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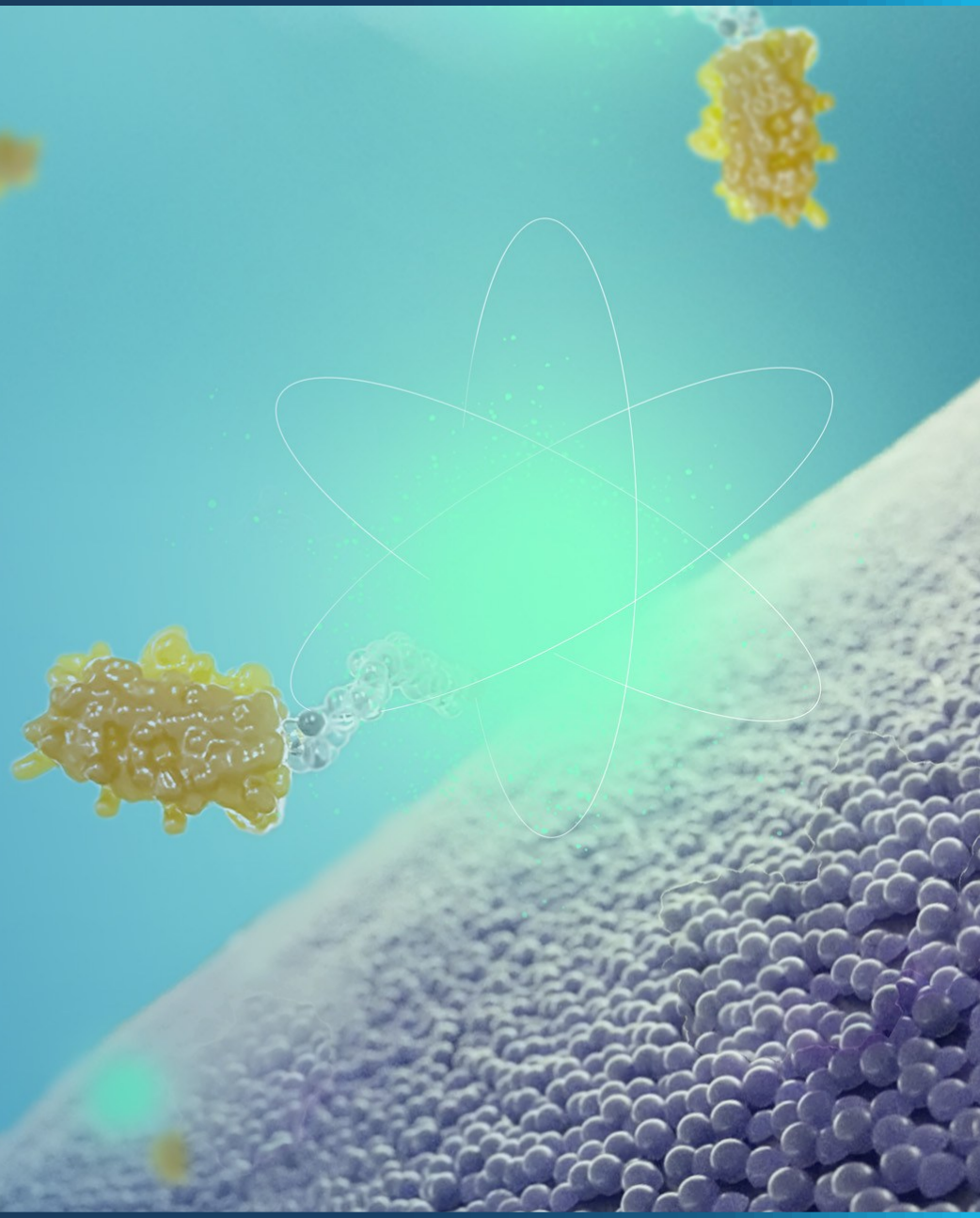
# Extending the Boundaries of Targeted Cancer Therapies with Radio-DARPins and Next-Gen Immune Cell Engagers



## Q3 Financials

October 30, 2025

Nasdaq, SIX Swiss Exchange: MOLN

# Disclaimer

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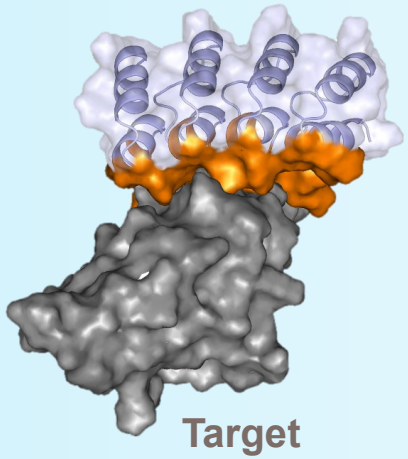
# Molecular Partners at a Glance

*Extending the Boundaries of Targeted Cancer Therapies*

**DARPin**
Designed Ankyrin Repeat Protein




## Our Company: MOLN

- Clinical-stage biotech company **pioneering DARPin therapeutics for patients**
- Operations & listing in Switzerland (SIX, 2014) and US (Nasdaq, 2021), founded 2004
- Financed until 2028 through key value inflection points (CHF ~105 M*)

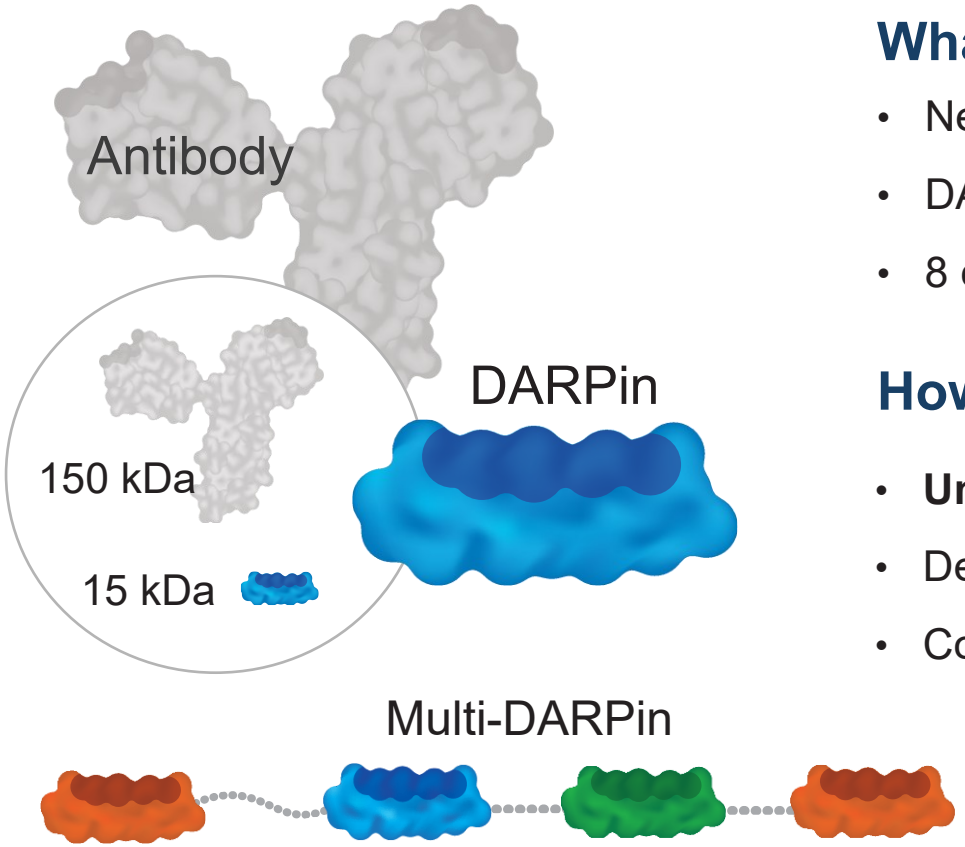
## Our Capabilities: Technology, Team, Collaborations

- Proprietary DARPin Platforms, including **Radio-DARPins** and **Switch / T cell engagers**
- Strong international team to execute up to clinical POC
- Global partnerships to access technology & capabilities (Orano Med)

## Our Pipeline: Patient Value

- Differentiated **Assets** with focus in **Oncology**,
- **MP0712 / Targeted radiotherapy** and **MP0533 / next-gen immune cell engagers** for patients across indications with high unmet medical need

# The DARPin Modality and Molecular Partners' Strategy




## What we invented

- New class of therapeutics: Designed Ankyrin Repeat Proteins **(DARPins)**
- DARPins **close the gap between small molecules and antibodies**
- 8 clinical-stage compounds, **>2500 patients treated**

## How we apply it

- **Unique DARPin solutions**, not addressable by antibody designs
- Demonstrate **true patient value** with **early clinical readouts**
- Combine our **capabilities with world-class partners**

# Our Pipeline – Targeted DARPin Therapeutics for Patients

| PLATFORM | CANDIDATE | RESEARCH | PRE-CLINICAL | PHASE 1 | PHASE 2 | PHASE 3 |
|---|---|---|---|---|---|---|
| Radio-DARPin Therapy (RDT) | **MP0712** | **SCLC & NECs** *$^{212}$Pb - DLL3* | | oranomed *Co-development** | | |
| | **MP0726** | **Ovarian Cancer** *$^{212}$Pb - MSLN* | oranomed *Co-development** | | | |
| | Undisclosed Programs | **Solid Tumors** | *Up to 8 programs** | | | |
| Next-Gen Immune Cell Engagers | **MP0533** | **r/r AML and AML/MDS** *CD33 x CD123 x CD70 x CD3* | | | | |
| | **Switch-DARPin T Cell Engager** | *CD3 x costim x TAAs* | | | | |
| | MP0621 (Switch-DARPin) | **HSCT** *cKit x CD16a x CD47* | | | | |
| | MP0317 | **Advanced Solid Tumors** *FAP x CD40* | | | | |



*The co-development agreement with Orano Med includes up to 10 targeted radiotherapy programs, including MP0712 and MP0726.
AML, acute myeloid leukemia; DLL3, Delta-like ligand 3; HSCT, hematopoietic stem cell transplant; MDS, myelodysplastic syndrome; MSLN, mesothelin; NEC, neuroendocrine cancer; r/r, relapsed/refractory; SCLC, small cell lung cancer; TAA, tumor-associated antigen.

