Alanis Therapeutics INC

PRECISION ANTIBODY THERAPEUTICS · MDS / AML

Blocking the bone marrow pathway that drives MDS and AML

ATI-D1, a first-in-class anti-Jagged-1 antibody, targets leukemic stem cells in the marrow niche — aiming for true disease modification across MDS and both primary and secondary AML.

Columbia University Spin-Out

V Foundation Grant Recipient

NCI SBIR Phase II Awardee

Non-Confidential Presentation · 2026

KEY SUCCESS FACTORS

Program Highlights

Columbia University spin-out

Built on a Columbia University × AvantGen collaboration — backed by multiple grants and awards (V Foundation; NCI SBIR Phase II) and a body of peer-reviewed work, including Cancer Cell 43:1007, 2025.

Protected & de-risked

Composition-of-matter patent pending plus a licensed, issued Columbia utility patent — and de-risked by CMC progress, with master cell bank established for cGMP and clinical trial, preliminary monkey PK completed and no overt adverse effects observed.

Novel, validated target

ATI-D1 blocks the oncogenic survival signal (Jagged-1/Notch1) that shelters leukemic stem cells in the MDS/AML marrow and seeds relapse — targeting the source, confirmed in mouse models and ex vivo human samples.

Strong management expertise

Management team with global oncology development and commercialization experience within heme malignancies to support the program

True disease modification

Aims to eliminate the leukemic stem cells current therapies leave behind — potentially restoring hematopoiesis and durably modifying disease, beyond the tumor control today's agents already achieve.

Clear path to value

Driving to a Phase 1 proof-of-concept trial and a licensing deal or pharma exit.

LEADERSHIP

A Management Team with the Internal Expertise to Execute

Operating semi-virtually, with global experience developing and commercializing oncology medicines — with a global imprint in heme and solid tumors

EXECUTIVE TEAM

Robert Goodenow, Ph.D.

Chief Executive Officer

Catherine Woods, Ph.D.

Head of Research

Elizabeth Song, Ph.D.

Head of Operations

BOARD OF DIRECTORS & ADVISORS

Xiaomin Fan, Ph.D.

Chairman, Founder · CEO, AvantGen

Robert Goodenow, Ph.D.

Director · CEO, Alanis

Cynthia Collins

Experienced Biotech CEO & Board Member

Azra Raza, M.D.

Chair, Clinical Advisory Board · Columbia

Stavroula Kousteni, Ph.D.

Chair, Scientific Advisory Board · Columbia

SCIENTIFIC ORIGIN

A Columbia University Spin-Out

Built on the research of recognized luminaries in MDS / AML.

Azra Raza, M.D.

Chan Soon-Shiong Professor of Medicine, Columbia University · Director, MDS Clinic

Medical oncologist focused on myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML); Principal Investigator for clinical studies at Columbia.

Stavroula Kousteni, Ph.D.

Professor, Physiology & Cellular Biophysics, Columbia University

Studies the bone marrow niche and hematopoietic stem cell fate in MDS and AML, defining the microenvironment that drives disease.

SHARED RESEARCH FOCUS

Examining the bone marrow microenvironment (the “niche”) in hematopoietic stem cell fate — particularly in the development of MDS and AML.

VALIDATION & TRANSLATION

Recipients of the V Foundation Bob Bast Translational Research Grant. Program anchored by key peer-reviewed publications and Columbia clinical-study capability.

