Molecular Partners

Investora, Zurich

September 14, 2023

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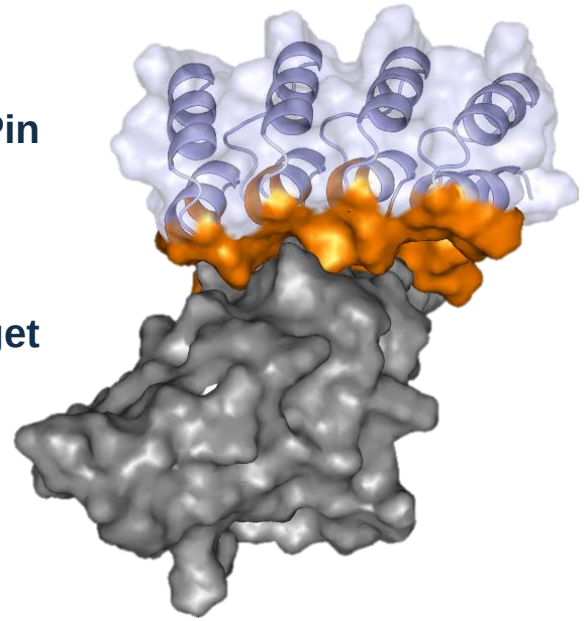
Any forward-looking statements speak only as of the date of this press release and are based on information available to Molecular Partners as of the date of this release, and Molecular Partners assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

Agenda



01 **Introduction & H1 Highlights**
Patrick Amstutz, CEO

02 **MP0317**
Patrick Amstutz, CEO

03 **MP0533**
Alex Zürcher, COO

04 **Radio DARPin Therapy**
Alex Zürcher, COO

05 **Outlook**
Patrick Amstutz, CEO

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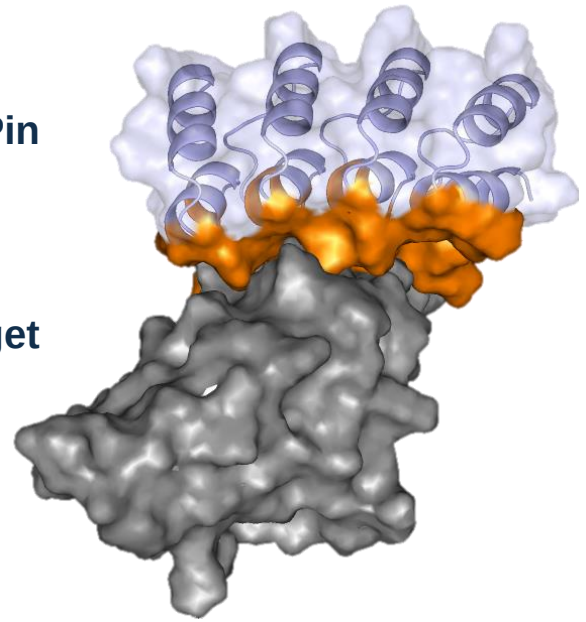
DARPin Modality and Molecular Partners' Strategy



