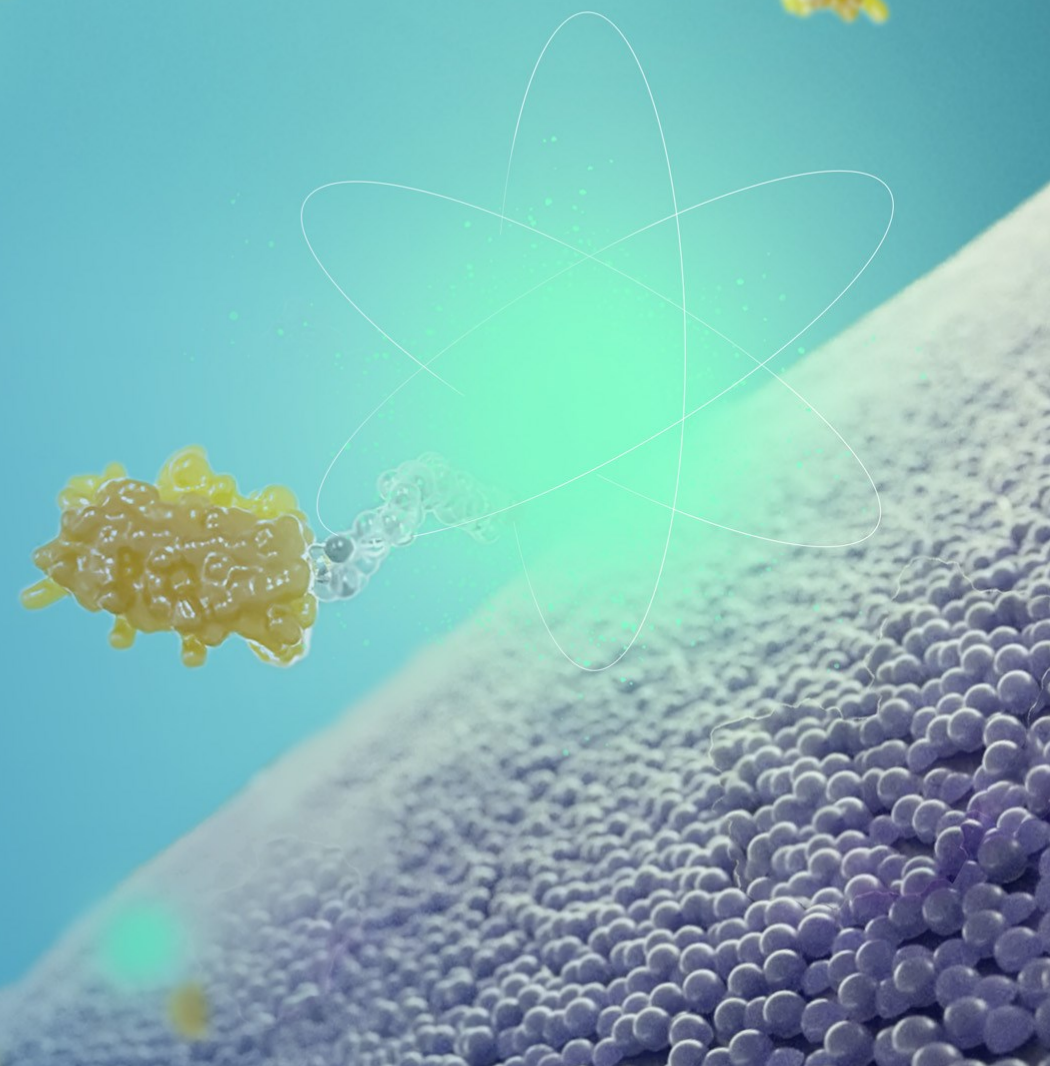




# Extending the Boundaries of Targeted Cancer Therapies with Radio-DARPin and Next-Gen Immune Cell Engagers

June 24, 2025

Nasdaq, SIX Swiss Exchange: MOLN



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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
- **Well financed** into 2028 through key value inflection points (CHF ~131 M\*)

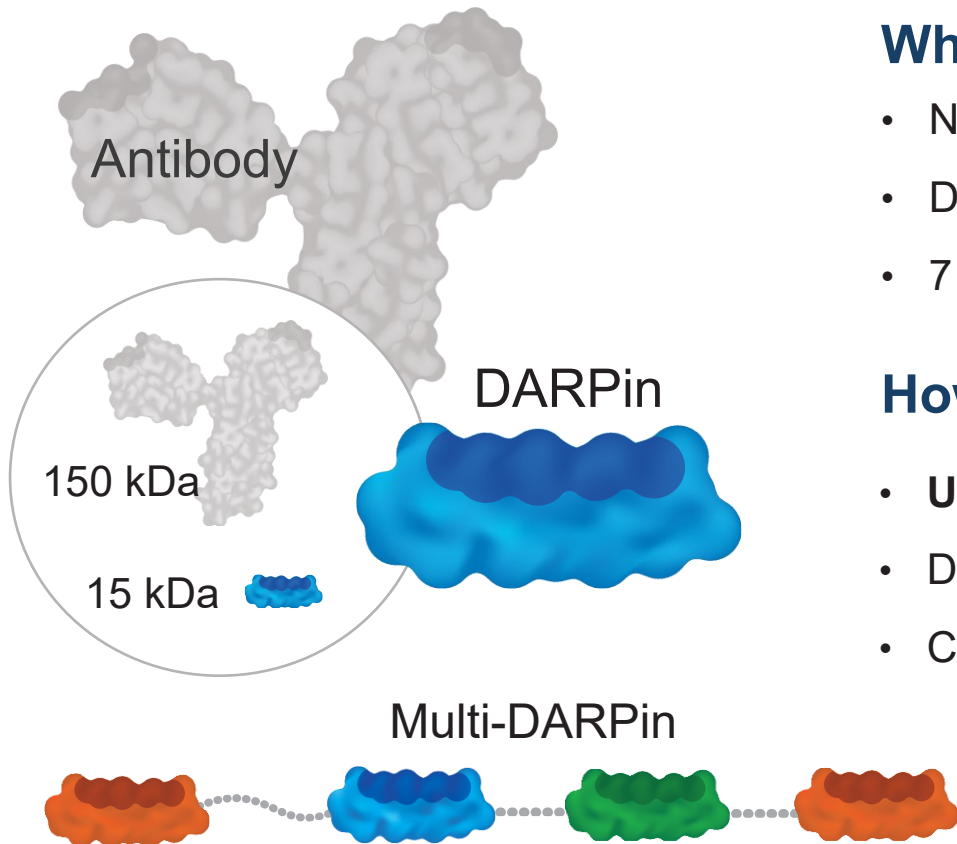
## Our Capabilities: Technology, Team, Collaborations