THE PROBLEM

Relapse, Progression & the Path to AML

~40%
5-yr US survival in high-risk MDS

30%
of MDS patients transform to AML

~30%
5-yr survival once AML develops

A shared driver

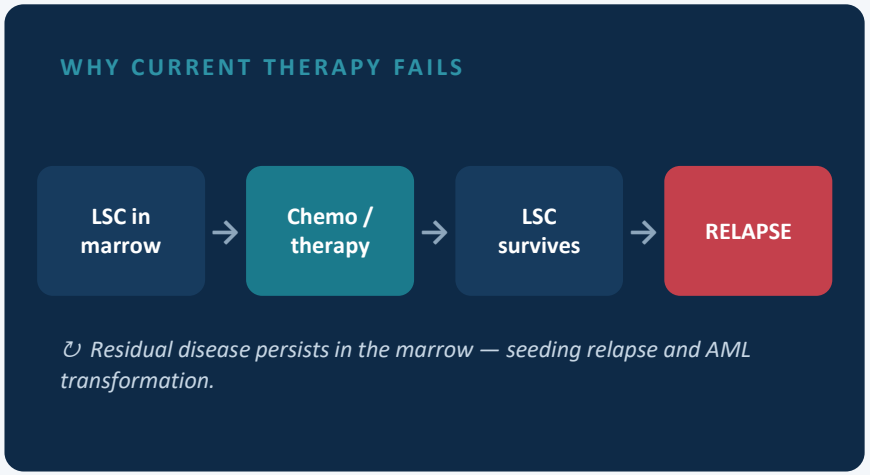
MDS and AML share a root cause — leukemic stem cells (LSCs) that survive in the marrow niche, where an oncogenic Jagged-1/Notch1 signal shelters them from therapy and drives relapse.

The consequence

Residual disease persists in the bone marrow microenvironment, driving relapse despite treatment and the urgent need to intervene early.

The Alanis approach

ATI-D1 (anti-Jagged-1) removes that niche survival signal to eliminate the LSCs current therapy leaves behind — with the potential to clear MDS, blocking progression to secondary AML, and treating primary AML.



Kroger et al;*heamtologica* 2025, 110 (2) Vendetti *Leukemia*, 2025 39, 2697

MARKET OPPORTUNITY

Large Unmet Need Across the MDS→AML Continuum

COMBINED MARKET OPPORTUNITY

$5B+

across MDS and AML

MDS >$2.5B
core lead indication

AML +$3B
AML expansion opportunity

Response rates fall short

High-risk MDS response rates are only ~30–40%, and ~30% of patients transform to AML — a near term initial entry point, with primary AML a major additional opportunity on the same mechanism.

Relapse remains a major problem

Relapse rates in high-risk MDS/AML reach ~50%. LSCs drive both MDS relapse and AML transformation, and current therapies leave them intact.

A multi-billion-dollar field with multiple entry points

The MDS market exceeds $2.5B and AML adds $3B+, together a $5B+ opportunity spanning the full MDS→AML continuum.

Sources: American Cancer Society; AbbVie investor disclosures; Nowicka et al., Biomedicines 2025, 13, 176.

Development Strategy

A Broad MDS + AML Opportunity, Entered Through MDS

AML

>10

approved / advancing targeted agents — a large, actively innovating AML field

MDS

Far fewer

targeted options — a less contested, more accessible entry point

Why this sequencing wins

We start broad across the Jagged-1⁺ MDS→AML continuum and let the data guide us. MDS offers the most direct, lower-burden entry to establish proof-of-concept and first-in-class positioning; AML — including front-line, where novel agents are gaining rapid traction — expands on the same mechanism of action as the signal emerges.

