Debio 1562M Anti-CD37 ADC

Non-Confidential Deck

May 2023

Debio 1562M Executive Summary

New generation of anti-CD37 ADC in AML

Debio 1562M is a **new generation ADC directed against CD37**, incorporating new Debiopharm proprietary linker technology (**Multilink**)

- CD37 **is a promising target in AML/MDS** suitable for an ADC approach as it can be easily internalized and is expressed in all patients
- **Potential to be first-in-class in AML/MDS** and **limited competition in CD37** space
- **Debio 1562M may have wide utility and commercial potential in NHL**

Debio 1562M pre-clinical data shows **significant improvement survival compared to naratuximab naked antibody** and demonstrates **stability, specificity and good tolerance**

It has showed **potent antitumour activity in in-vivo AML models,** incl. **superiority versus SOC** (venetoclax + azacytidine)

Current dev status: completion of **pre-clinical data package including GLP toxicity study** by **May 2024**. **CTA/IND submission** by **October 2024**

Expected entry into **clinic Q1 2025**, time to **market 2030** with **patent protection up to 2043 + max 5 years** (country by country)

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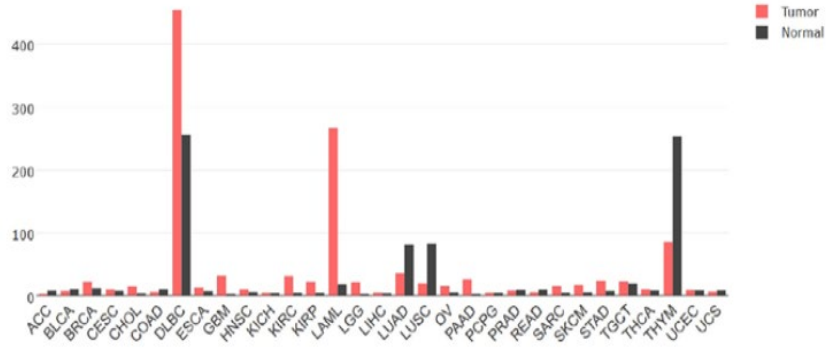
The Target

CD37

Debio 1562M
CD37

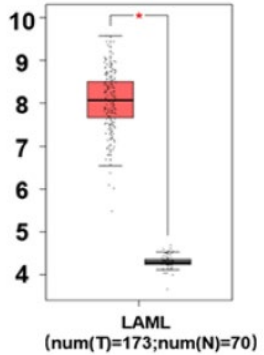
CD37 is broadly expressed on AML cell lines and on primary blasts

CD37 mRNA expression (TCGA & Gtex database)

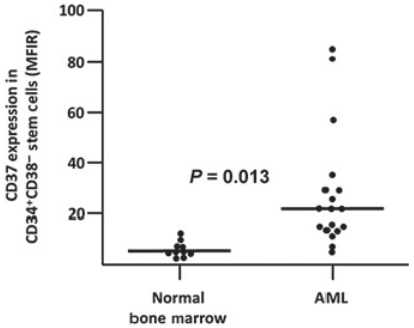


Zhang et al, Bioscience Report, 2020

CD37 mRNA AML vs healthy donors



CD37 protein expression in AML vs healthy stem cells



Pereira et al, Molecular cancer Therapeutics, 2015

- CD37 has widespread surface expression in AML cell lines and primary blasts, with minimal to no expression on normal cells
- CD37 is expressed across a wide range of AML subtypes and could be a target for targeted therapy irrespective of specific mutations

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CD37

CD37 expression is associated with poor prognosis in AML (ELN status and OS)

CD37 high expression as a potential biomarker and association with poor outcome in acute myeloid leukemia

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CD37 Expression in Acute Myeloid Leukemia Provides New Target for Directed Therapy

Karilyn Larkin MD [1 2], Erin Guth MS * [2], Bonnie K. Harrington DVM [3], Nicole Grieselhuber MD PhD * [1 2], Natarajan Muthusamy DVM, PhD [1 2], John C. Byrd MD [1 2]

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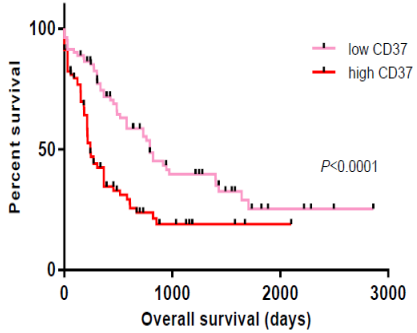