What we invented

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

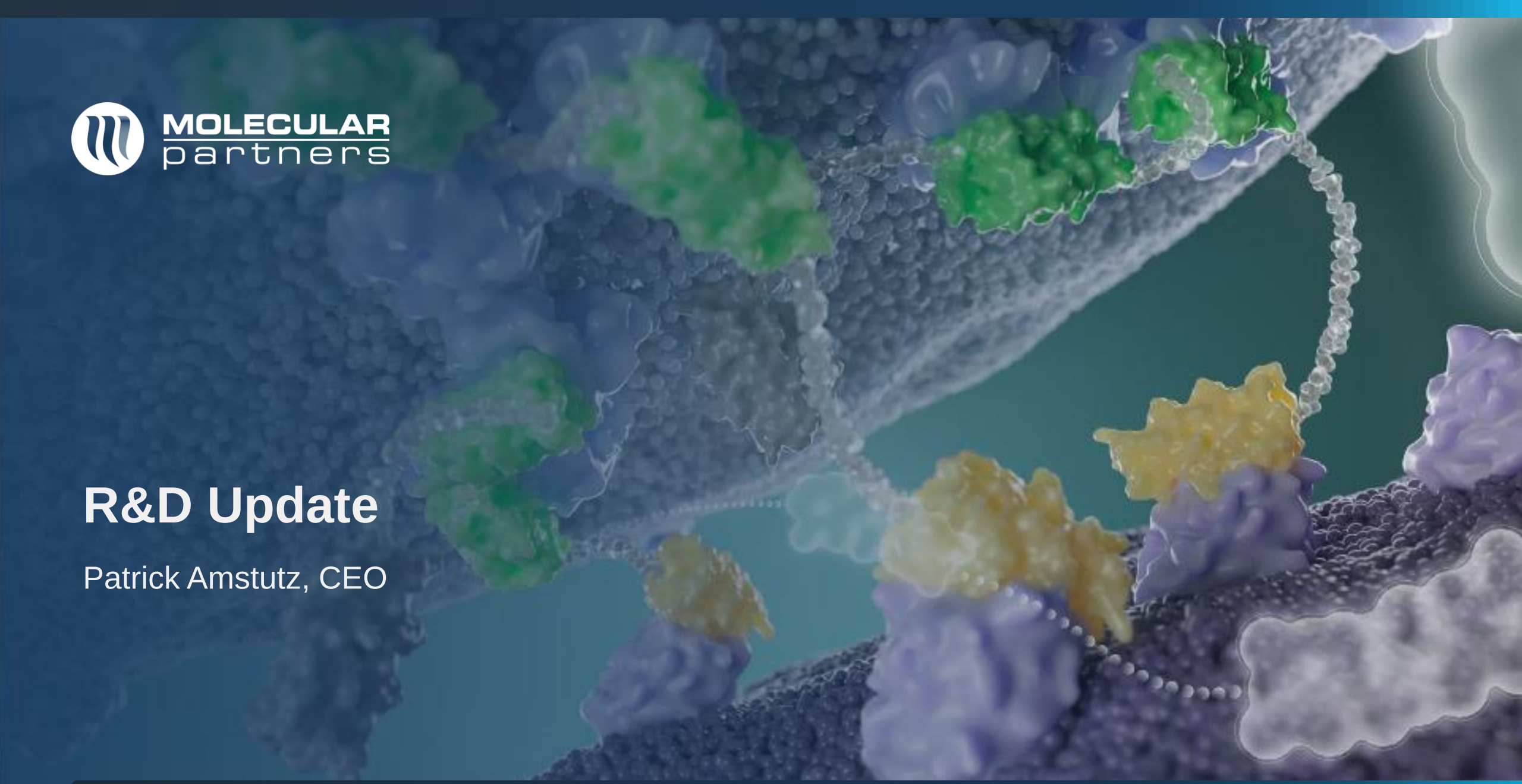
How we apply it

- **Unique DARPin solution** for a defined medical problem not addressable by antibody designs
- Demonstrate **true patient value** with **early clinical read out**
- Combine our **capabilities with world-class partners** to deliver innovative therapeutics

Highlights H1 2023

MP0533	• Novel tetra-specific T cell engager for R/R AML and high-risk MDS • Phase 1 dose-escalation study well on track, 7 sites open in Europe • **Currently enrolling at cohort 4 dose-level**
MP0317	• Bi-specific FAP-dependent, tumor-targeting CD40 agonist • Phase 1 study in R/R solid tumors recruiting at highest planned dosing • ASCO 2023 presentation: **favorable safety profile and proof of mechanism in** patients
Radio DARPin Therapy Platform	• RDT platform successfully being optimized with focus **on reducing accumulation in kidney** • Selected tumor-associated protein DLL3 as a first in-house target • Novartis collaboration further progressing
Operations	• Strong financial position with CHF ~218 M in cash (incl. short term deposits) as of June 30, 2023 • **Capitalized well into 2026**