The ATI-D1 Difference

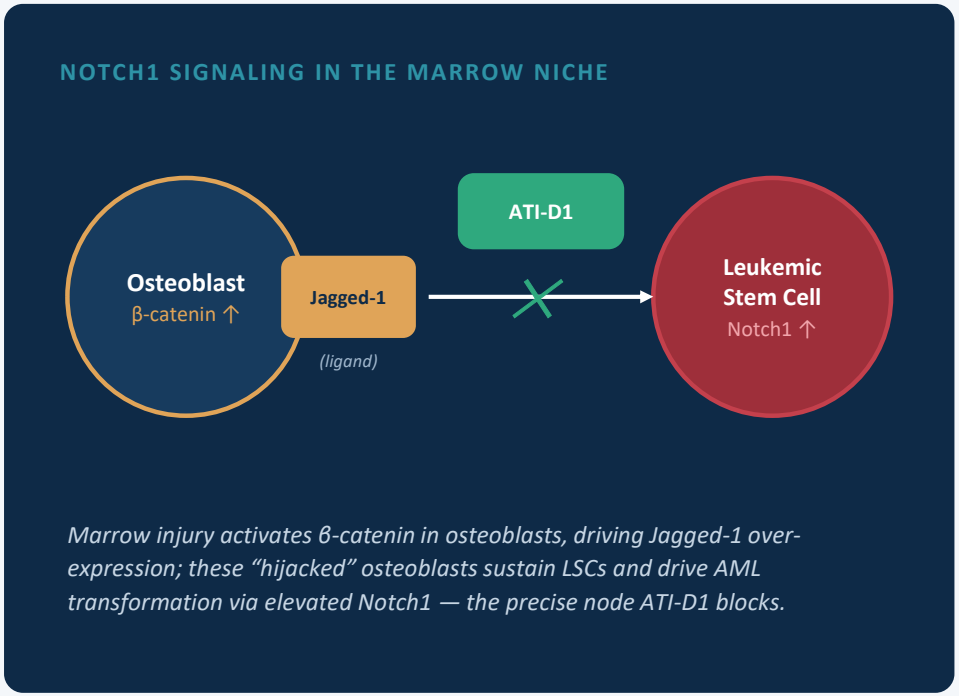
1. **Current agents miss the source of the disease**
   HMAs, luspatercept and imetelstat improve symptoms but none eliminate LSCs or block AML transformation.

2. **ATI-D1 targets the root cause**
   It attacks LSC survival in the marrow niche — present in ~70% of high-risk MDS patients.

3. **Built-in expansion path**
   AML — including front-line — advances in parallel on the same mechanism; we follow the efficacy signal into the largest opportunity.

Targeting the Jagged-1 / Notch1 Pathway

Dysregulated signaling in the marrow activates the β-catenin cascade driving Jagged-1 overexpression & Notch1 signaling to the leukemic stem cells fueling MDS/AML.



Marrow injury activates β-catenin in osteoblasts, driving Jagged-1 over-expression; these "hijacked" osteoblasts sustain LSCs and drive AML transformation via elevated Notch1 — the precise node ATI-D1 blocks.

Disease progression

Rising Jagged-1⁺ osteoblasts deplete the marrow, worsen anemia and elevate blast counts — fueling AML transformation.

A precise, druggable node

The osteoblast–LSC Notch1 interaction is a defined, targetable axis rather than a diffuse mutation landscape.

Blocking restores balance

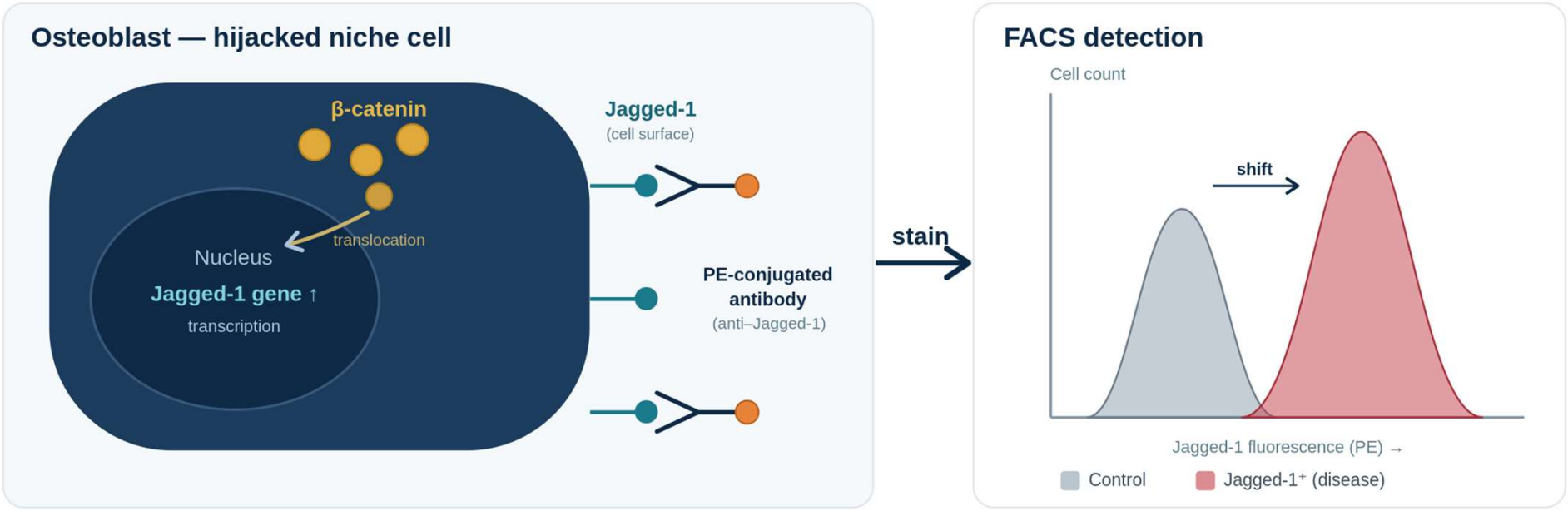
Inhibiting Jagged-1 removes the survival signal that shelters LSCs, opening the door to restored hematopoiesis.