CD37 transcript in 200 annotated AML cases from TCGA (high and low defined by median dichotomization)

Bioscience Report, 2020

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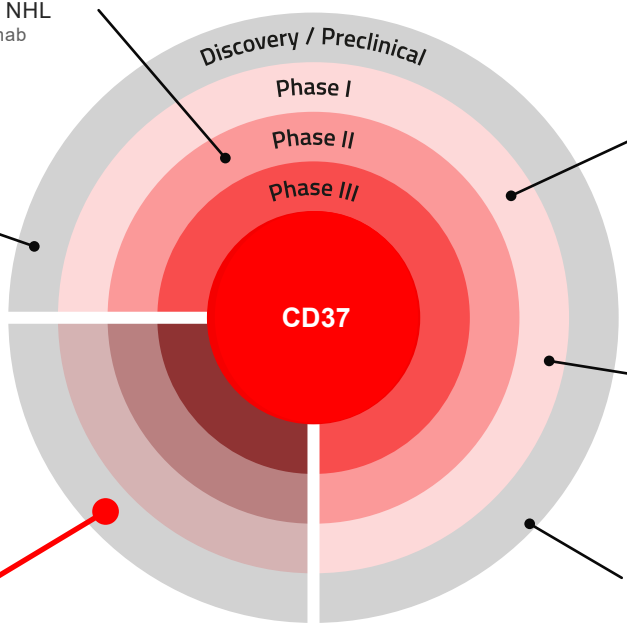
Competitive Landscape: CD37

Debio 1562M is a potential first-in-class anti-CD37 ADC in development for AML/HR-MDS



GEN-3009 ***(DuoHexaBody-CD37)***
in r/r NHL
Genmab

a. Alpha 37
212PB-NNV003 (CLL)
b. Humalutin
177Lu-NNV003 (NHL)
c. CD37 CAR-T
d. Anti-CD37 mAb (NHL, autoimmune diseases)
Nordic Nanovector

CAR-T CD37
in Heme malignancies
Massachusetts general hospital (IST)

PSB202 ***(anti-CD20/CD37 Ab)***
in relapsed indolent B-cell malignancies
Sound Biologics

HDP-102 ***(anti-CD37 ADC)***
in NHL
Heidelberg Pharma

Debio 1562M ***(anti-CD37 ADC)***
in AML/HR-MDS
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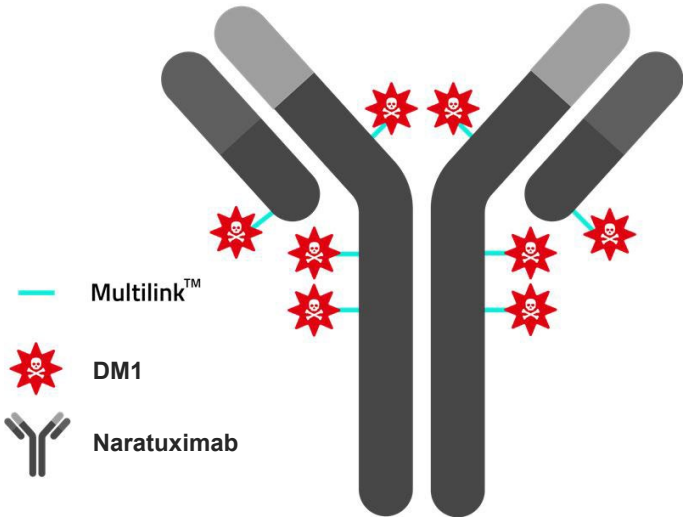
Our asset

A new generation anti-CD37 ADC
with proprietary linker technology

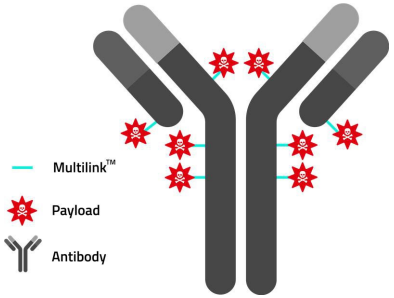
Debio 1562M is an antibody drug conjugate targeting CD37



Debio 1562M (DAR8)