# Corporate Highlights – Q3 2025

| | |
|---|---|
| **MP0712** | • MP0712 ($^{212}$Pb x DLL3) **IND-enabling studies completed,** IND filed<br>• Initiated imaging and dosimetry with $^{203}$Pb-labeled MP0712 |
| **Radio-DARPin Therapy (RDT)** | • **Strategic collaboration** with **Orano Med expanded to ten** $^{212}$Pb programs<br>• Lead candidate MP0726 targeting mesothelin (MSLN) nominated based on pre-clinical data presented at AACR and SNMMI 2025 |
| **MP0533** | • **Improved response rate and antitumor activity in low disease burden patients** of ongoing Phase 1/2a reported at EHA 2025<br>• Implemented amended dosing scheme, with cohort 9 fully recruited and cohort 10 ongoing |
| **Switch-DARPin** | • **Logic-gated T cell activation with co-stimulation** in solid tumors presented at AACR 2025 |
| **MP0317** | • Study protocol approved for combo IIT with standard-of-care in cholangiocarcinoma |
| **Operations** | • **Strong financial position** with CHF 105 M in cash as of September 30, 2025<br>• Completed strategic review of operations and organization, extending runway into 2028<br>• Appointed Martin Steegmaier, PhD, as CSO and member of Executive Committee* |



*Effective October 1, 2025.
IIT, investigator-initiated trial; IND, investigational new drug.

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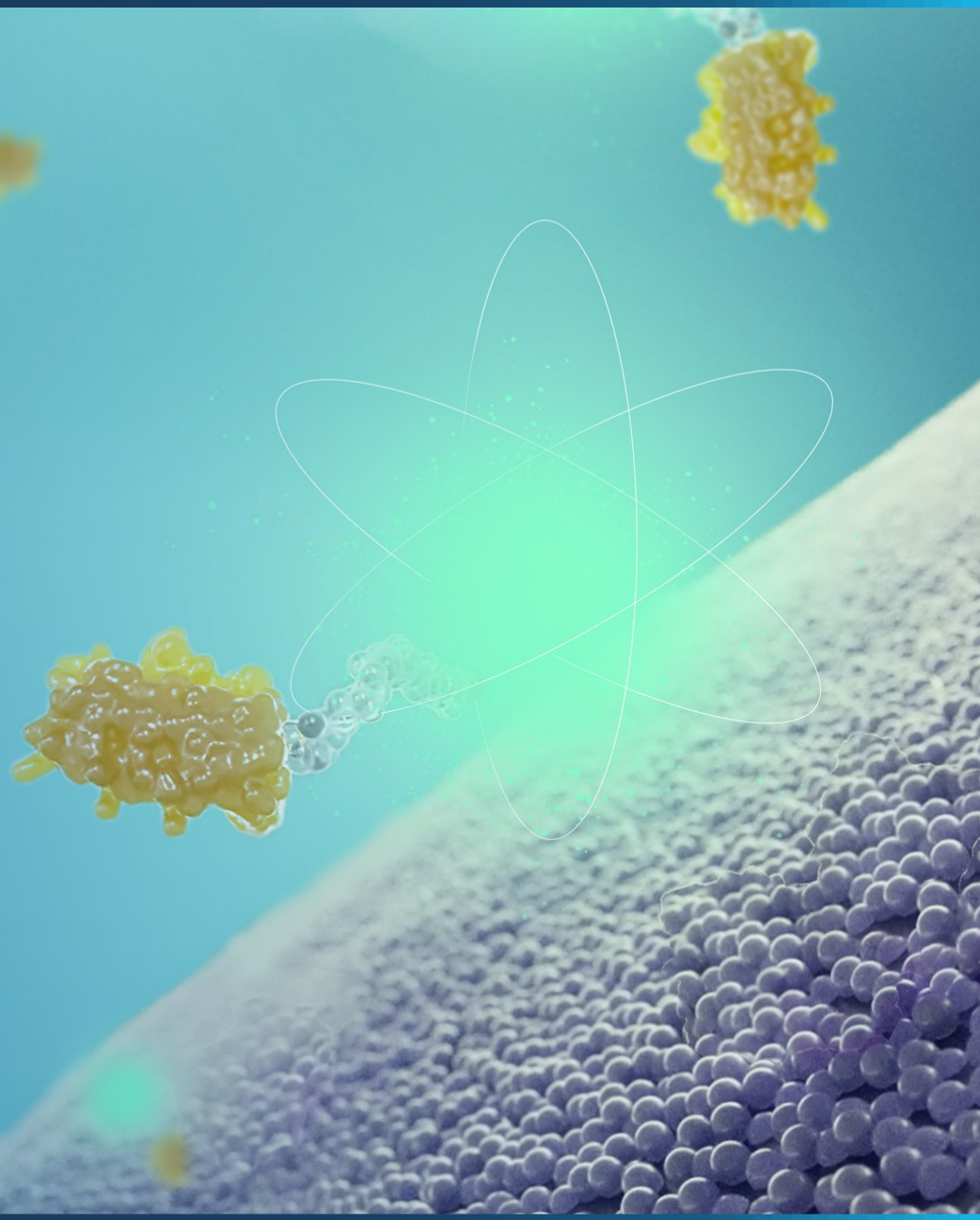
# MP0712 & Radio-DARPin Therapy

Custom-engineered to create vectors ideal for radiopharmaceuticals



# Radio-DARPins as Versatile Therapeutic Candidates

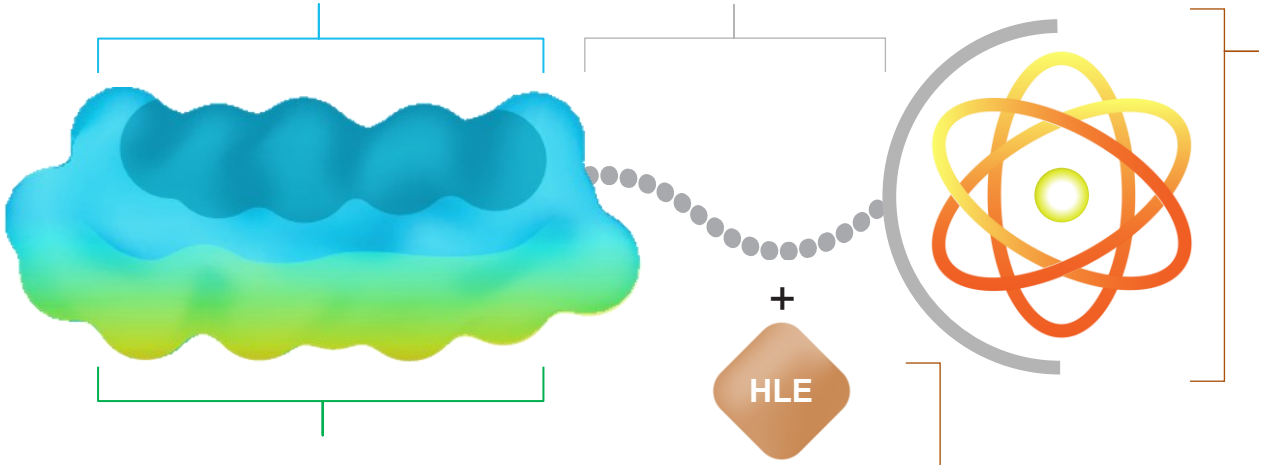
*Combining versatile DARPin features with the power of $^{212}$Pb for next-gen Targeted Alpha Therapy*

## DARPin: IDEAL VECTOR FOR RADIOPHARMACEUTICALS

- Proven selective targeting
- High affinity, tumor retention
- Broad target space
- Small size

## LINKER & CHELATOR

- Established DOTAM




## $^{212}$Pb: ALPHA-EMITTING THERAPEUTIC ISOTOPE

- Proven clinical efficacy
- Fast & high energy deposition
- Safe profile
- Ideal waste management

## SURFACE ENGINEERING

- High stability
- Reduce kidney accumulation

## HALF-LIFE EXTENDER

- Half-life tuning
- Promote tumor uptake

# MP0712, the first $^{212}$Pb-DLL3 Targeted Radiotherapeutic for SCLC

## SCLC: critical unmet need, limited treatment options

- Median progression free survival (mPFS) ~3 months[1,2]
- 5-year overall survival (OS) ~3%[1,2]

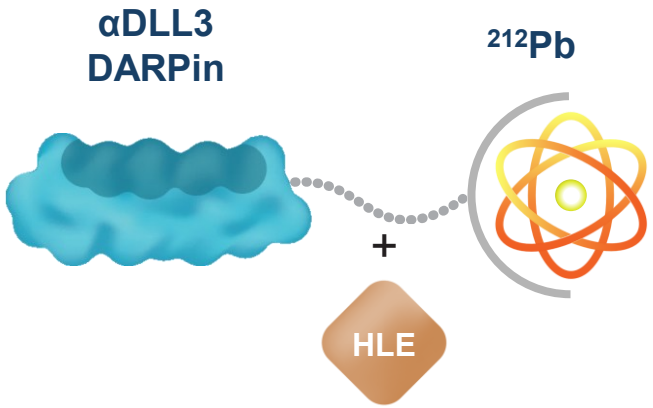
## DLL3: a validated target for SCLC

- Expressed in >85% of SCLC patients[3] and in neuroendocrine cancers
- No expression in healthy tissues
- Tarlatamab[4], approved DLL3 targeting drug (T cell engager)
  - ORR ~40%, DOR 9.7 months, PFS 4.3 months

## MP0712: targeted delivery of alpha radiation with $^{212}$Pb

- DLL3 DARPin optimized for selective delivery of payload to tumor
- $^{212}$Pb payload: high energy alpha emissions in short time frame
- Potential for combinations with immunotherapy

### MP0712 product composition

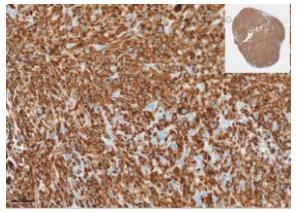



1.Treatment of refractory and relapsed small cell lung cancer, UpToDate; 2. SEER;
3. Rojo et al., Lung Cancer 2020; 4. Phase 2 DeLLphi-301 study (NCT05060016).
DOR, duration of response; HLE, half-life extension; ORR, overall response rate; SCLC, small cell lung cancer.