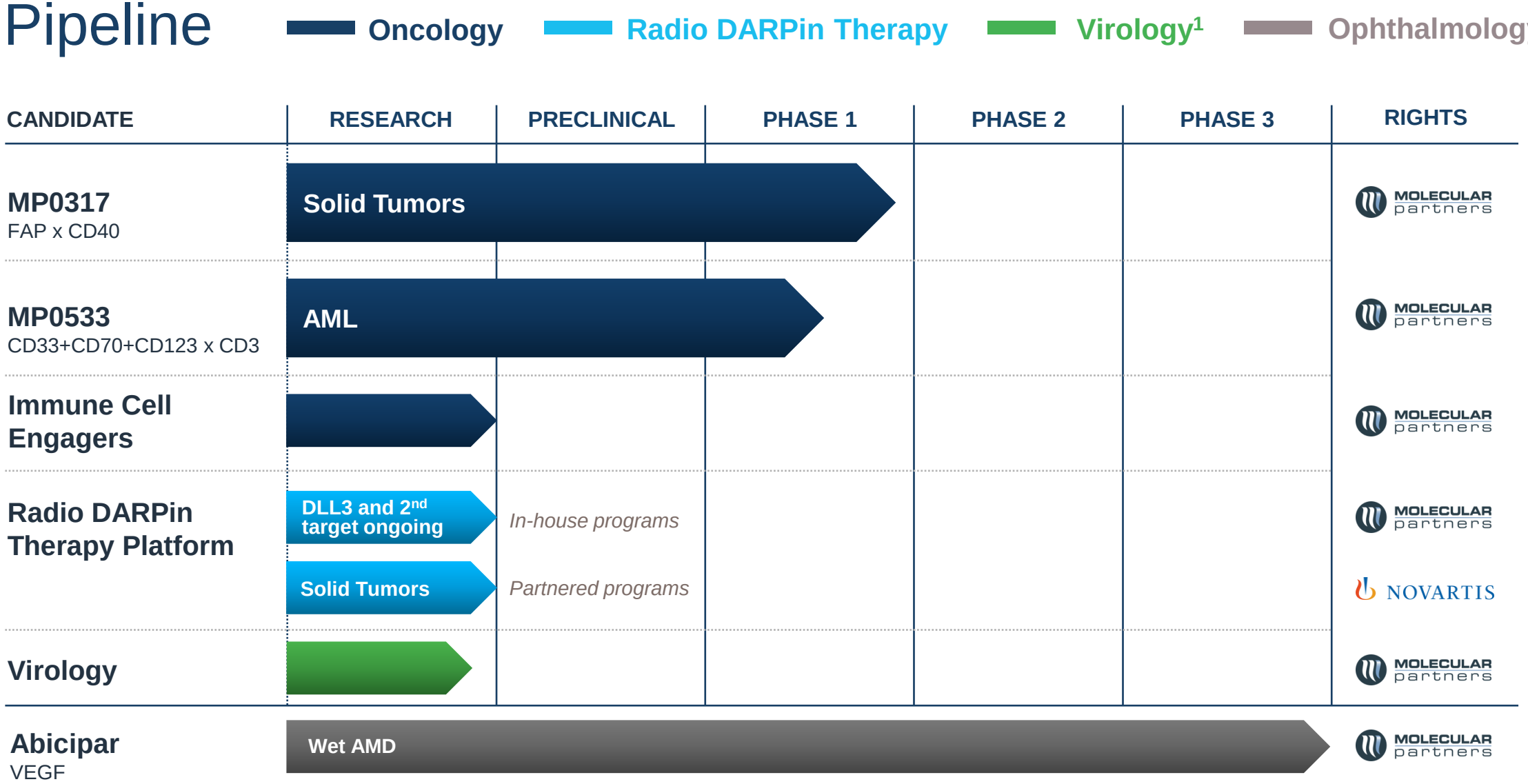
AML, acute myeloid leukemia; ASCO, American Society of Clinical Oncology; DLL3, Delta-like ligand 3; MDS, myelodysplastic syndrome; RDT, Radio DARPin Therapy; R/R, relapsed/refractory.