- Humanized monoclonal antibody **naratuximab**
- Cytotoxic payload: **DM1**
- Linker: new peptidic cleavable linker **Multilink™** allowing high DAR and fast intracellular release of payloads

Multilink™ is a new generation linker technology enabling the development of novel, potent, stable and safe ADCs



Multilink™ allows:

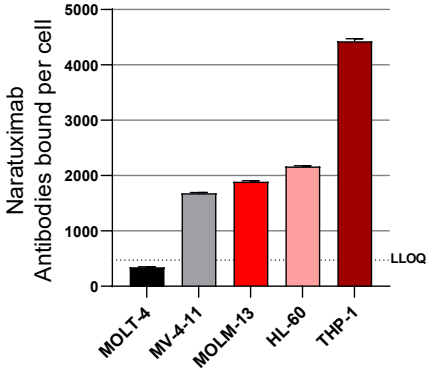
- **Fast payload release** thanks to exopeptidase activity of cathepsin B
- **High stability** without premature payload release
- **Good solubility** to prevent aggregation
- **DAR increase**
- **Homogenous high DAR**

Evidence to date

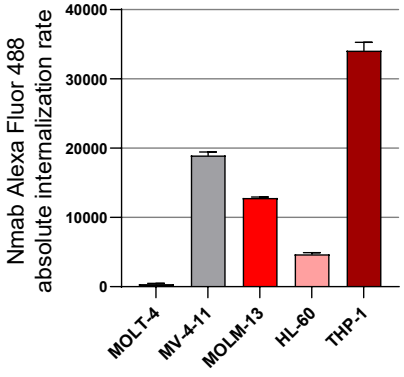
Pre-clinical data

Debio 1562M demonstrates rapid internalization and potent nM activity

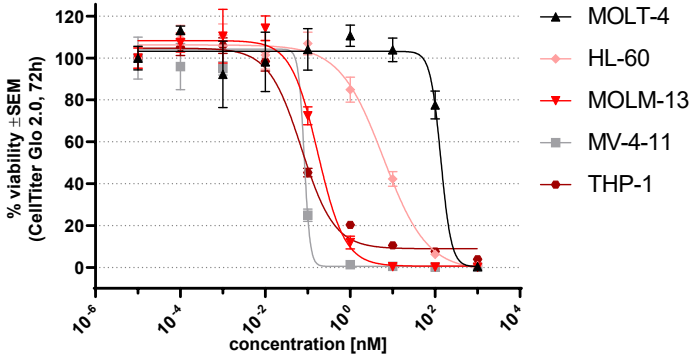
CD37 expression on cell lines



Antibody Internalization after 2h incubation



ADC Cytotoxicity assay 72h



World ADC London 2023

	MOLT4	HL-60	MOLM-13	MV-4-11	THP-1
IC50 (nM)	136.9	6.06	0.17	0.08	0.07

Naratuximab is efficiently internalized in CD37 expressing cells and Debio 1562M has nM antiproliferative activity which correlates with internalization rate.

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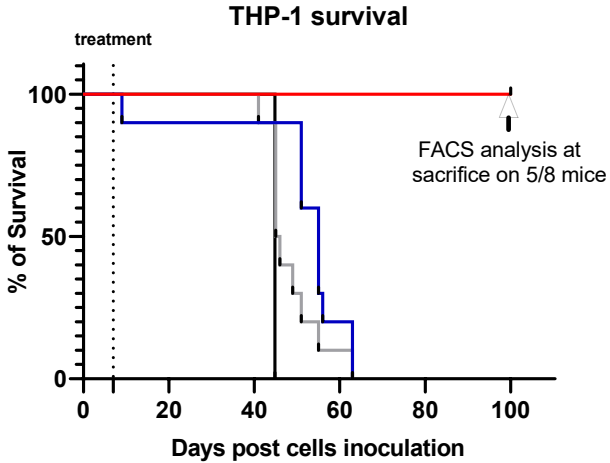
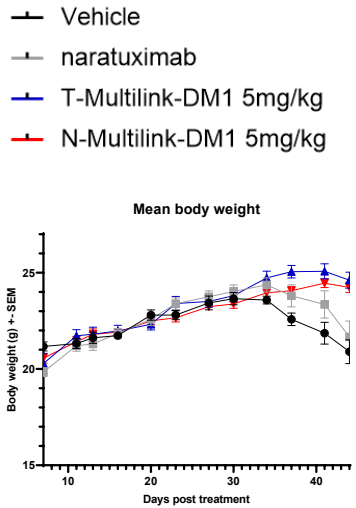
Debio 1562M significantly improves survival compared to naratuximab naked antibody