Sources: Kode et al., Nature 2014;506:240 & Leukemia 2016;30:1. Rothzerg et al., J Cell Physiol 2023;238:1478.

MECHANISM

β-Catenin Translocation Drives Jagged-1, Detected by FACS

β-catenin → nucleus → Jagged-1 — activated β-catenin drives Jagged-1 overexpression, quantified as surface Jagged-1 by flow cytometry.



1 β-catenin → nucleus

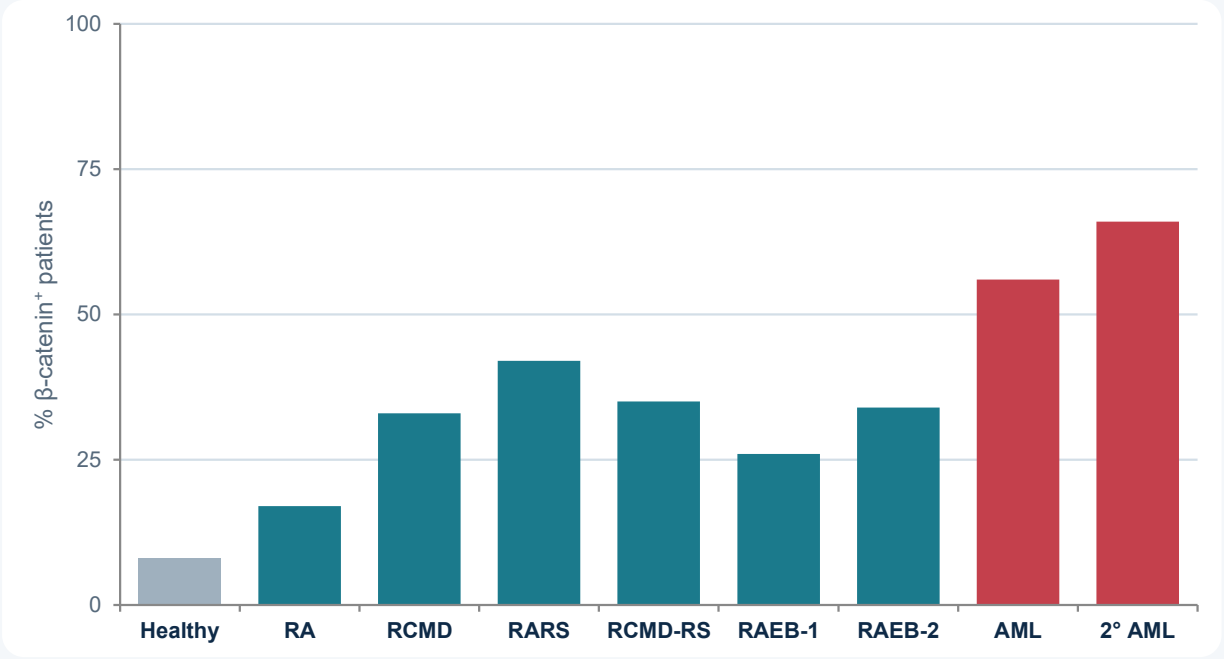
2 Jagged-1 overexpression

3 Detected by FACS

BIOMARKER

Jagged-1 / Notch1 Over-Expression Correlates with Disease Severity

Detected by FACS in bone marrow samples across the MDS→AML continuum — the osteoblastic signal is highest in AML, correlating with disease severity.