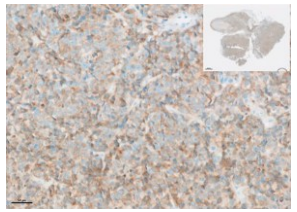
# MP0712: Potent Efficacy at Clinically-Relevant Dose

**DLL3 expression & distribution by IHC**

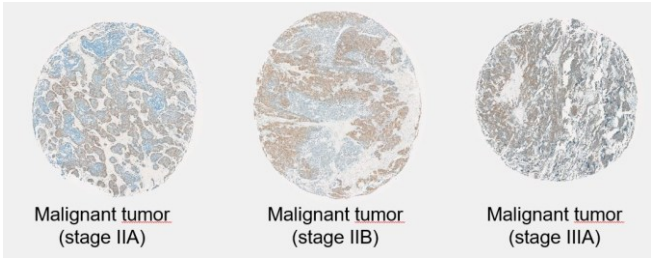
hDLL3-MC38 tumors



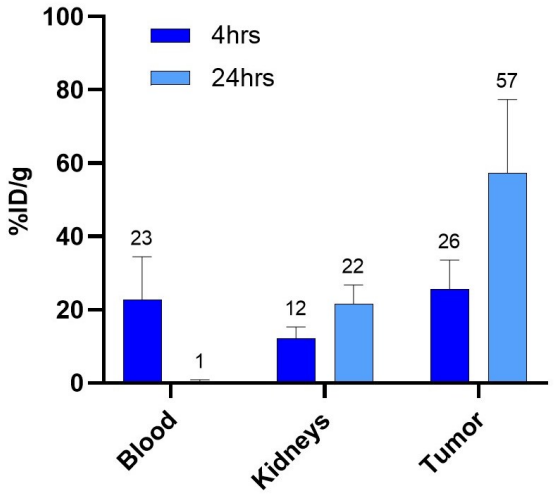
NCI-H82 tumors



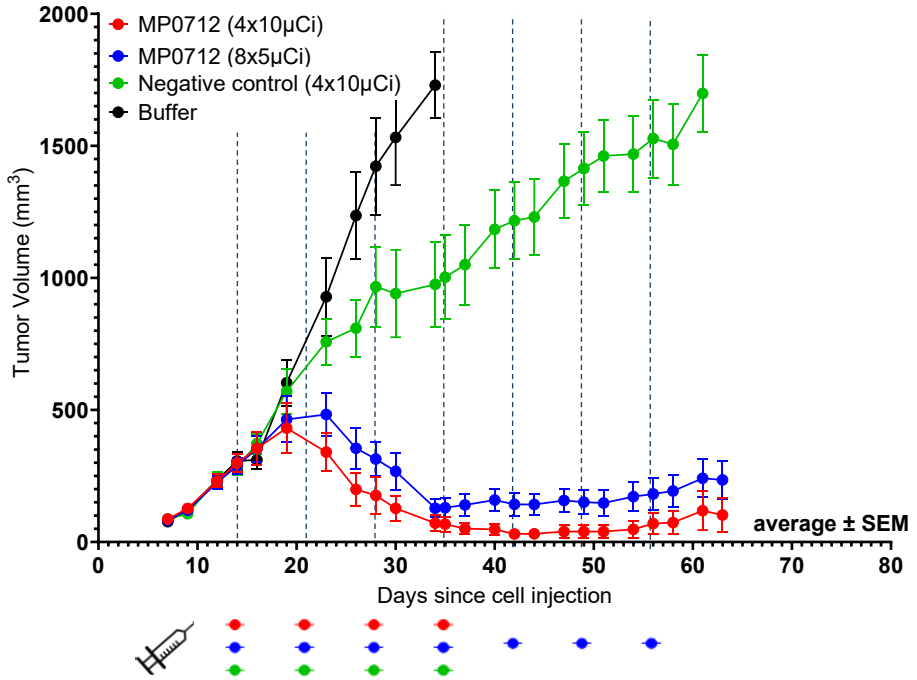
Human SCLC tumors




*Mice xenografted **i.v.** with*
***NCI-H82 tumor cells***




*R2G2 mice xenografted **s.c.** with*
***NCI-H82***




- **MP0712 reached T:K ratios > 2 in mouse model matching clinically relevant DLL3 expression levels**
- **MP0712 induces complete and durable tumor regression in NCI-H82 tumor model at 10 µCi injected every week**



*Steiner et al, TRP 2024 (oral presentation)*
*Croset et al, EANM 2024 (oral presentation)*
*Lizak et al, SNMMI 2024 (oral presentation)*

NCI-H82 i.v. model: $^{212}$Pb-DOTAM-DARPin - single injection - dose: 10 µCi (0.01 mg/kg)
Efficacy study in NCI-H82 s.c. model / MP0712 and negative control injected 4 x 10 µCi at 0.01 mg/kg or 8 x 5 µCi at 0.01mg/kg every 1; 10 µCi = 370 kBq

# Outline of MP0712 Clinical Development Strategy

- Patients: Focus on small cell lung cancer (SCLC), secondly on neuro-endocrine cancers (NECs)
- Imaging and dosimetry ongoing under Section 21, initial data* to be presented at TRP 2025
- **Phase 1 study to start in H2 2025, initial safety and efficacy data in 2026**

***PHASE 1/2a STUDY***

**Phase 1: $^{212}$Pb Dose Escalation**
Main objective: safety, RP2D; N=15–27 patients
Phase 1 includes an imaging and dosimetry step with $^{203}$Pb

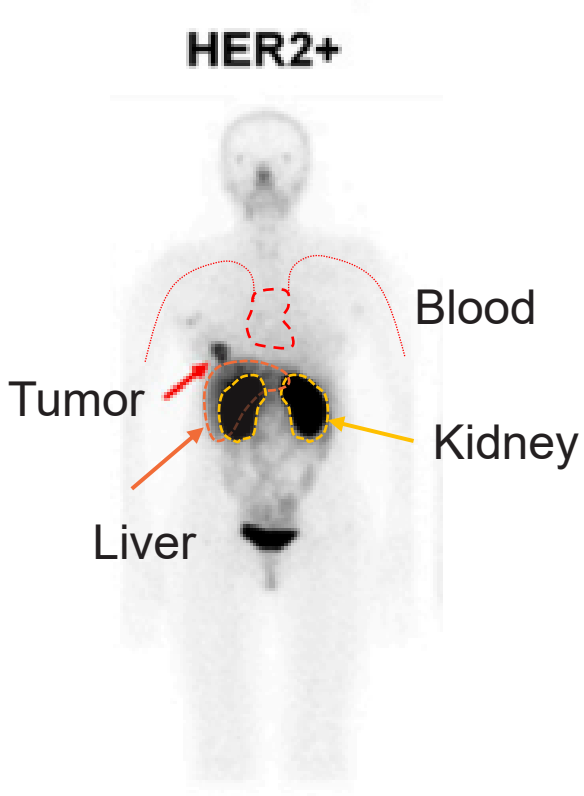
**Phase 2a – Dose Expansion and PoC – SCLC+NEC**
Main objective: efficacy signals, confirm RP2D; N=30 patients

**Registration study**
2L+ SCLC patients

Phase 2
- 1–2L combination with IO SCLC
- Registration in patients with other NECs

**Molecular Partners has received and accepted a request from Nuclear Medicine Research Infrastructure (NuMeRI) in South Africa to provide MP0712 for imaging use under the legal framework in South Africa for compassionate care (also referred to as Section 21 of the Medicines and Related Substances Act). This approach enables the generation of first images applying MP0712 labelled with 203Pb in patients with SCLC. While the decision of where and how to share data from the image work under Section 21 remains at the discretion of NuMeRI, the Company anticipates providing an update on MP0712 in H2 2025.*

# What are we looking for in images coming from Section 21?




**Phase I Trial of $^{99m}$Tc-(HE)$_3$-G3, a DARPin-Based Probe for Imaging of HER2 Expression in Breast Cancer**

Olga Bragina[1,2], Vladimir Chernov[1,2], Alexey Schulga[2,3], Elena Konovalova[3], Eugeniy Garbukov[4], Anzhelika Vorobyeva[2,5], Anna Orlova[2,6], Liubov Tashireva[7], Jens Sörensen[8], Roman Zelchan[1,2], Anna Medvedeva[1], Sergey Deyev*[2,3], and Vladimir Tolmachev*[2,5]

**$^{203}$Pb Imaging of a Patient with Tumor Lesions:**

- ✓To inform **dosimetry** of therapeutic drug ($^{212}$Pb)
- ✓To understand **biodistribution** of drug

**Tumor > Kidney, Liver**

+ acceptable blood levels

**MP0712 Outlook:**

- ➢ Update on early imaging work in 2025 (TRP Summit)
- ➢ Phase 1 start in 2025, with initial clinical data 2026

# MP0726, $^{212}$Pb x MSLN Radio-DARPin for Ovarian Cancer (OC)

## OC: high medical need and marginal progress

- > 50% patients die within 5 years post-diagnosis (diagnosis often in late stage)
- Poor treatment options: ~80% recurrence rate post 1L chemo, limited 2L options (FRα-targeted Tx relevant for only 40% patients)