Experimental conditions:

- Disseminated model
- cells injected in tail vein 7 days before treatment
- 8 mice /group
- 1 iv injection
- Vehicle = PBS

In vivo efficacy in THP-1 model





Residual disease quantification (FACS day 97)

Animal ID.	Blood CD45+%	Bone Marrow CD45+%
G4-4828	0,05	0,071
G4-4836	0,01	0,061
G4-4860	0,01	0,05
G4-4865	0,10	0,01
G4-4868	0,04	0,05

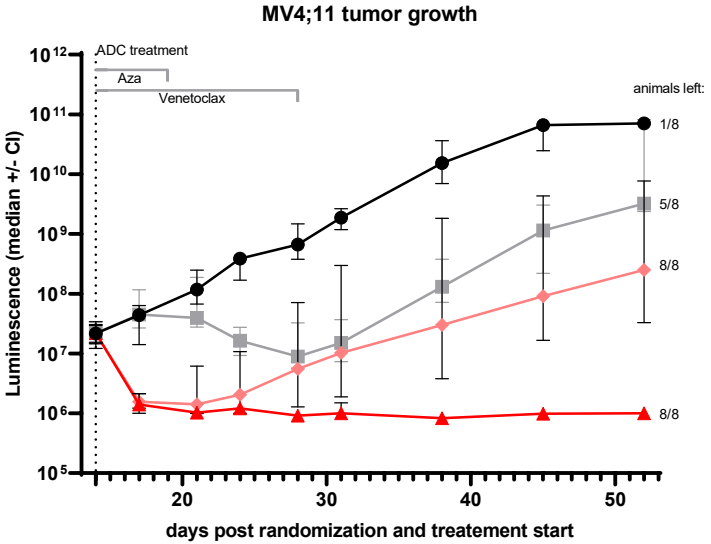
no tumor cells were detected at d97

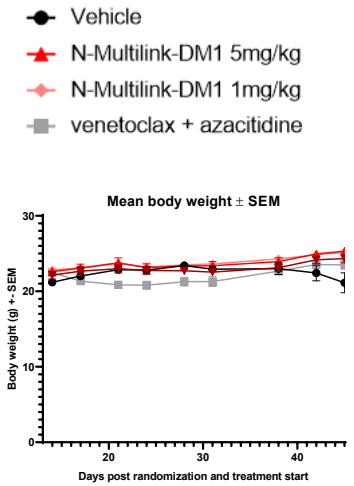
World ADC London 2023

Debio 1562M demonstrates potent sustained in vivo antitumoural activity versus standard of care

Experimental conditions:

- Disseminated luciferase model
- Cells injected in tail vein 14 days before treatment
- 8 mice /group
- 1 iv injection for Debio 1562M
- Azacitidine: 3.5mg/kg QDx5, iv
- Venetoclax: 100mg/kg QDx14, po
- Vehicle = PBS





World ADC London 2023

Single dose of Debio 1562M at 5mg/kg is sufficient to observe a sustained antitumoral response compared to venetoclax + azacitidine standard of care regimen