R&D Update

Patrick Amstutz, CEO

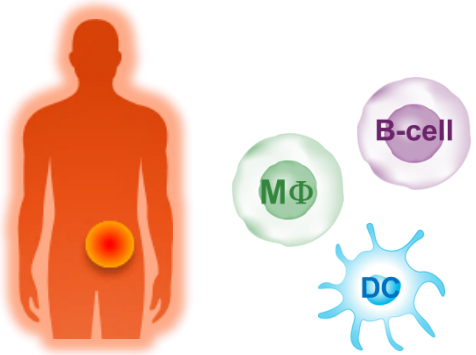
Pipeline



1) Ensovibep: Molecular Partners was informed by Novartis that the Emergency Use Authorization (EUA) application from the U.S. Food and Drug Administration (FDA) for ensovibep was withdrawn effective January 25, 2023. As previously disclosed, ensovibep is not presently in clinical development.
2) The Company continues to evaluate potential business opportunities for abicipar outside of Molecular Partners.

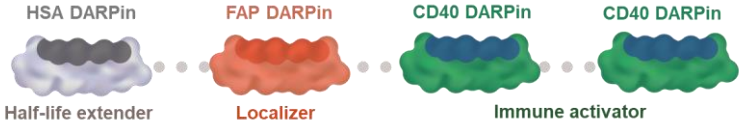
MP0317: Unlocking CD40 Activity by Local Activation

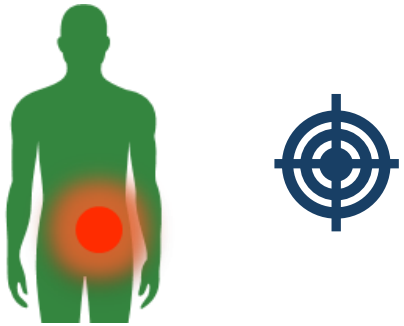
Problem: Toxicity of CD40 Antibodies Has So Far Limited Their Activity



- **CD40 agonists** can activate **B cells, DCs and MΦ** to enhance the efficacy of IO drugs, especially in “cold tumors”
- **Systemic activation of CD40 via mAbs** has been hampered by **significant toxicities** and therefore limited to **low dosing**, likely insufficient to reach meaningful efficacy