- Proprietary DARPin Platforms, including **Radio-DARPin** 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**,
- **Targeted radiotherapy / MP0712** and **next-gen immune cell engagers / MP0533** 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**
- 7 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)	<b>MP0712</b>	<b>SCLC &amp; NECs</b> <i><sup>212</sup>Pb - DLL3</i>		 <b>oranomed</b> Co-development*		
	<b>MP0726</b>	<b>Ovarian Cancer</b> <i><sup>212</sup>Pb - MSLN</i>		 <b>oranomed</b> Co-development*		
	Undisclosed Programs	<b>Solid Tumors</b>		Up to 8 programs*		
Next-Gen Immune Cell Engagers	<b>MP0533</b>	<b>r/r AML and AML/MDS</b> <i>CD33 x CD123 x CD70 x CD3</i>				
	<b>Switch-DARPin T Cell Engager</b>	<i>CD3 x costim x TAAs</i>				
	MP0621 (Switch-DARPin)	<b>HSCT</b> <i>cKit x CD16a x CD47</i>				
	MP0317	<b>Advanced Solid Tumors</b> <i>FAP x CD40</i>				



# 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

- 5y overall survival (OS) ~30%; fast-progressing disease
- Leukemic stem cells drive relapse

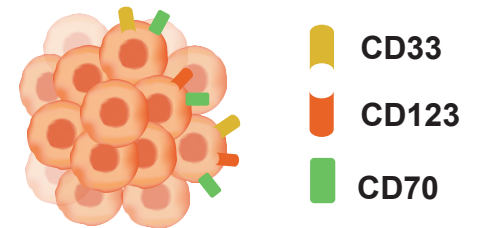
## CD123, CD33, CD70: broadly expressed targets on AML cells

- 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)

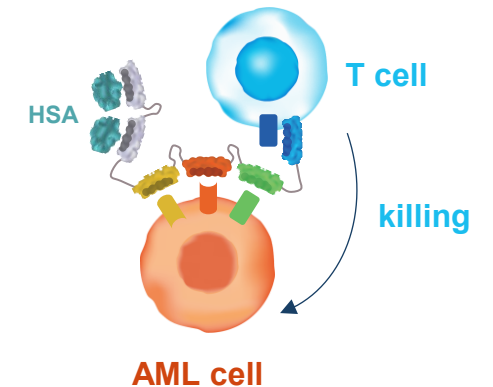
## MP0533: avidity-driven, tetraspecific T-cell engager

- 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

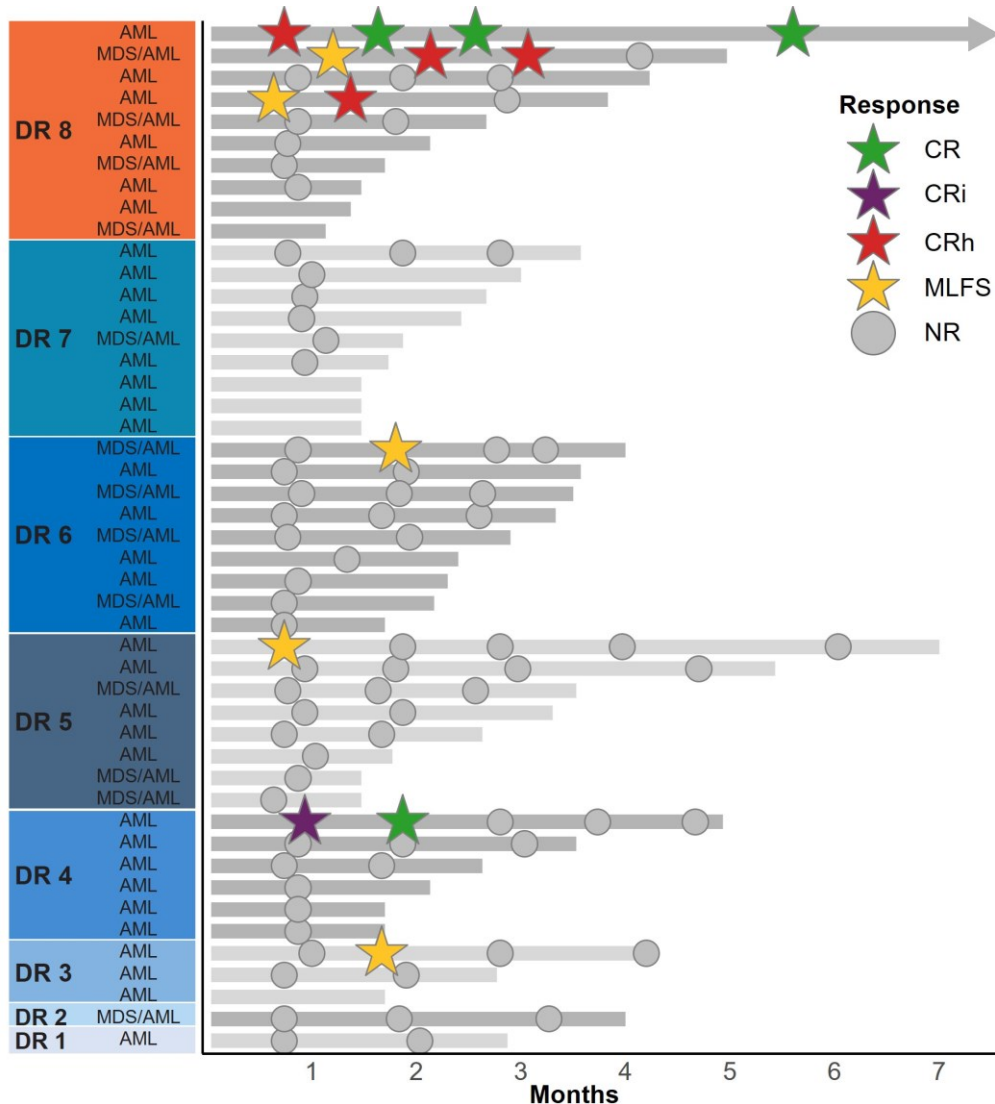
### AML cells & targets



### MP0533 & Mode of Action



# Encouraging clinical responses observed with intermediate densification



## Improved response rate and depth observed to-date in Cohort 8:

- **DR 1–7** – 4 patients (of 33 evaluable) 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 / 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 of at least 6 months.