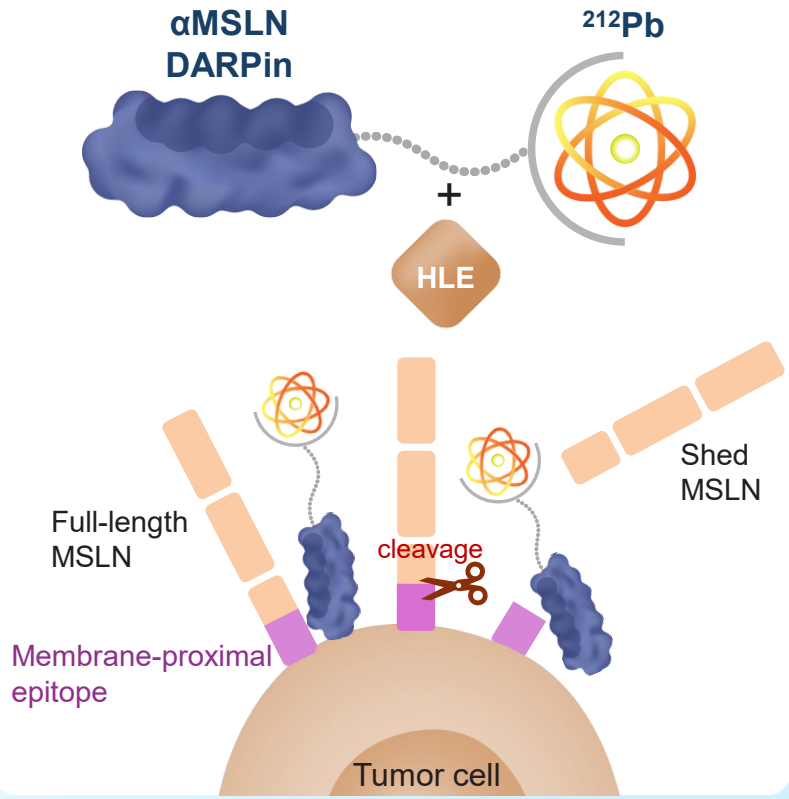
## MSLN: a promising target for OC as 1st indication

- Highly expressed in OC (>80% prevalence), expression maintained in metastases
- Shed MSLN detected in serum of OC patients, might limit efficacy of MSLN-targeted therapies[1,2,3,4] (e.g., CAR T/NK, ADC, TCE in development)

## RDT x MSLN: targeted delivery of alpha radiation with $^{212}$Pb

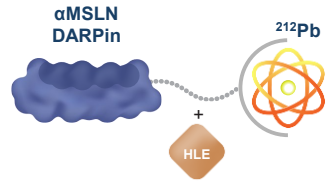
- MSLN DARPin targets **membrane-proximal epitope** (and not shed MSLN)
- $^{212}$Pb payload: high energy alpha emissions in short time frame
- Potential for combinations with immunotherapy (incl. next-gen TCEs)

## Product composition

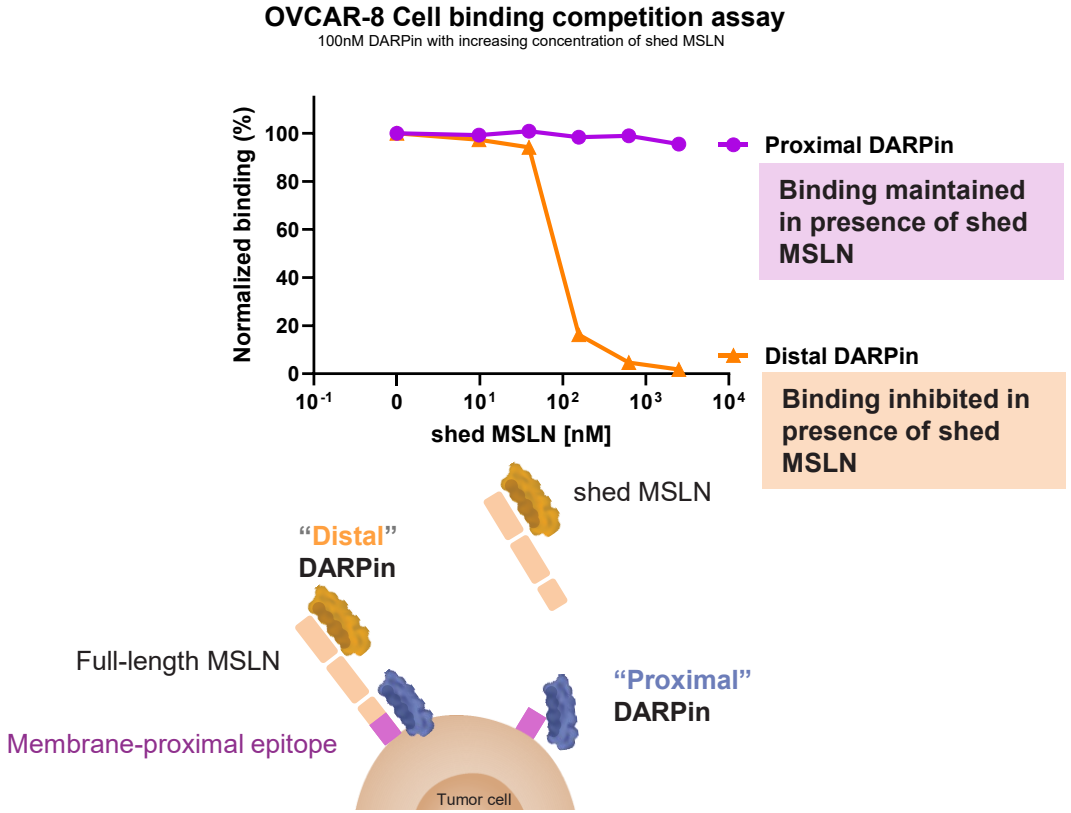



1. Awuah et al. 2016; 2..Zhang et al. 2011; 3.Smith et al. 2024 (ASCO poster); 4.Pastan et al, 2024.
CAR, chimeric antigen receptor; FRα, folate receptor alpha; MSLN, mesothelin; NK, natural killer cell; OC, ovarian cancer; Tx, treatment.

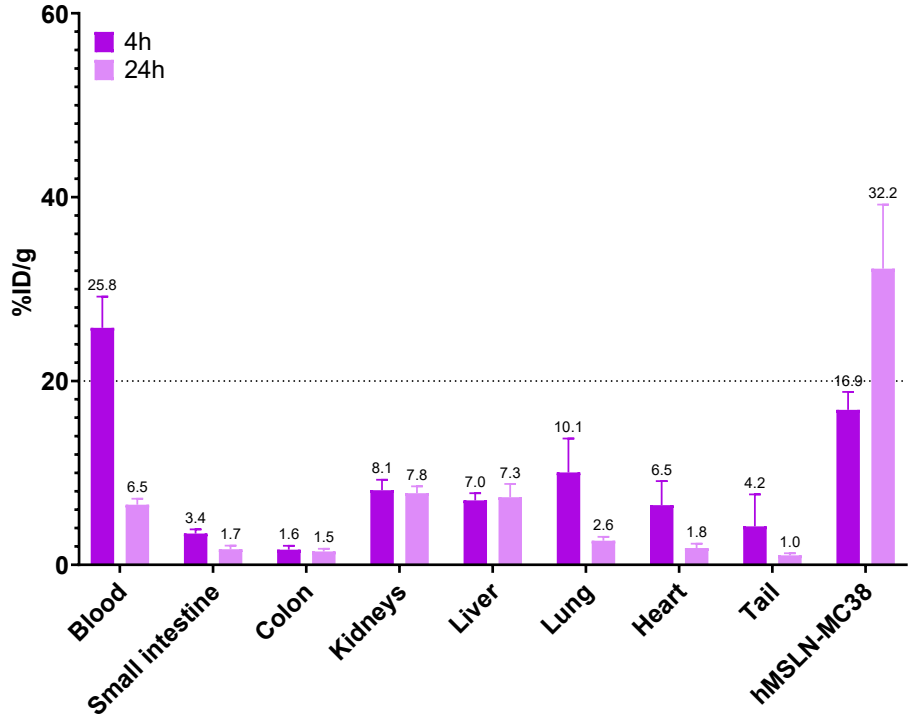
# Attractive Biodistribution Profile of MSLN Radio-DARPin




## Cell binding maintained despite shed MSLN




## Favorable biodistribution in hMSLN-MC38 tumor model






Wullschleger S, et al., AACR 2025.

Mice xenografted s.c. with hMSLN-MC38 (Biocytogen)
Dose: 10 µCi of $^{212}$Pb at 0.01 mg/kg of MSLN DARPin

# Global Partnership to Develop $^{212}$Pb Radio-DARPin Therapeutics

*Combining DARPin versatility with the power of $^{212}$Pb for next-gen Targeted Alpha Therapy*

**MOLECULAR PARTNERS**
***PIONEERS of DARPin THERAPEUTICS***


**ORANO MED**
***PIONEERS of TARGETED ALPHA THERAPY***

## FULL VALUE CHAIN PARTNERSHIP

### World class technologies & capabilities combined

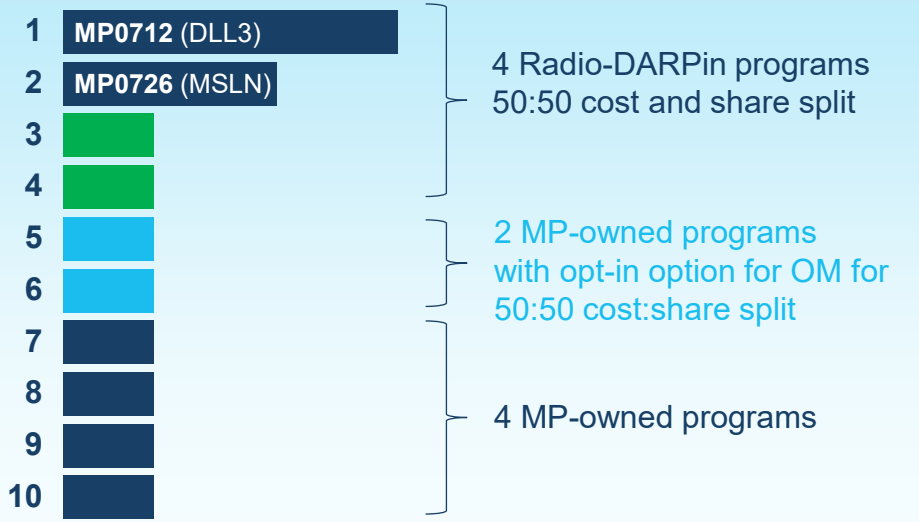
INDIANA, US:
Industrial scale manufacturing
Global shipping hub
ATLab US