WHO DISEASE CLASSIFICATION — INCREASING SEVERITY →

Source: Mosialou et al., Cancer Cell 2025;43:1007

up to ~70%

of MDS/AML patients over-express the Jagged-1 pathway

>450

patient samples across the full MDS→AML continuum

Elevated across all MDS subtypes vs healthy marrow — and highest in AML and secondary AML, correlating with disease severity.

Tested across MDS subtypes (RA, RCMD, RAEB-1/2) and AML. Source: Mosialou et al., Cancer Cell 2025;43:1007.

EX VIVO EVIDENCE

ATI-D1 Activity in Human Patient-Derived MDS/AML Samples

Clonal suppression, tumor-cell death and restored hematopoiesis.

MEASURED CHANGES IN DISEASE STATE

Metric	Change	Disease state
Proliferating cells	0%	Healthy (low)
Proliferating tumor cells	↓ 60–100% in 86% of patients	MDS low / high
Dead tumor cells	↑ 50–100% in 50% of patients	MDS low / high
Myeloid cells	↑ 110%	AML low / high
Erythroid cells	↑ 100%	AML low / high

Suppresses MDS/AML clonal proliferation

Halts expansion of the malignant clone in patient samples.

Eliminates MDS/AML clonal progenitors

Drives death of the disease-initiating progenitor population.

Restores normal hematopoiesis

Recovers normal blood-cell production, including in AML samples.

Source: Mosialou et al., Cancer Cell 2025;43:1007.

IN VIVO EFFICACY

Reverses MDS→AML Progression in an Engineered Mouse Model

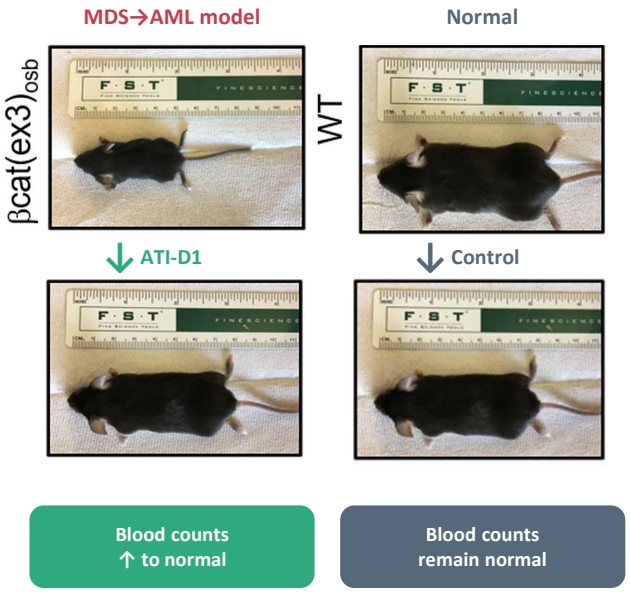
Also restores normal hematopoiesis in bone marrow damaged by malignancy

THE MODEL

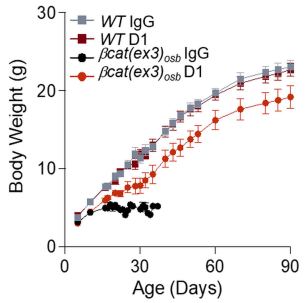
Mice engineered to express activated β-catenin (BCAT) — and consequently Jagged-1 — in osteoblasts are born frail with disease identical to human MDS, transforming to AML by day 10 and ultimate death. This mirrors the human MDS→AML progression seen clinically.

Treated with anti-Jagged-1

Treated model mice thrive, survive free of disease and show normal blood — evidence of potential to block the full MDS→AML continuum.