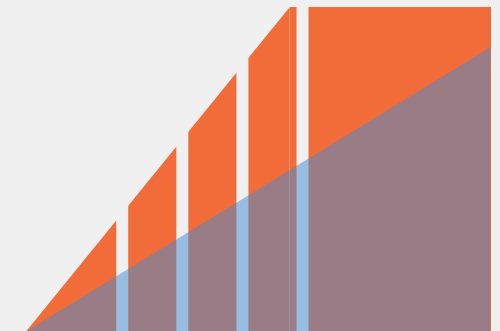
### Dose escalation (DR 1–7)

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

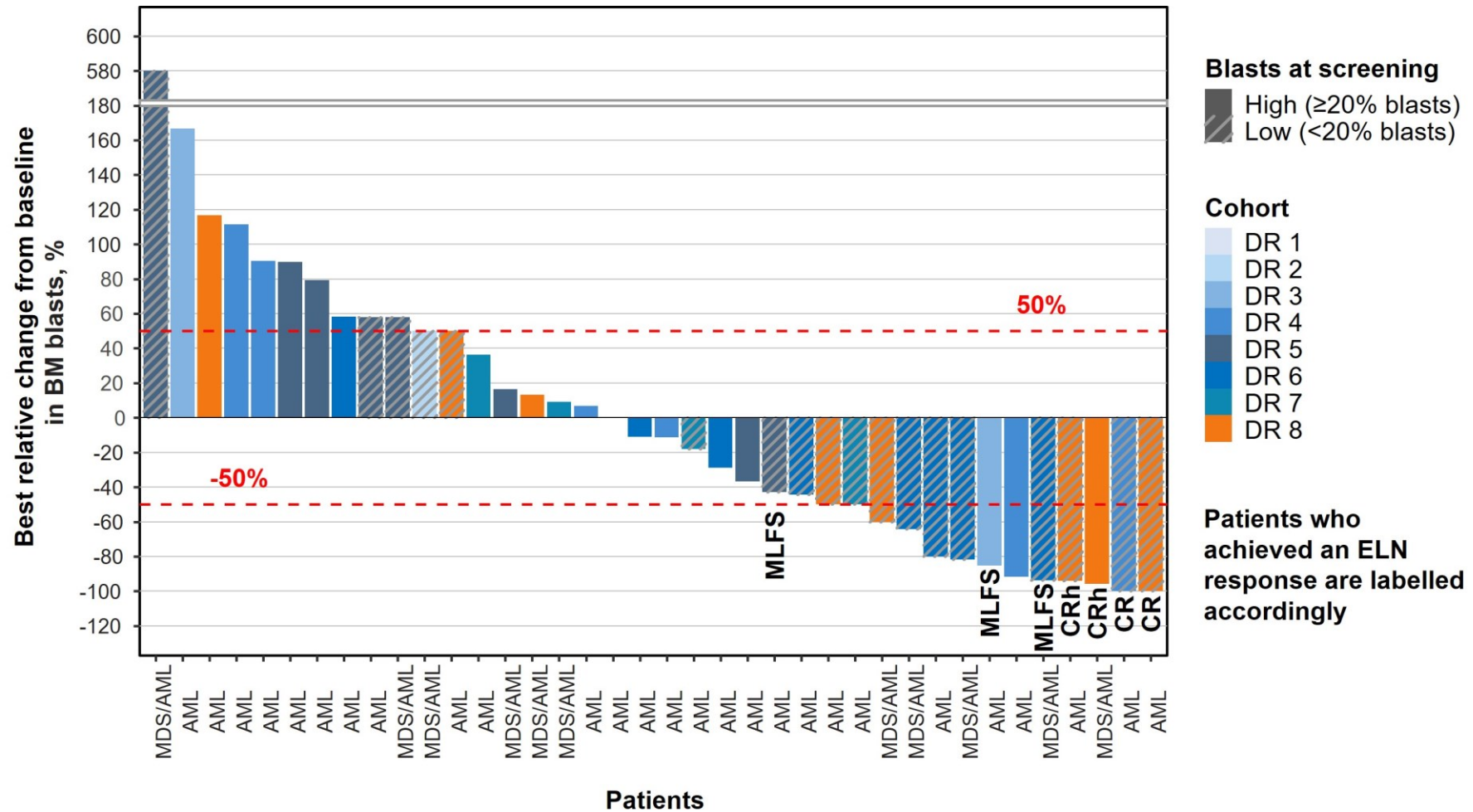


### Intermediate densification (DR 8)

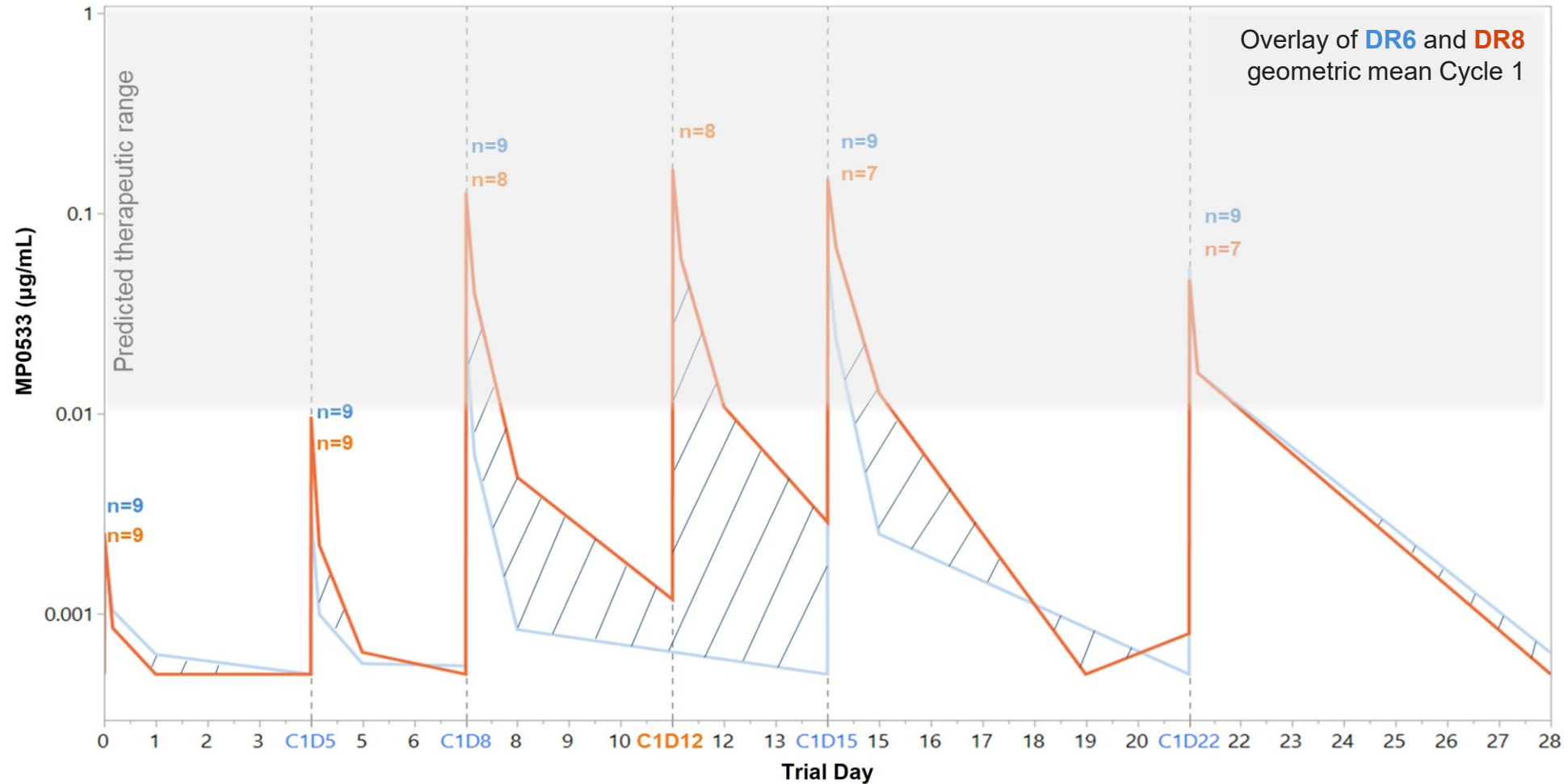
- **Additional Day 12 dose for steeper & faster dose escalation, addressing TMDD**