TEXAS, US:
Preclinical development
GMP supply for early clinical phases

SWITZERLAND:
Preclinical assessment
DARPin engine, fast & high throughput

FRANCE:
$^{212}$Pb starting material
ATLab Europe

### Pipeline of ten $^{212}$Pb radiotherapy products



# Our Partner Orano Med – Pioneer of Targeted Alpha Therapy

## Targeted Alpha Therapy with $^{212}$Pb

**Alpha therapy**

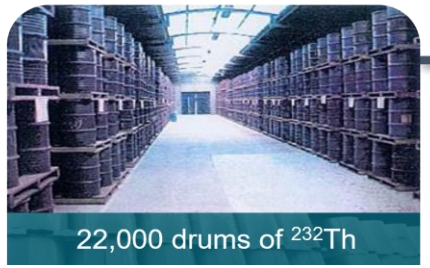
- **High cytotoxicity**: DNA double-strand break, high energy deposition, no need for receptor internalization
- **Targeted effect**: short range of action with potential to target microlesions, less impact on healthy tissues

**Lead-212 ($^{212}$Pb)**

- **Short-half life** (~11 h): out-patient administration, easy waste management, high-dose rate, flexible dosing
- **Clean decay** with single alpha emission and effective chelating agent, limiting circulation of free daughter isotopes

## Orano Med as Pioneer of $^{212}$Pb Targeted Alpha Therapy

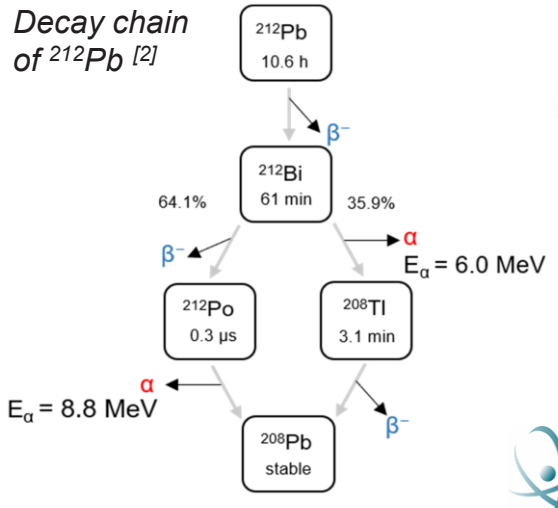
- Unique, independent **supply of $^{212}$Pb** as alpha emitting therapeutic isotope
- **Large scale GMP manufacturing** capabilities
- Fully integrated research and preclinical development platform
- **Clinical capabilities** demonstrated with $^{212}$Pb and lead program AlphaMedix™, outlicensed to Sanofi in Sept 2024, in Phase 2
- Strong collaboration partner with MP since early 2023





Lead-212 is obtained **chemically** by **successive extractions and purifications** of the descendants of thorium-232

*Decay chain of $^{212}$Pb* [2]




oranomed



1. Zimmermann, *J Nucl Med*, 2023.
2. Li et al., *Materials* 2021.

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# MP0533

Tetra-specific T-cell Engager for AML

# MP0533 Enables T Cell-Mediated Killing of AML Blasts and Stem Cells

## r/r AML: critical unmet need, quick relapse despite new treatments

- 5-year OS ~30%; fast-progressing disease
- Leukemic stem cells drive relapse

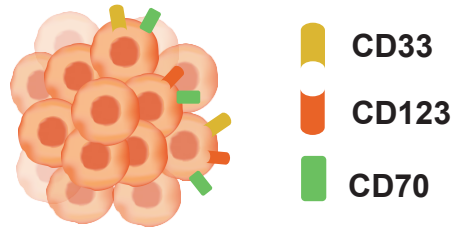
## CD123, CD33, CD70: broadly expressed targets on AML cells

- Co-expressed on blasts and leukemic stem cells across patients
- Single or no expression on healthy cells
- Clinically validated targets with mono-targeting treatments (ADCs, mAbs)

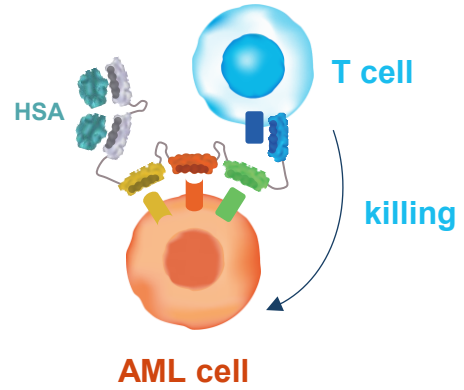
## MP0533: avidity-driven, tetra-specific T-cell engager

- Preferential killing of AML blasts and leukemic stem cells, while sparing healthy cells
- Broad patient population: amenable to chemo-resistant patients, mutation-agnostic
- Attractive therapeutic index with acceptable safety and demonstrated efficacy

**AML cells & targets**



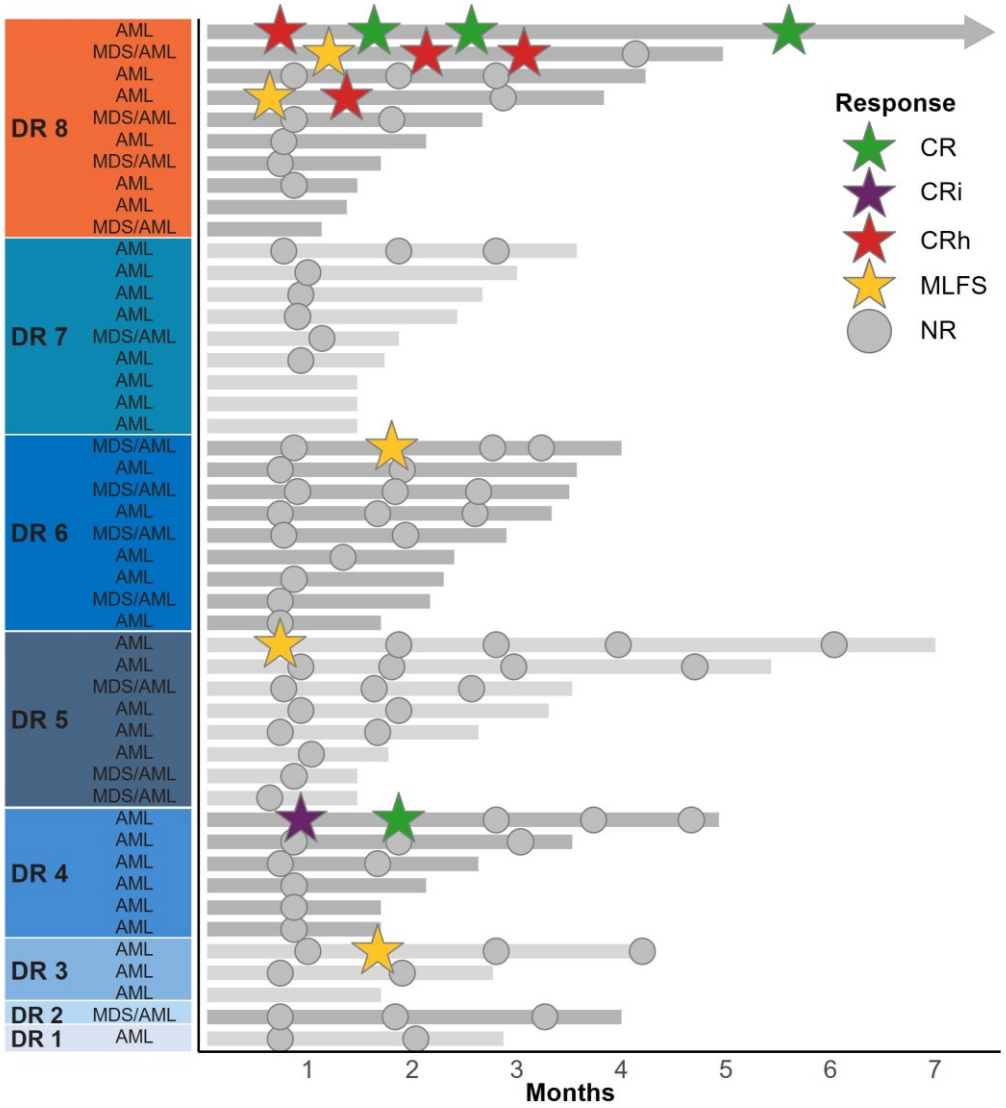

**MP0533 & mode of action**






ADC, antibody drug conjugate; HSA, human serum albumin; mAb, monoclonal antibody; r/r, refractory / relapsing; OS, overall survival.