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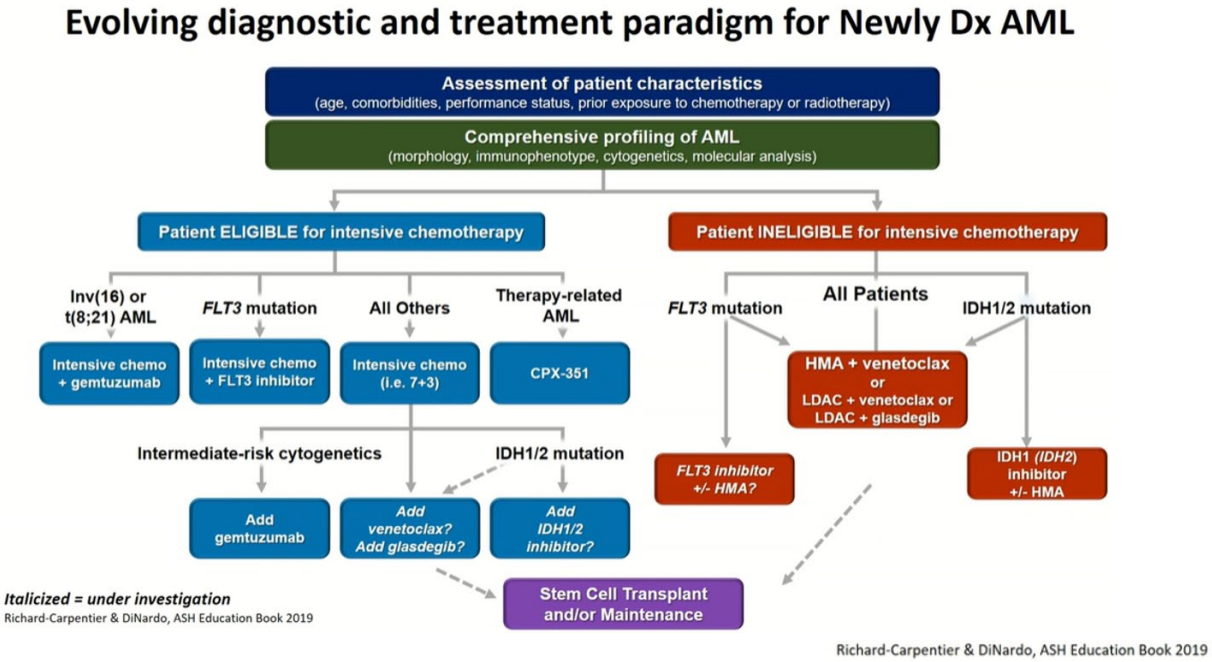
Unmet medical need & commercial opportunity

AML/MDS

AML is an indication with high unmet medical need

Estimated **26%** **5-year survival rate**



Richard-Carpentier & DiNardo, ASH Education Book 2019

- In 1L, there is a distinction between fit and unfit population eligible for intensive chemotherapies followed by ASCT; but **10-40%** of patients are refractory and **50%** relapse
- Treatment of **r/r AML** include salvage chemotherapy, targeted agents, HMA alone, or enrollment in clinical trials. Prognosis remain poor with a **mOS** of **6 months**

ASCT = Autologous Stem Cell Transplant; **r/r** = relapsed/refractory; **HMA** = Hypomethylating agent; **LDAC**= Low dose cytarabine

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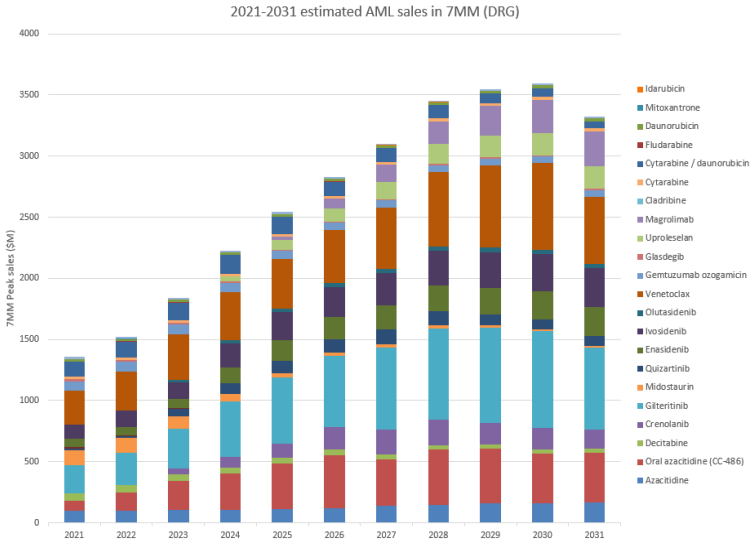
AML/MDS Market

AML/MDS market is estimated to reach $4,5B in 2031 in the 7 MM

- **AML market is expected to grow from 1,4B in 2021 to ~ $3,3B in 2031**



Source: DRG

- Moreover, **expected market in HR-MDS ~ $1,2B in 2031**

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Value Proposition

AML/MDS TOTAL MARKET POTENTIAL in 2031

Estimated $3,3B in AML

Estimated $1,2B in HR-MDS

CLEAR PATH TO MARKET IDENTIFIED

2030
Expected time to market

EXPECTED PATENT PROTECTION

Composition of matter
Expiration date: 2043 + max 5 years (country-by-country)

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Interested in discussing further?

Contact information

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