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



# Improved MP0533 exposure achieved with steeper and denser step-up dosing regimen in DR8



# Further dose densification to demonstrate full potential of MP0533

## Protocol amendment to optimize MP0533 exposure

Summary of Cohorts DR 1-8 data (as presented at EHA 2025):

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

**Outlook:** Initial data from DR 9 in H2 2025

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

- To improve the exposure profile of MP0533 in patients
- To increase the depth and duration of clinical responses

### How:

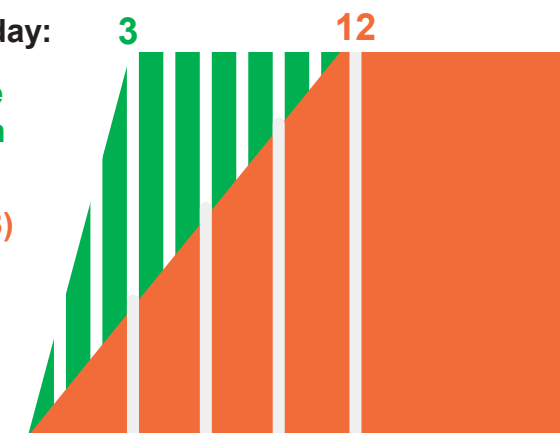
- Dose densification (accelerated step-up dosing & higher dose frequency) to overcome target-mediated drug disposition
- Premedication with B cell depleting agent to mitigate loss of exposure

### Amended Dosing Scheme\*

Target dose reached on day:

Further dose densification (DR 9-10)

(versus DR 8)





# MP0712 & Radio-DARPin Therapy

Custom-engineered to create  
vectors ideal for radiopharmaceuticals



# Radio-DARPin as Versatile Therapeutic Candidates

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

## DARPin: IDEAL VECTOR FOR RADIOPHARMACEUTICALS

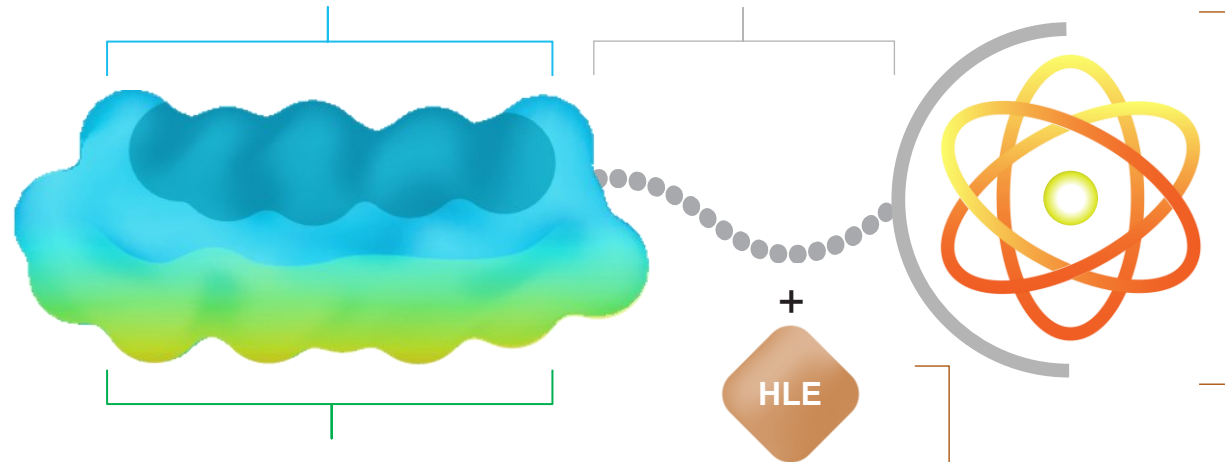
- Proven selective targeting
- High affinity, tumor retention
- Broad target space
- Small size

## LINKER & CHELATOR

- Established DOTAM

## $^{212}\text{Pb}$ : 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 $^{212}\text{Pb}$ -DLL3 Targeted Radiotherapeutic for SCLC

## SCLC: critical unmet need, limited treatment options

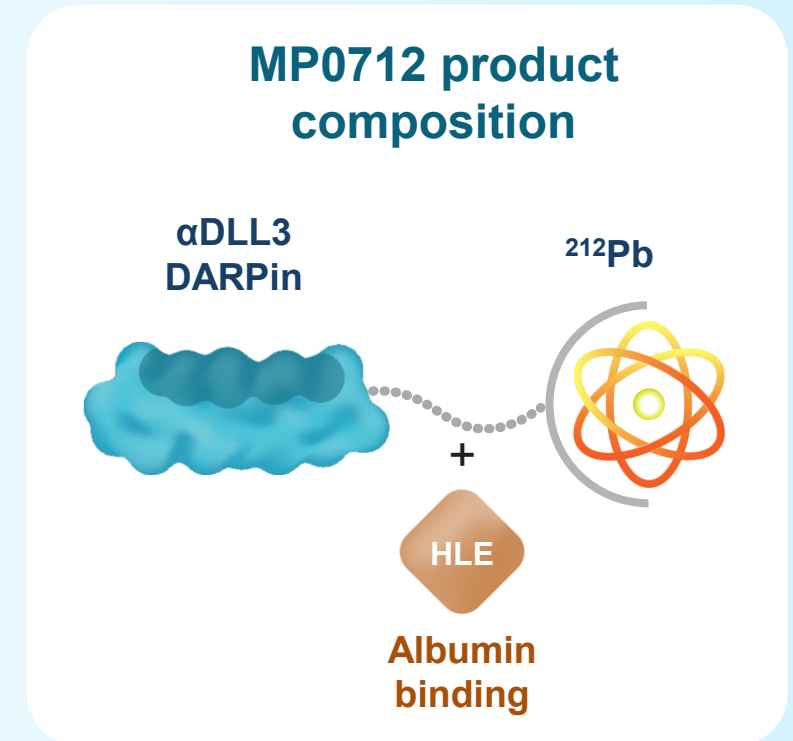
- Median progression free survival (mPFS) ~3 months<sup>1,2</sup>
- 5y overall survival (OS) ~3%<sup>1,2</sup>