# Encouraging Clinical Responses Observed with Intermediate Densification

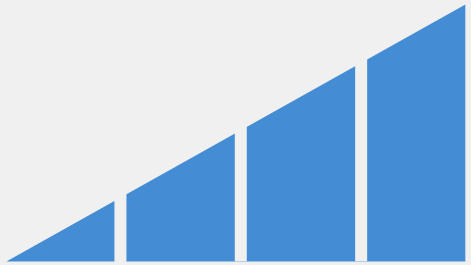



**Improved response rate and depth observed in Cohort 8:**

- **DR 1–7 –** 4 of 33 evaluable patients achieved a response: 1 CR (DR 4) and 3 MLFS (1 each DR 3, 5, 6)
- **DR 8 –** with the accelerated step-up dosing, 3 of 8 evaluable patients responded after cycle 1: 1 CR and 2 CRh as best overall response
- One patient in DR 8 is still on treatment and shows a response duration > 12 months

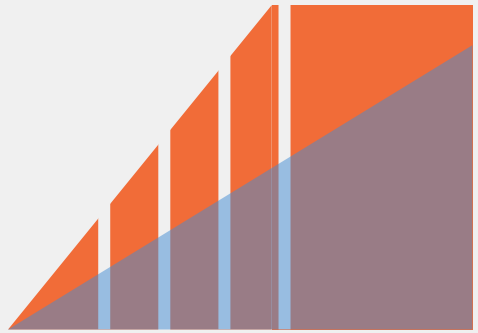
## Dose escalation (DR 1–7)

- Limited clinical activity
- Loss of exposure driven by TMDD and ADAs in some patients



## Intermediate densification (DR 8)

- **Additional Day 12 dose** for **steeper & faster dose escalation,** addressing TMDD



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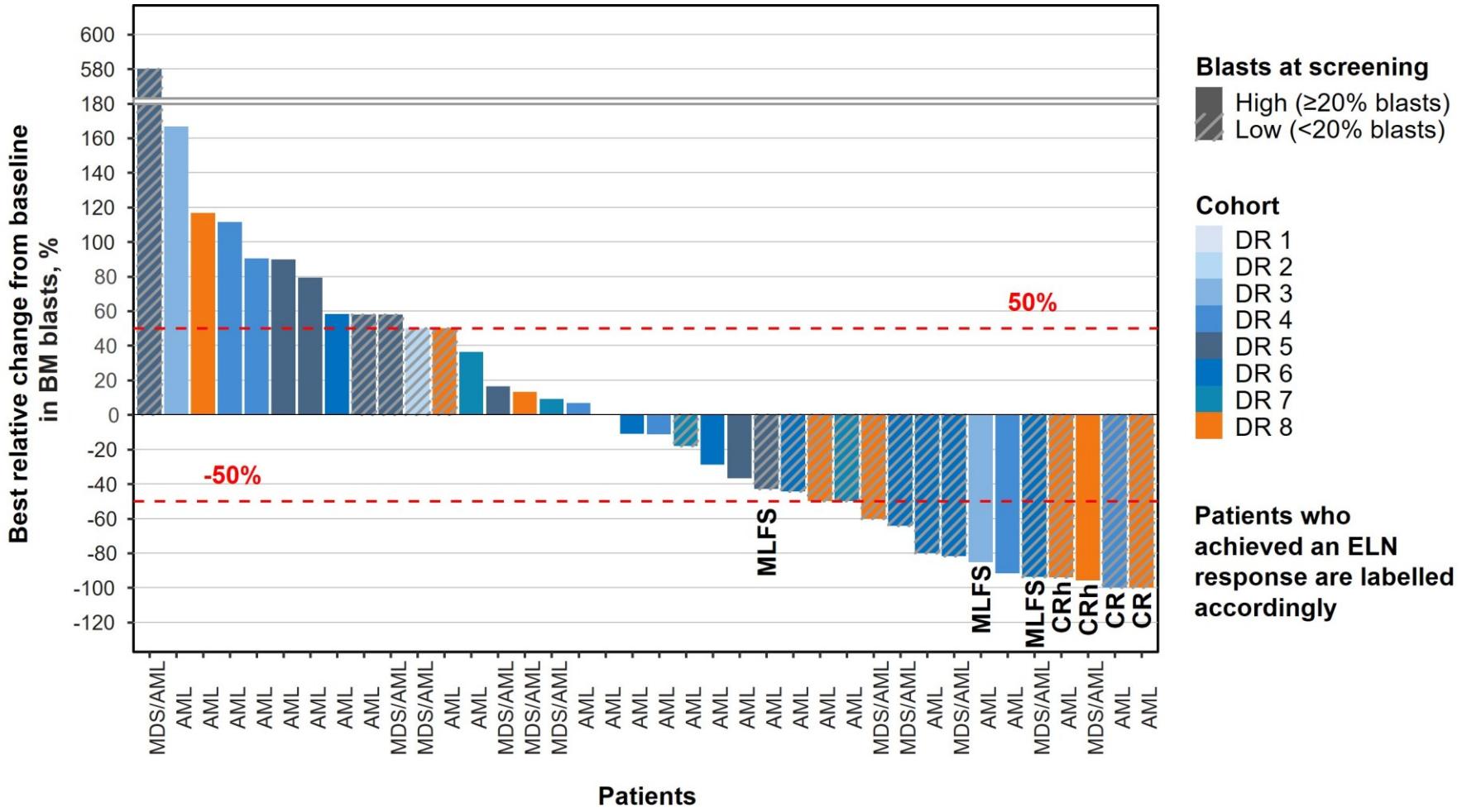
Bories, et al. EHA 2025 Poster Presentation
Data cut-off: 14 April 2025
*Preliminary data as study is ongoing, subject to final data validation.*

Response was assessed according to ELN 2022 criteria: Döhner et al. Blood 2022;140(12)1345-77.
ADA, anti-drug antibody; CR, complete response; CRh, CR with partial hematologic recovery; CRi, CR with incomplete hematologic recovery; DR, dosing regimen; ELN, European LeukemiaNet; MLFS, morphologic leukemia-free state; TMDD, target-mediated drug disposition.

# Encouraging Blast Reduction Observed, Particularly in Patients with Lower Disease Burden at Baseline*

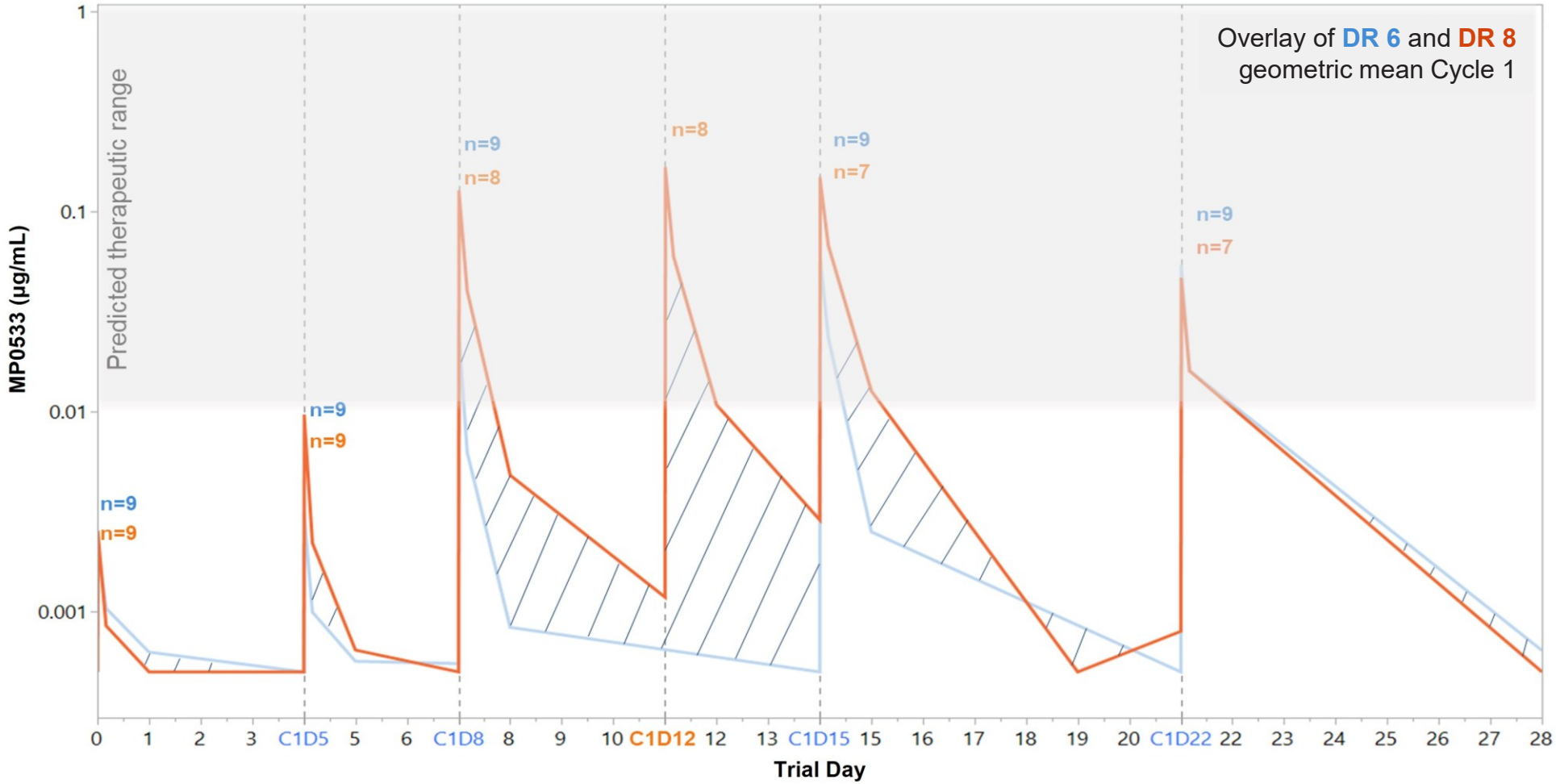





Bories, et al. EHA 2025 Poster Presentation
Data cut-off: 14 April 2025
*Preliminary data as study is ongoing, subject to final data validation.*

*Lower disease burden defined as patients with baseline blast <20% in bone marrow.
BM, bone marrow.