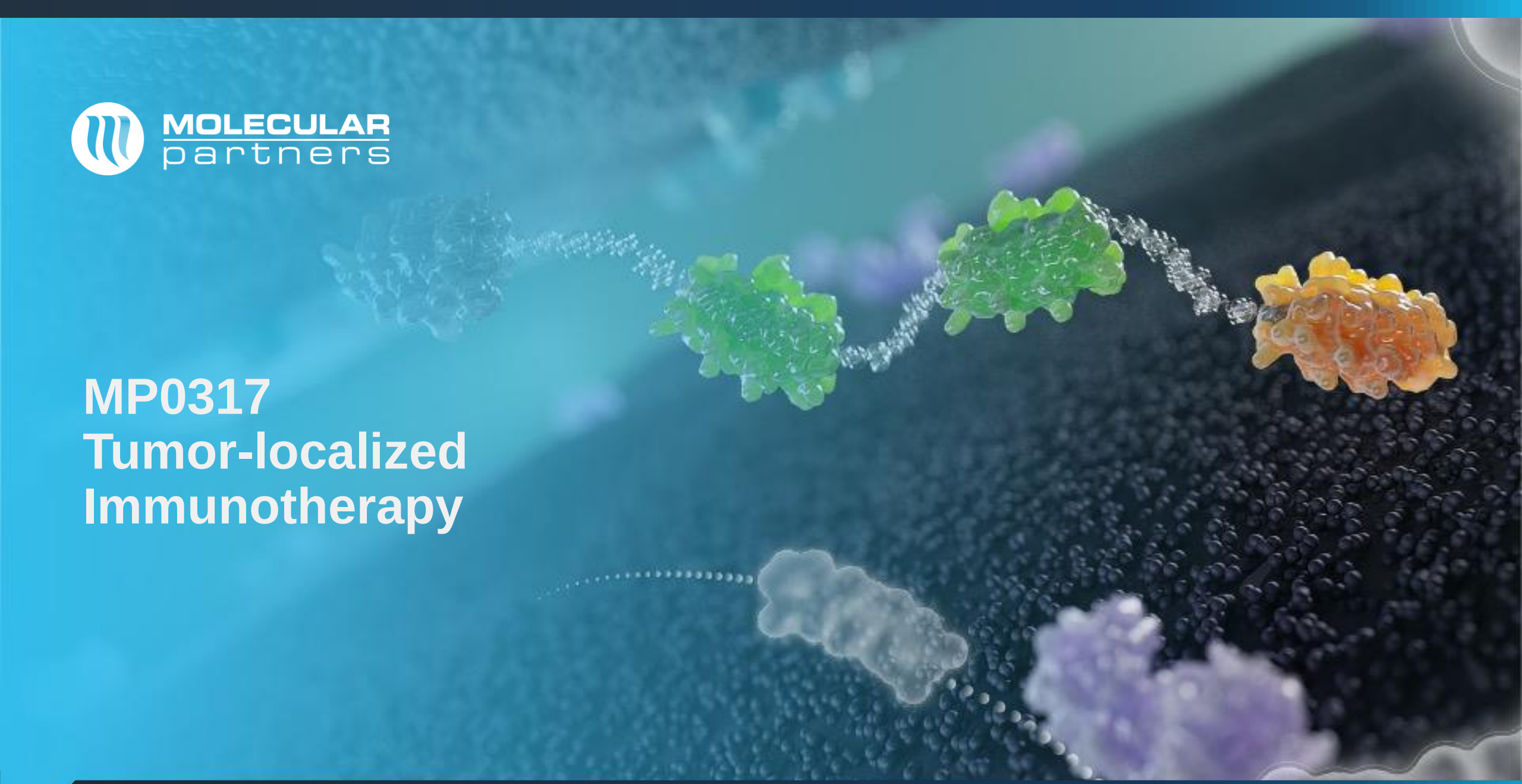
Solution: MP0317 – FAP-dependent tumor-localized CD40 activation





- **FAP is a validated tumor target** overexpressed in at least 28 different cancer types and its expression is not downregulated during disease progression
- **MP0317** is designed to bind tumor-localized FAP and induce CD40-mediated **activation of immune cells in the tumor**, thereby overcoming systemic toxicity and allowing a **wider therapeutic dosing range**

DC, dendritic cell; FAP, fibroblast activation protein; HSA, human serum albumin; MΦ, macrophage; mAB, monoclonal antibody.