## DLL3: a validated target for SCLC

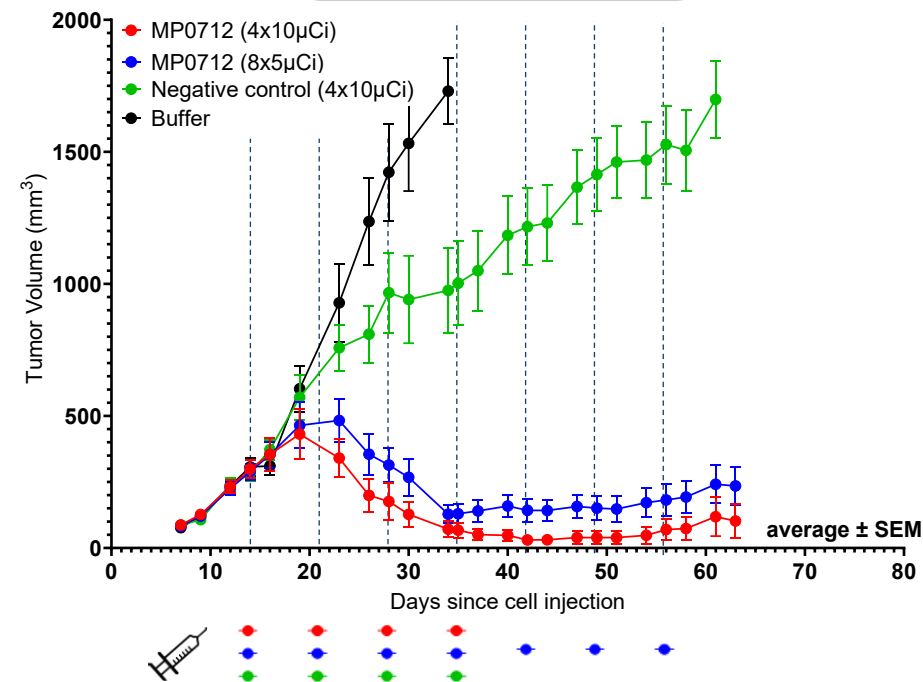
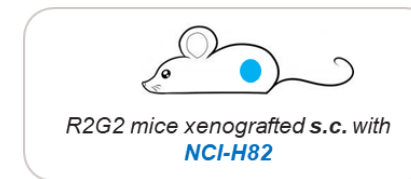
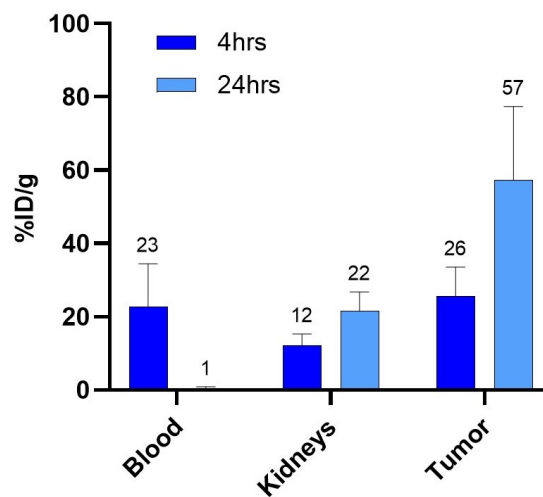
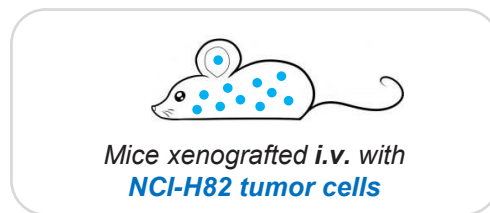
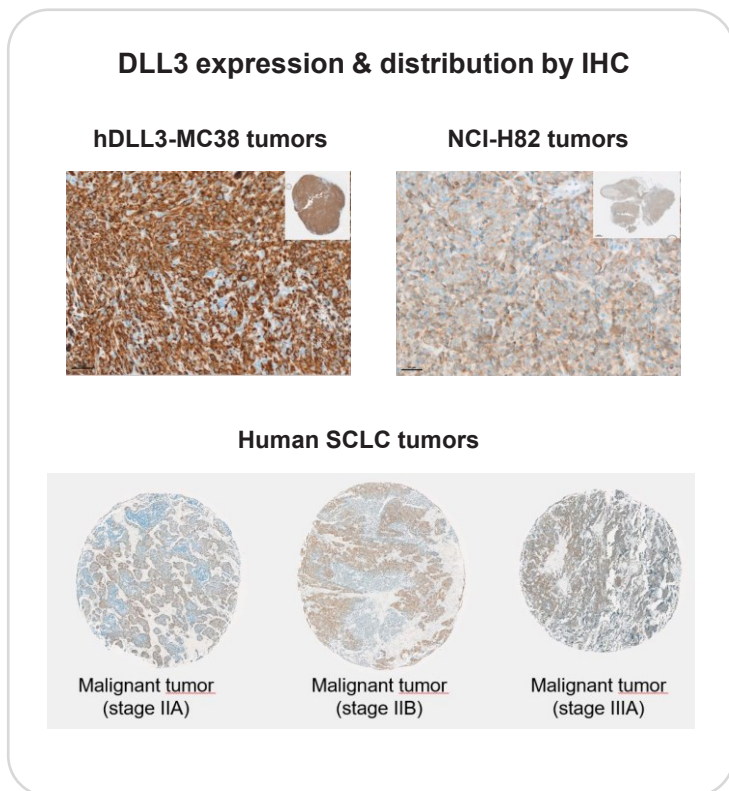
- Expressed in >85% of SCLC patients<sup>3</sup> and in neuroendocrine cancers
- No expression in healthy tissues
- Tarlatamab<sup>4</sup>, approved DLL3 targeting drug (T cell engager)
  - ORR ~40%, DOR 9.7 months, PFS 4.3 months

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

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



# MP0712: Potent Efficacy at Clinically-Relevant Dose



- 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 10µCi injected every week

# Outline of MP0712 Clinical Development Strategy

- Patients: Focus on Small Cell Lung Cancer (SCLC), secondly on Neuro Endocrine Cancers (NECs)
- Imaging and dosimetry on-going, initial data\* expected by YE 2025
- **Phase 1 study to start in H2 2025, initial safety and efficacy data in 2026**

## PHASE 1/2a STUDY



### Phase 1: $^{212}\text{Pb}$ Dose Escalation,

Main objective: Safety, RP2D;  $N = 15\text{--}27$  patients

Phase 1 includes an imaging and dosimetry step with  $^{203}\text{Pb}$

### Phase 2a – Dose Expansion and PoC – SCLC+NEC;

Main objective: Efficacy signals, confirm RP2D;  $N = 30$  patients

### Registration study

2L+ SCLC patients

### Phase 2s

- 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  $^{203}\text{Pb}$  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.*