# Improved MP0533 Exposure Achieved with Steeper and Denser Step-up Dosing Regimen in DR 8



# Further Dose Densification to Demonstrate Full Potential of MP0533

*Protocol amendment to optimize MP0533 exposure*

## Summary of DR 1–8 data[1]

| | N (evaluable patients) | Days exposed to predicted therapeutic range in cycle 1 | Patients with >50% blast reduction | Response rate (number of responders) |
|---|---|---|---|---|
| DR 1–7 | 33 | < 2 days | 30% | 12 % (4) |
| DR 8 | **8** | **4 days** | **60%** | **37.5 % (3)** |

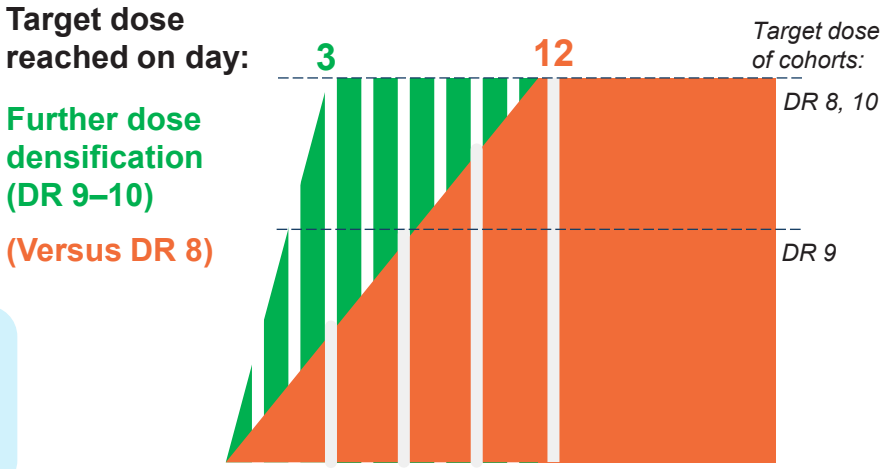
## Objectives of protocol amendment (DR 9–10):

- Improve the exposure profile of MP0533 in patients
- Increase depth and duration of clinical responses

## How:

- Dose densification (accelerated step-up dosing & higher dose frequency) to overcome TMDD
- Premedication with B cell-depleting agent to mitigate loss of exposure

## Amended Dosing Scheme*




## Outlook: Initial data from DR 9 to be presented at ASH 2025

- Dosing of patients in DR 10 on-going
- Combo trials (Aza/Ven) initiation in 2026 pending decisional data of cohorts 9-10

1. Bories, et al. EHA 2025 Poster Presentation
Data cut-off: 14 April 2025
*Preliminary data as study is ongoing, subject to final data validation.*

*Dosing scheme not to scale. DR, dose regimen; TMDD, target-mediated drug disposition.

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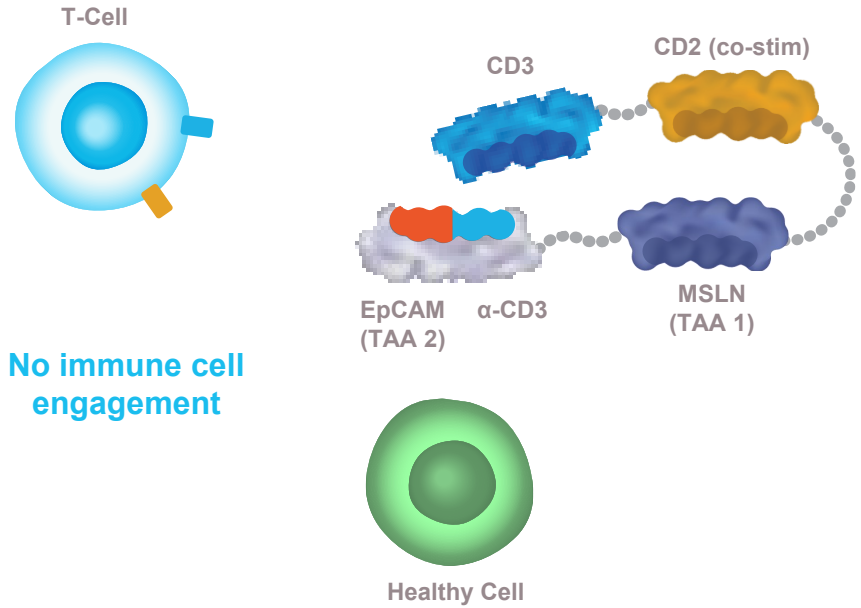
# Switch-DARPin Platform

Next-generation T cell engagers

# CD3 Switch-DARPin for Next-Gen TCEs with Enhanced Function

*Tackling current limitations of TCEs in solid tumors*

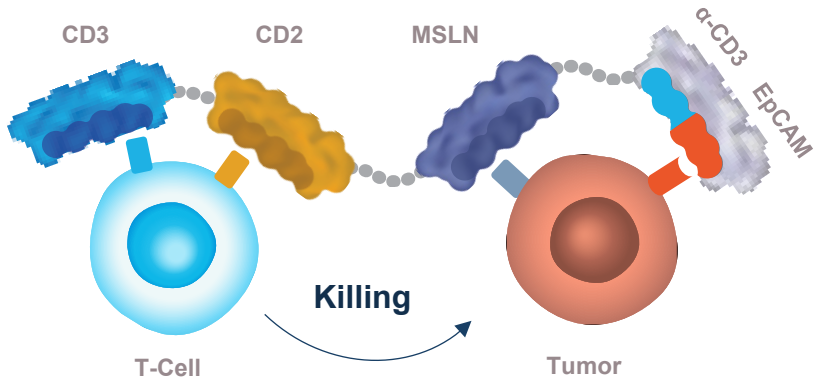
**OFF** **CD3 DARPin masked by 2-in-1 Switch in absence of TAAs**




No immune cell engagement

- TCE is silent and inactive in circulation

**ON** **Binding to TAAs releases CD3 Switch-DARPin**




Immune cell-mediated killing

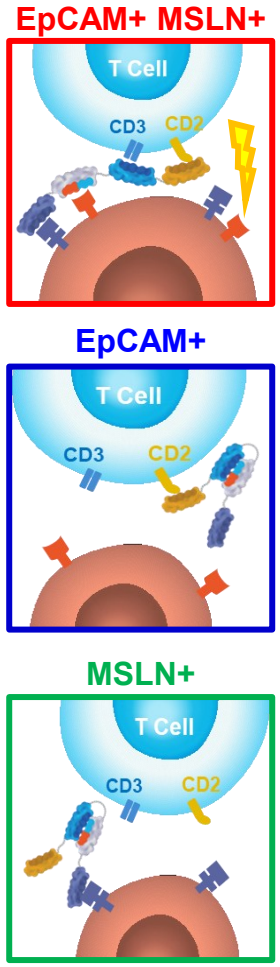
- TCE is activated to kill the tumor cell
- TCE is co-stimulated (no exhaustion)

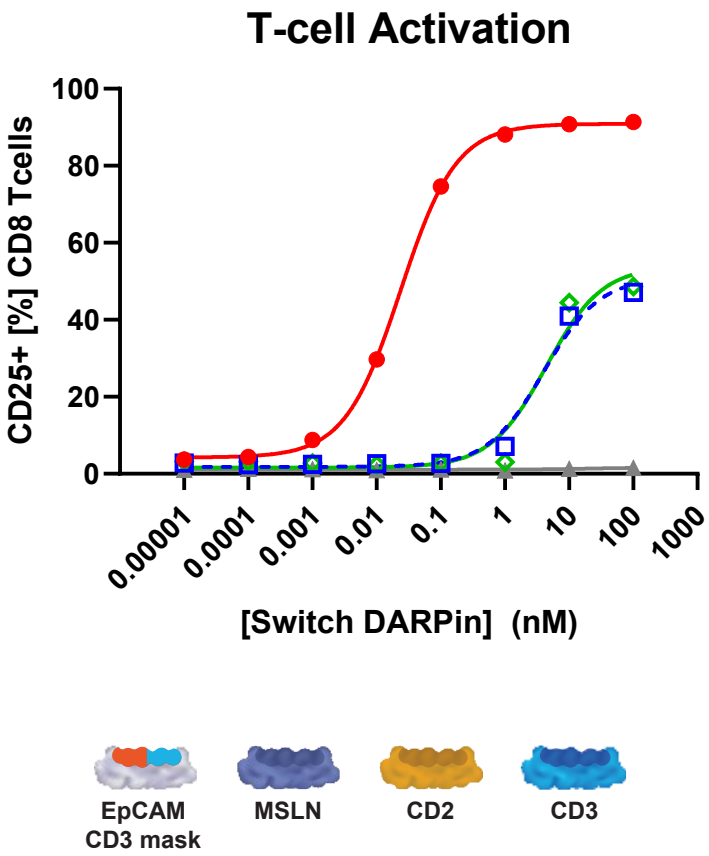
**Next update** on CD3 Switch TCE at SITC 2025

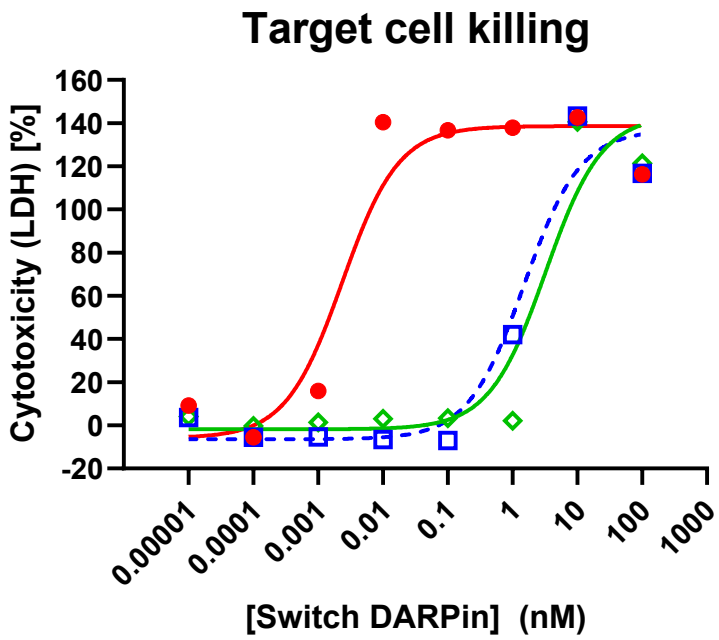


TAA, tumor associated antigen; TCE, T cell engager.