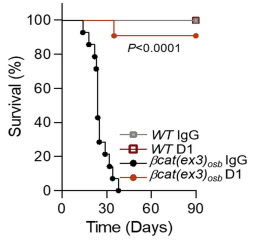


Body weight over time



ATI-D1 treated mice (red) gain weight at a rate approaching normal (grey)

Survival

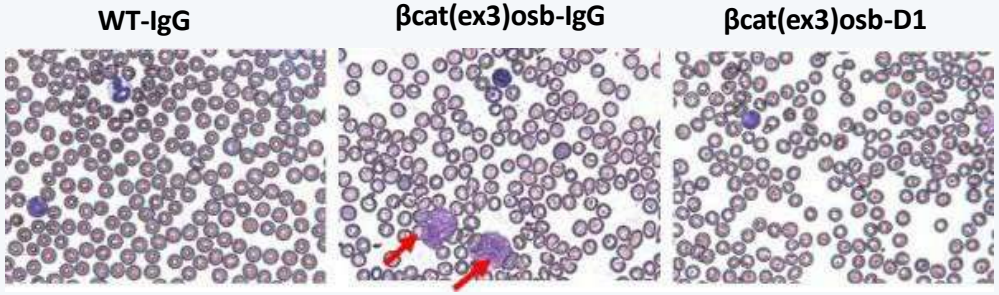


ATI-D1 treated mice (red) show improved survival vs control treated (black)

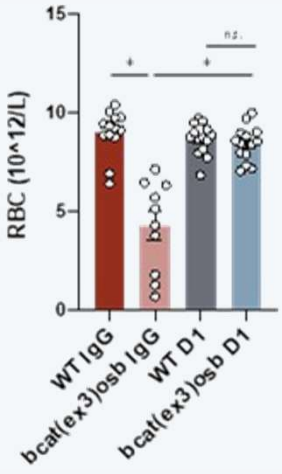
Source: Mosialou et al., Cancer Cell 2025;43:1007.

IN VIVO EFFICACY

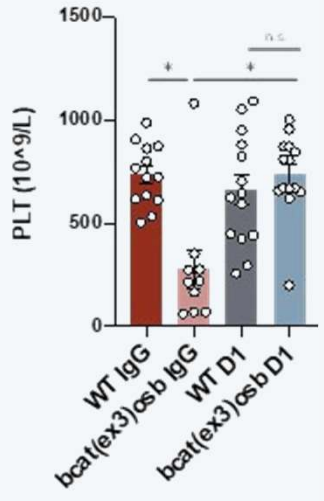
ATI-D1 Eliminates Excess Blasts *and* Restores Normal Hematopoiesis



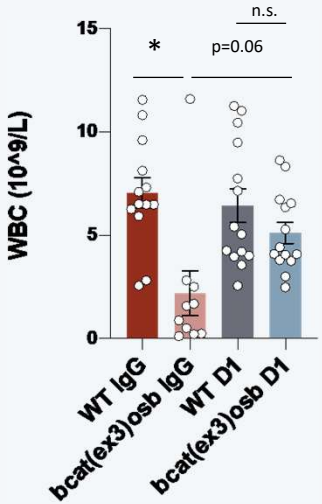
ATI-D1 treatment rescues anemia

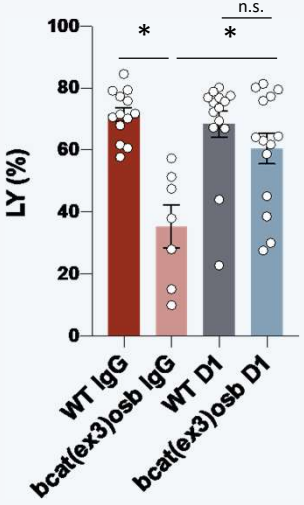


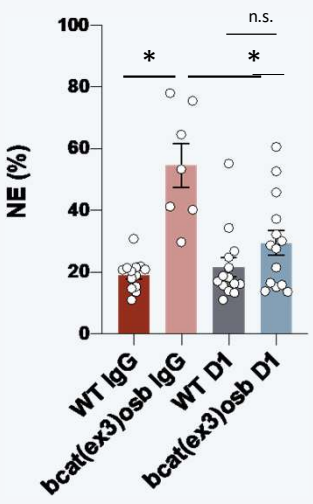
ATI-D1 treatment reverses thrombocytopenia