# $^{212}\text{Pb}$ x MSLN Targeted Radio-DARPin for Ovarian Cancer

*Combining distinctive DARPin features with the power of  $^{212}\text{Pb}$  for next-gen targeted alpha therapy*

## Ovarian Cancer (OC): high medical need and marginal progress

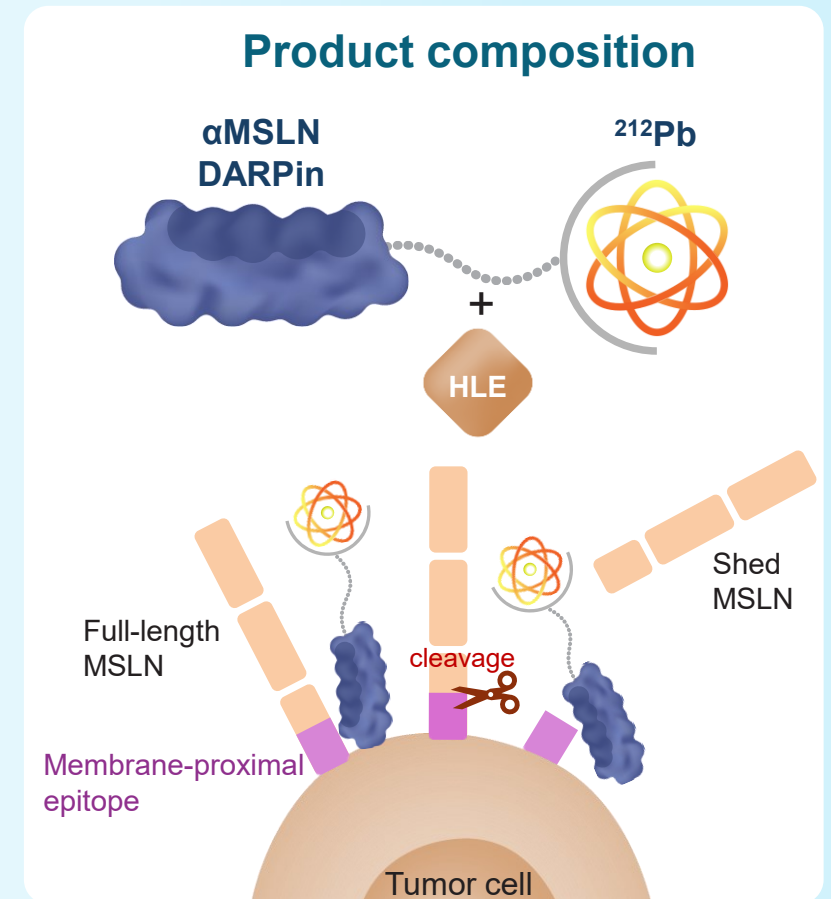
- > 50% patients die within 5y post-diagnosis (diagnosis often in late stage)
- Poor treatment options: ~80% recurrence rate post 1L chemo, limited 2L options (FR-alpha targeted Tx relevant for only 40% patients)

## Mesothelin (MSLN): a promising target for OC as 1<sup>st</sup> 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<sup>1,2,3,4</sup> (e.g., CAR T/NK, ADC, TCE in development)

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

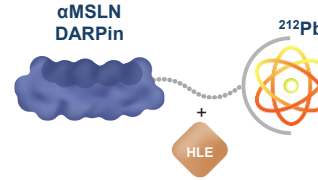
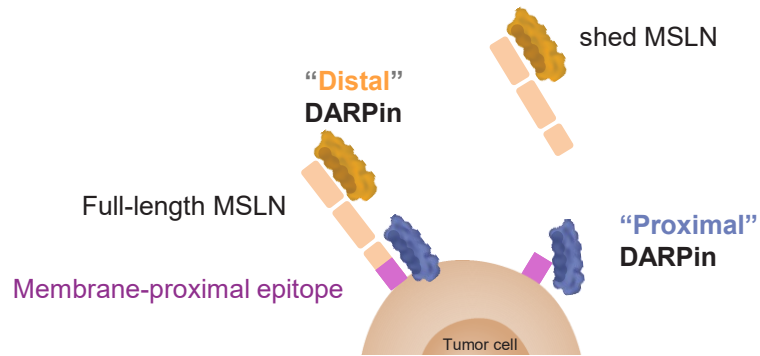
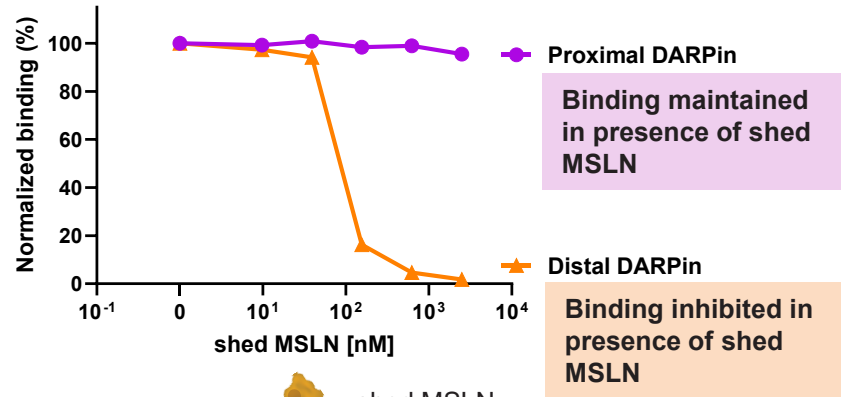
- MSLN DARPin targets **membrane-proximal epitope** (and not shed MSLN)
- $^{212}\text{Pb}$  payload: high energy alpha emissions in short time frame
- Potential for combinations with immunotherapy (incl. next-gen TCEs)