# MSLN x EpCAM x CD2 x CD3 Switch-DARPin Enables “AND-Gate” for Preferential Targeting of Double vs Single TAA Expressing Cells



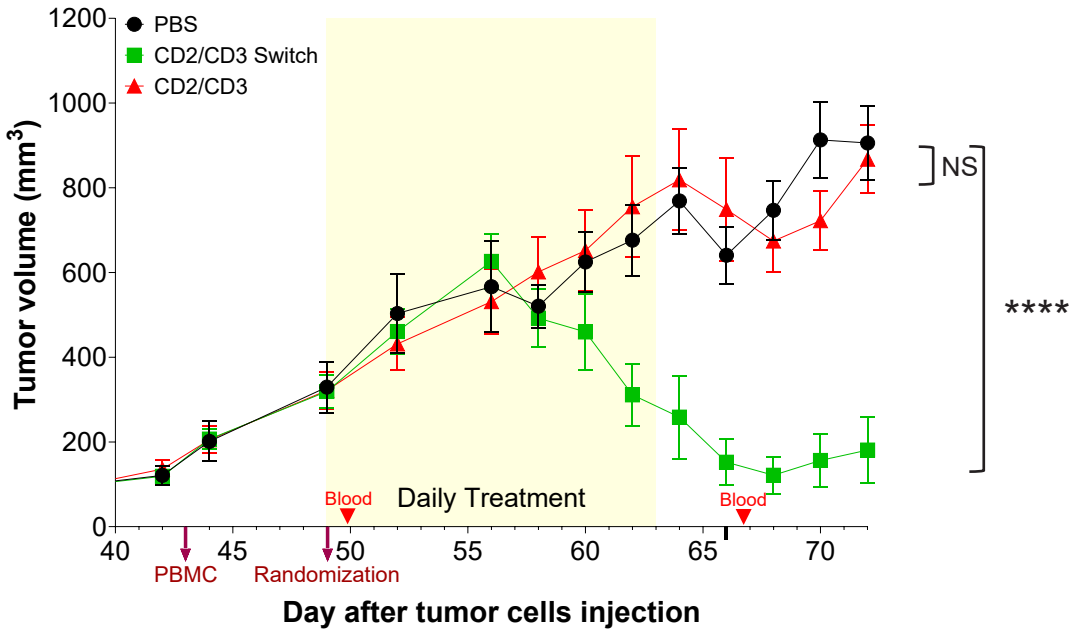



*Bianchi et al, AACR 2025 (poster presentation)*

EpCAM; epithelial cellular adhesion molecule; MSLN, mesothelin.

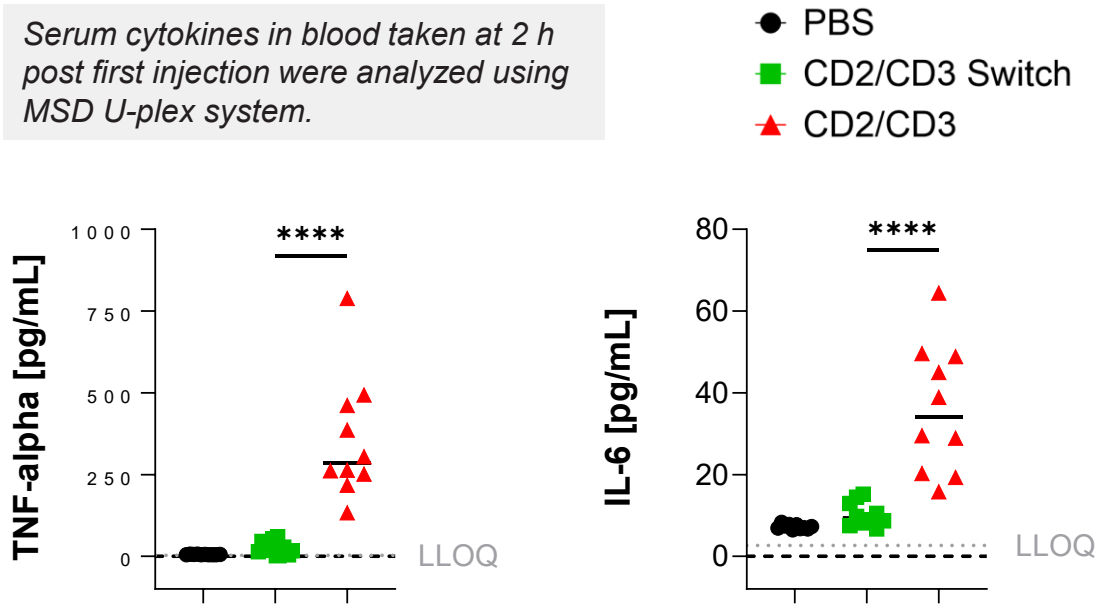
# CD3 Switch-DARPin with CD2 Co-Stimulation Induces Tumor Regression

## Antitumor activity in OVCAR-3 xenograft model




## Safety of CD2/CD3 Switch: *in vivo* cytokine release

*Serum cytokines in blood taken at 2 h post first injection were analyzed using MSD U-plex system.*

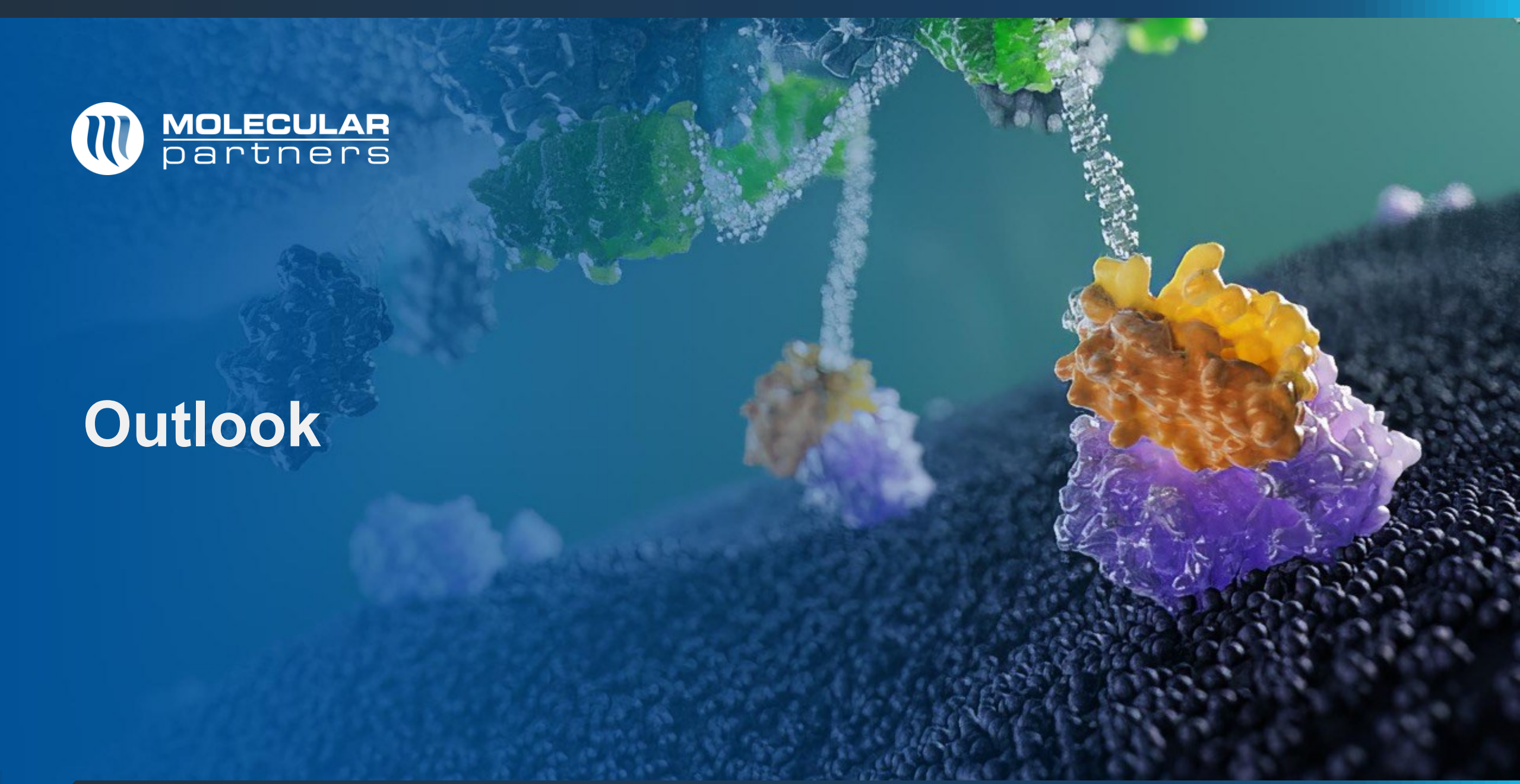



- Masking of CD3 allows the safe use of strong CD3 and co-stimulation binders in one molecule
- Also confirmed in human whole blood cytokine release assay



*Robinson et al, SITC 2024 (poster presentation)*
*Bianchi et al, AACR 2025 (poster presentation)*

TNF, tumor necrosis factor; IL-6, interleukin-6;
PBS, phosphate buffered saline; PBMCs, peripheral blood mononuclear cells.



# Outlook

# Outlook and Upcoming Milestones

| | |
|---|---|
| **MP0712** | • **First-in-Human Phase 1 study expected to start in 2025**<br>• Update on early imaging work planned at TRP 2025, with full data at TWC 2026<br>• Initial safety data anticipated in H1 2026 |
| **Radio-DARPin Therapy (RDT)** | • Progress second RDT program **MP0726** in 2026<br>• Nomination of additional $^{212}$Pb x RDT programs in collaboration with Orano Med |
| **MP0533** | • **Initial data from amended dosing scheme** (cohort 9) at ASH 2025<br>• Combo trials (aza/ven) initiation in 2026 pending decisional data of cohorts 9-10 |
| **Switch-DARPin** | • **Preclinical update on CD3 Switch-DARPin T cell engager program** at SITC 2025<br>• Selection of a first Switch-DARPin candidate |
| **MP0317** | • Phase 2 investigator-initiated combo study to start in France |

**CHF ~105 M** cash* (incl. short-term time deposits) ensures funding until 2028



*Financials as per September 30, 2025.
IND, investigational new drug.

MOLECULAR partners

*Twenty Years of Pioneering*
*DARPin Therapeutics for Patients*

# Thank You