ATI-D1 treatment restores normal WBC, lymphocytes & neutrophil counts







Source: Mosialou et al., Cancer Cell 2025;43:1007

BREADTH OF ACTIVITY

ATI-D1 is Active Regardless of Tumor Mutational Status

Now collaborating with BEAT AML (Blood Cancer United) to correlate jagged-1 expression with ATI-D1 ex vivo activity, mutational status and patients' clinical outcomes

21 of 22

Jagged-1⁺ patient samples responded

ATI-D1 suppressed clonal expansion or induced tumor-cell death across diverse co-mutational backgrounds.

Source: Mosialou et al., Cancer Cell 2025;43:1007.

Selected for Jagged-1 over-expression

All 22 patients were selected for Jagged-1 over-expression. Their co-mutation profiles spanned ASXL1, FLT3, TP53 and IDH1/2, among others — the full spectrum of clinically relevant mutations.

Biomarker predicts response — not mutation subtype

Response tracked with Jagged-1 over-expression rather than any specific mutation. This positions Jagged-1 as a single, unifying biomarker for patient selection across cytogenetically distinct MDS and AML.

CMC DEVELOPMENT & MANUFACTURING

At the Midpoint of Development — Advancing Toward Clinical Testing

A de-risked CMC path: GMP antibody in hand, advancing toward Phase 1/2 clinical testing.

~8.0 g/L
Master cell bank titer, created & characterized

3 yrs
To clinical proof-of-concept

GMP ampules banked at Charles River Labs; 50 L pilot run completed and tested in a pilot non-human primate PK study.

Master Cell Bank
Created & characterized (~8.0 g/L)

GMP Banking
Ampules banked at Charles River Labs

Process Development
Scale-up & analytical methods

50 L Pilot Run
Tested in pilot PK study

Final Formulation
In progress

Clinical Batch
Planned for IND-enabling

Stability Testing
Planned

CLINICAL PLAN

Phase 1b/2 in MDS/AML: Path to Potential Accelerated Approval

DOSE ESCALATION

3 + 3 Design

- Open-label
- Incremental dose ranging
- Primary: safety, PK & RP2D
- Secondary: Efficacy signal & biomarker correlates

→

RP2D

cohort expansion

→

MDS Expanded Cohort

30% ORR assumption

n ≥ 20

AML Expanded Cohort

≥20% ORR assumption

n ≥ 20

Population

MDS: R/R after HMA therapy or HMA-ineligible. AML: Jagged-1 (Notch1-activated) marrow, R/R or no options.

Efficacy read-outs

MDS: ORR (IWG 2023), transfusion independence, cytopenia reduction. AML: ORR (ELN 2022) & hematologic improvement.

Dose groups

Four groups with an added level below MTD may refine the optimal dose.

Biomarker & PI

Secondary: response vs osteoblastic Jagged-1 expression. Lead investigator: Azra Raza, M.D., Columbia.

ROADMAP

Development Timeline, Milestones & Spend

Stage 1 Preclinical & IND-enabling / Clin Pharm	Stage 2 Phase 1a/b First-in-human	Stage 3 Phase 2 Potential accelerated approval	Stage 4 Phase 3 Confirmatory
2026–2027	**2028–2029** ◆	**2030–2031**	**TBD**
• CMC development/GMP Product • NHP PK/Toxicology • IND Package	• IND submission • Clinical data / safety • Safety/Signal/marker correlates	• FDA Phase 2 meeting • Phase 2 Clinical Trial • Data package for potential AA	• Confirmatory trial • Full approval • Market Launch

Alanis Therapeutics INC

Advancing precision antibodies across the MDS→AML continuum.

FOR MORE INFORMATION, PLEASE CONTACT

Robert Goodenow, Ph.D.

Chief Executive Officer

Robert.Goodenow@alanistx.com

949.291.9018

alanistx.com

6162 Nancy Ridge Dr., Suite 150, San Diego, CA 92121