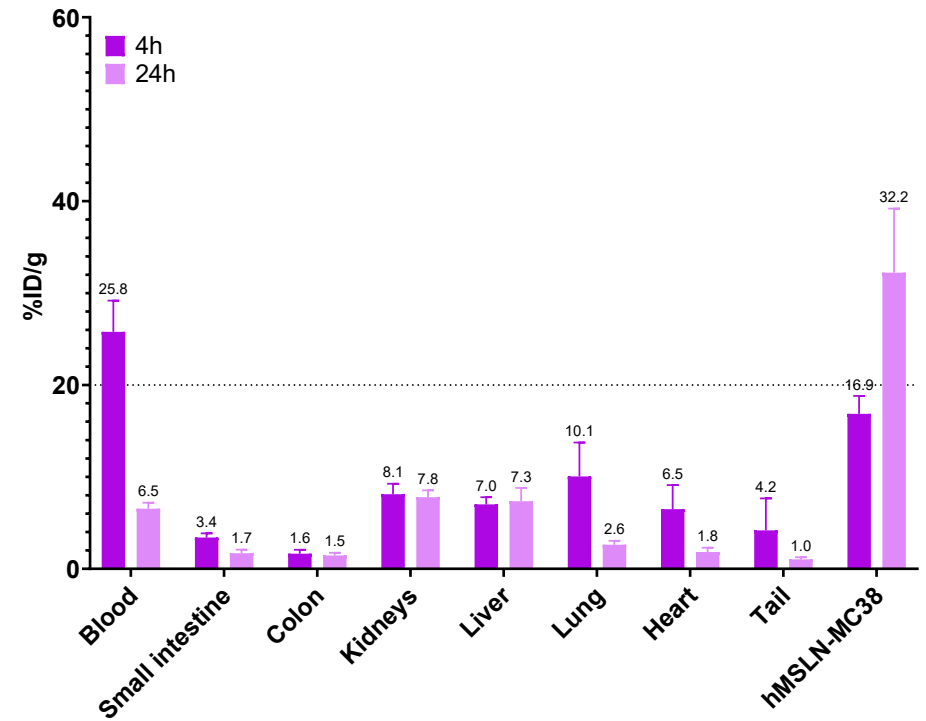
# Attractive biodistribution profile of MSLN Radio-DARPin

## Cell binding maintained despite shed MSLN

OVCAR-8 Cell binding competition assay  
100nM DARPin with increasing concentration of shed MSLN



## Favorable biodistribution in hMSLN-MC38 tumor model



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

Combining DARPin versatility with the power of  $^{212}\text{Pb}$  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



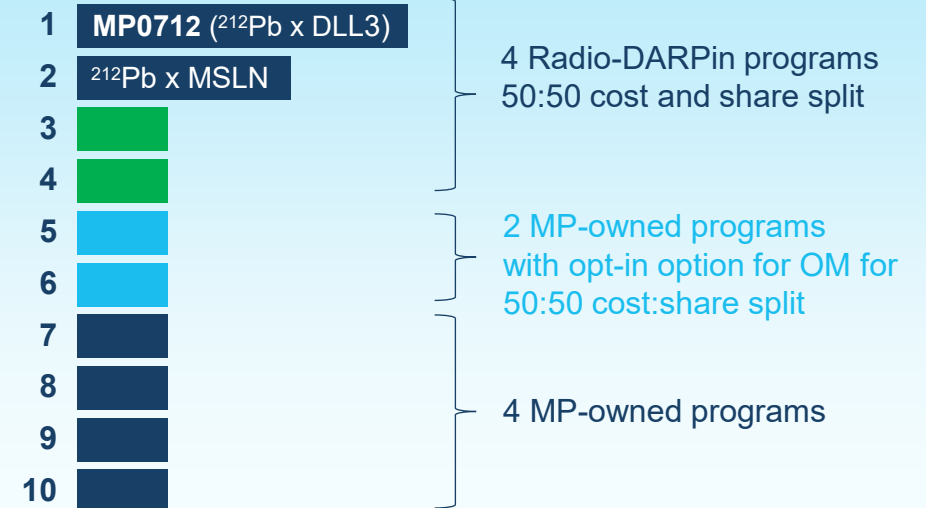
INDIANA, US:  
Industrial scale manufacturing  
Global shipping hub  
ATLab US

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

SWITZERLAND:  
Preclinical assessment  
DARPin engine, fast &  
high throughput

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

### Pipeline of Ten $^{212}\text{Pb}$ Radiotherapy products



# Our Partner Orano Med – Pioneer of Targeted Alpha Therapy

## Targeted Alpha Therapy with $^{212}\text{Pb}$ :

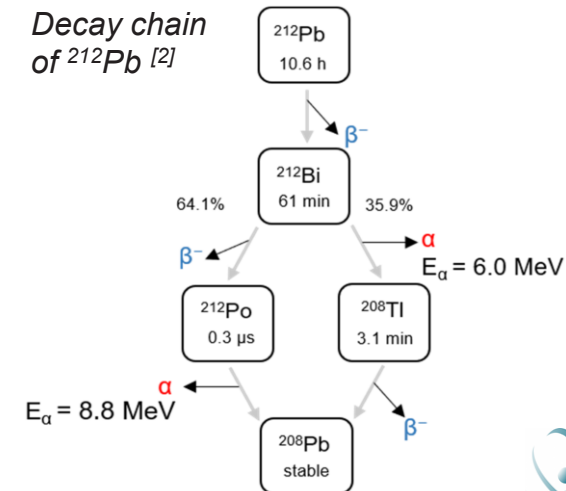
- **Alpha therapy:**
  - **High cytotoxicity:** DNA double-strand break, high energy deposition, no need for receptor internalization
  - **Targeted effect:** short range of action with potential to target microlesions, less impact on healthy tissues
- **Lead-212 ( $^{212}\text{Pb}$ ):**
  - **Short-half life** (~11h): 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 $^{212}\text{Pb}$ Targeted Alpha Therapy:

- Unique, independent **supply of  $^{212}\text{Pb}$**  as alpha emitting therapeutic isotope
- **Large scale GMP manufacturing** capabilities
- Fully integrated research and preclinical development platform
- **Clinical capabilities** demonstrated with  $^{212}\text{Pb}$  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



