenging to cure.

CD37 Expression in AML

- CD37 (TSPAN26) is a trans-membrane protein belonging to the tetraspanin superfamily (Hemler 2005).
- In AML, increased CD37 expression on blasts and leukemic stem cells has been reported, at both mRNA and protein levels (Lu 2025; Pereira 2015; Yan 2021).
- This heightened expression is specific to malignant cells when compared to normal hematopoietic stem cells (Caulier 2024).
- Elevated CD37 expression is correlated with a poor patient outcome in AML (Fang 2024; Jeremy 2024).
- CD37 expression is observed across all subtypes of AML and Myelodysplastic syndrome (MDS).

Debio 1562M Clinical Development in AML

- Debio 1562M is an antibody-drug conjugate against CD37, utilizing Debiopharm's proprietary Multilink™ cleavable linker technology.
- Eight molecules of a DM1 (mertansine) derivative, a highly potent anti-tubulin binder inducing mitotic catastrophe and cell death, are conjugated to naratuximab humanized antibody.
- Specifically designed linker exploiting a new catalytic property of cathepsin B confers to Debio 1562M an excellent plasma stability resulting in a safe toxicologic profile in mice.

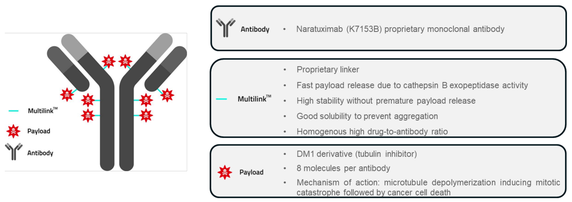


Figure 1: Schematic representation of Debio1562M

STUDY DESIGN

- This is a global, multicenter, open-label, first-in-human Phase 1/2 clinical trial investigating Debio1562M as a monotherapy.
- Study results will provide insights into the clinical potential of Debio1562M in patients with R/R AML, and Higher Risk-MDS (HR-MDS) for whom no standard therapy of proven benefit is available.

Phase 1: Dose Escalation

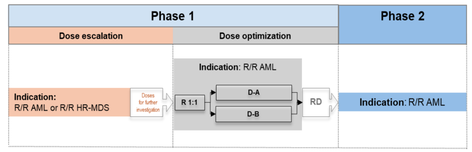
- Explore different dose levels using an adaptive Bayesian logistic regression model guided escalation with overdose control.

Phase 1: Dose Optimization

- A subsequent randomized, 2-arm portion will be conducted to define the recommended dose (RD).

Phase 2

- A single-arm Phase 2 part will evaluate the antileukemic activity of Debio1562M monotherapy at the established RD.



Abbreviations: AML=acute myeloid leukemia; D-A/D-B=dose level and/or dosing schedule A or B; HR-MDS=higher-risk myelodysplastic syndrome; R=randomization; RD=recommended dose; R/R=relapsed/refractory.

Figure 2: Study overview

STUDY OBJECTIVES

PHASE 1: Dose Escalation

Primary objective

- To characterize the safety and tolerability of Debio1562M in R/R AML and R/R HR-MDS.

Secondary objectives

- To assess the preliminary antileukemic activity.
- To characterize the pharmacokinetics (PK).

PHASE 1: Dose Optimization

Primary objective

- To characterize the safety and tolerability and identify the RD of Debio1562M in R/R AML.

Secondary objectives

- To assess the preliminary antileukemic activity.
- To further characterize the safety and tolerability.
- To characterize the PK.

PHASE 2

Primary objective

- To assess the antileukemic activity of Debio1562M in R/R AML.

Secondary objectives

- To further characterize the safety and tolerability.
- To characterize the PK.

PATIENT POPULATION

Key inclusion criteria

- Patients with R/R AML (no selection based on mutation status or karyotypes) (R/R HR-MDS will be included only in dose escalation) for whom no standard therapy of proven benefit is available.
- Eastern Cooperative Oncology Group (ECOG) performance status ≤2.
- Patients with prior autologous or allogeneic bone marrow transplant are eligible.
- Adequate baseline laboratory values.

Key exclusion criteria

- Evidence for active central nervous system leukemia involvement.
- Clinically active infection.
- Clinically significant cardiac dysfunction and cardiopulmonary disease.
- Evidence of peripheral neuropathy Grade ≥2.
- Immunization with live vaccine within 4 weeks prior to the start of treatment.

STUDY SITES AND STATUS

- Enrollment is currently ongoing in United States of America.
- For participating sites, please see NCT06969430.

Sample size

- Approximately 134 participants will be enrolled in this trial.

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