MP0317
Tumor-localized Immunotherapy

Overview of CD40 agonists & safety profiles

MP0317: First CD40-FAP Showing Tolerable Profile

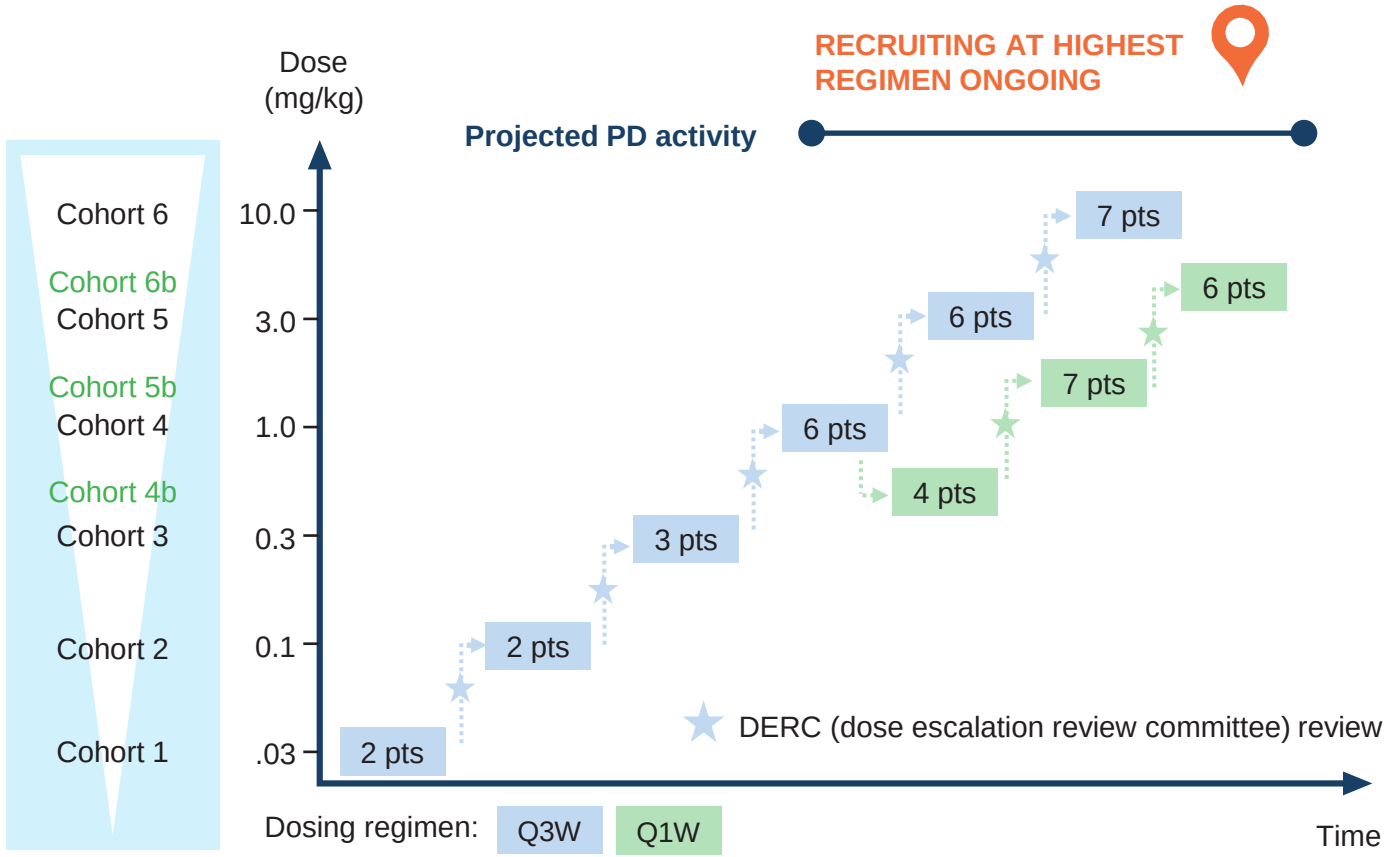
		COMPOUND	STAGE	EXAGGERATED SYSTEMIC IMMUNITY	PRESENTLY EXPLORED DOSES	RIGHTS
CD40 BISPECIFICS	LOCALIZED AGONIST (3RD GEN)	**MP0317** ***(FAP x CD40)***	**Ph1**	**No**	**10 mg/kg**	MOLECULAR partners
		RG6189* *(FAP x CD40)*	Ph1	Not Disclosed	ND	Roche
		GEN1042 *(CD40 - 4-1BB)*	Ph2	No	100 mg** (1.3 mg/kg**)	Genmab & BIONTECH
CD40 MABS	TUNED FC (2ND GEN)	**SEA-CD40**	Ph2	Yes	0.03 mg/kg	Seagen
		Giloralimab / ABBV-927*	Ph2	Yes	ND	abbvie
		Sotigalimab / APX005M	Ph2	Yes	0.3 mg/kg	Apexigen
		Mitazalimab	Ph2	Yes	0.9 mg/kg	ALLIGATOR bioscience
		CDX1140	Stopped (Ph2)	Yes	1.5 mg/kg	Celldex therapeutics
	FULL FC (1ST GEN)	**Selicrelumab**	Stopped (Ph1)	Yes	0.2 mg/kg	Roche