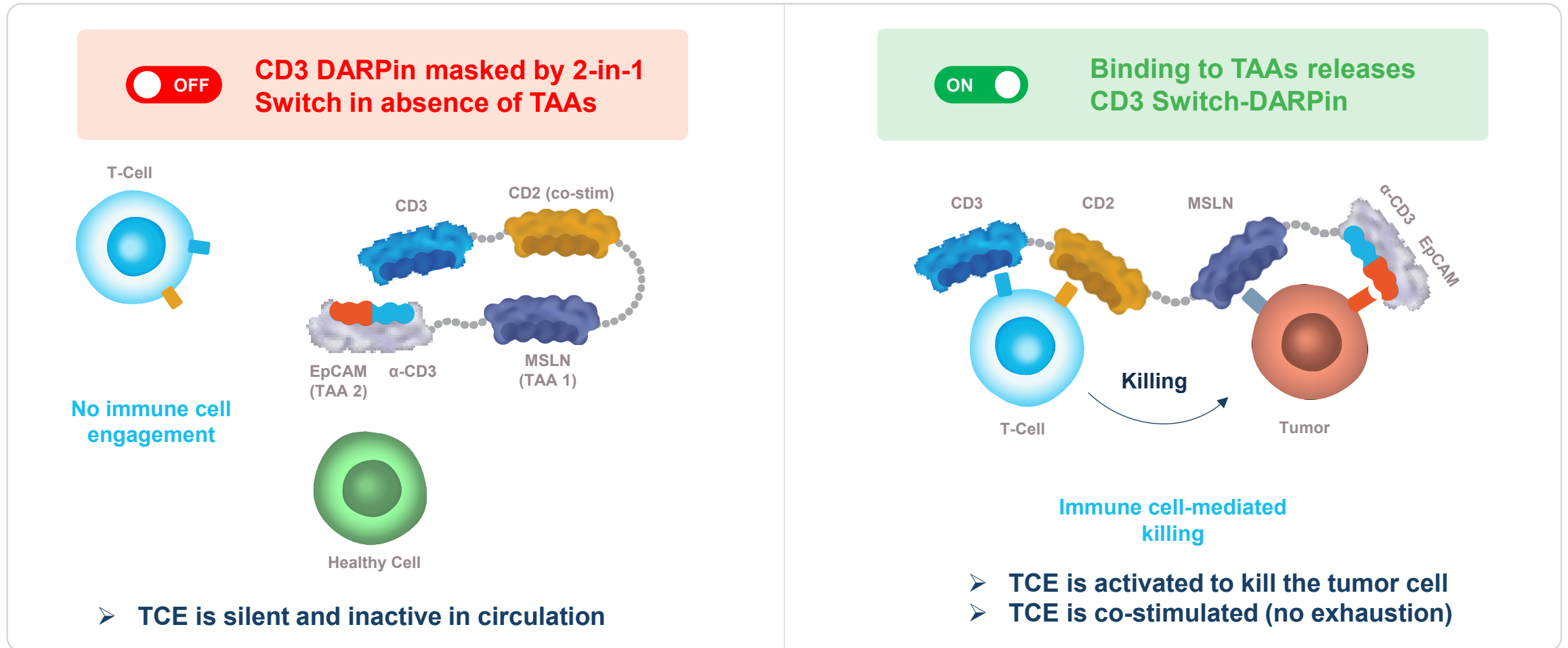


# Switch-DARPin Platform

Next-generation T cell engagers

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

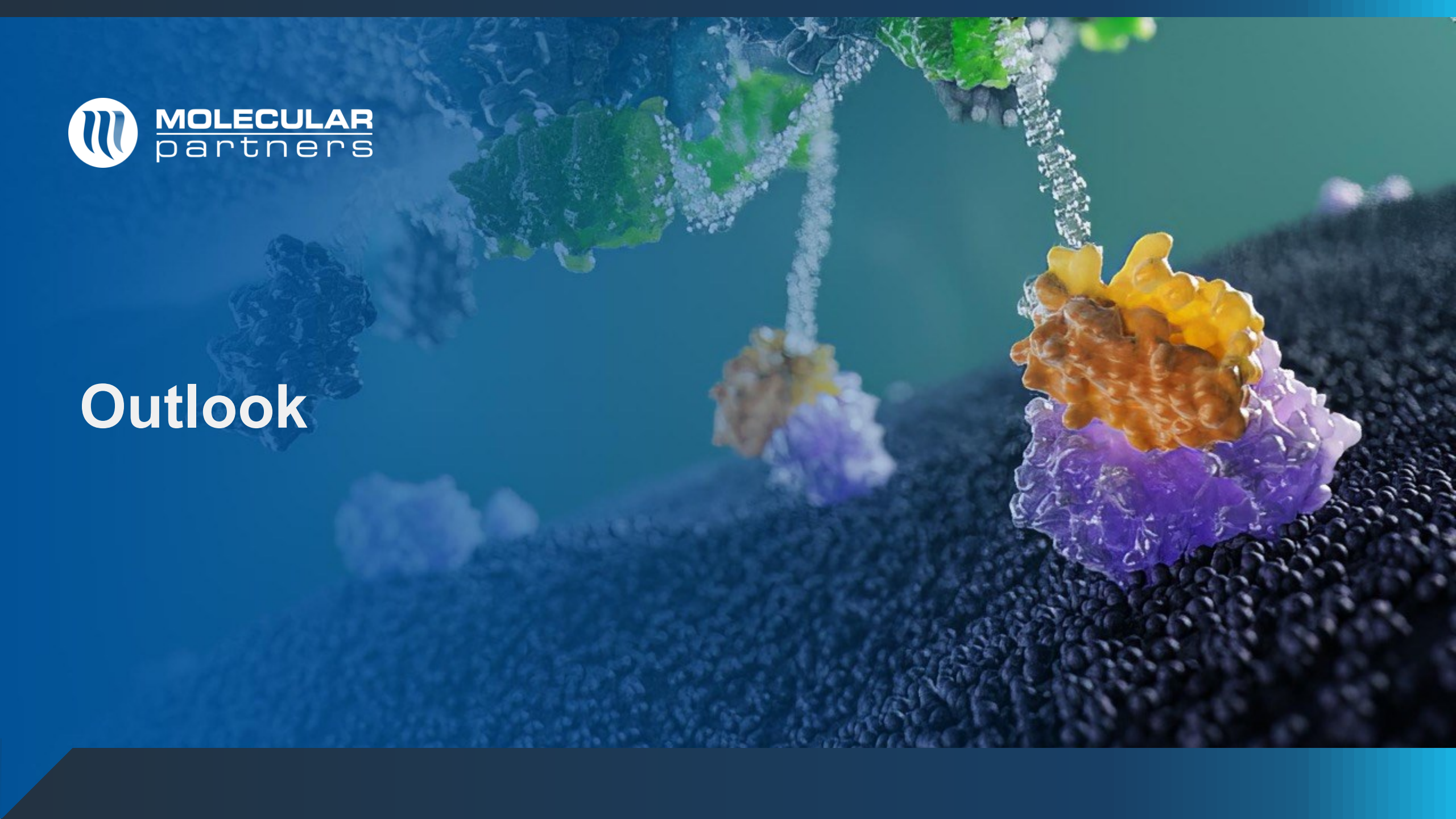
*Tackling current limitations of TCEs in solid tumors*



Preclinical update on CD3 Switch T cell engager at AACR 2025



# Outlook



# 2025 Outlook and Upcoming Milestones

## MP0712

- **First-in-Human studies to start in 2025** (Phase 1)
- Initial clinical data by end 2025 (imaging & dosimetry)
- Initial efficacy and safety data in H1 2026

## Radio-DARPin Therapy (RDT)

- MSLN preclinical update at AACR and SNMMI 2025, therapeutic candidate selection
- Additional  $^{212}\text{Pb}$  x RDT programs nominated, in collaboration with Orano Med

## MP0533

- Comprehensive clinical data from Phase 1 cohort 8 at EHA 2025
- Protocol implementation of improved dosing regime, H1 2025
- **Data from additional cohorts on amended dosing scheme in H2 2025**

## Switch-DARPin

- Preclinical update on CD3 Switch T cell engager at AACR 2025
- Evaluation of partnering opportunities with Switch platform, including MP0621 (cKit) & T-cells

**CHF ~131 million cash\*** (incl. short-term time deposits) ensures **funding into 2028**



*Twenty Years of Pioneering  
DARPin Therapeutics for Patients*

# Thank You