** flat dose (est. 75 kg/pt)

Sources: Vonderheide R et al 2013 Oncoimmunology; Barlesi F et al 2020 BMJ JITC; O Hara M et al 2021 Lancet Oncol; Calvo E et al 2019 JCO; Van Laethem et al 2022 JCO; Johnson M et al 2021 J Immunother Cancer; Bajor DL et al 2022 JCO; Smith KE et al 2021 Expert Opinion on Biological Therapy; Grilley-Olson 2018 ASCO; Padron et al 2022 Nat Med; Moreno et al 2023 Investigational New Drugs; Lindstedt et al 2022 SITC; Byrne et al 2021 Clin Canc Res; Soto et al 2023 ASCO Gastrointestinal Cancer Symposium; Elghonaimy et al 2022 Keystone Symposia; Coveler AL et al 2023 J Immunother Cancer; Sanborn et al 2020 SITC,

MP0317 Phase 1 Study Design & Status

First-in-human, multicenter, dose-escalation study in adults with advanced solid tumors



Primary Study Objectives

- MP0317 safety and tolerability
- Recommended dose for expansion and combination

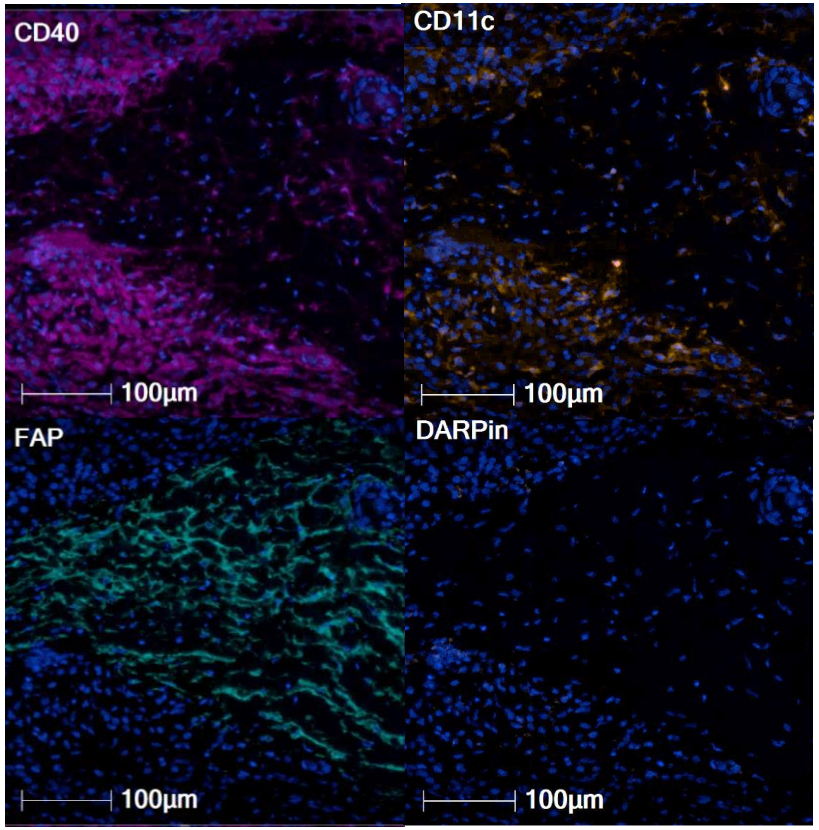
Initial Data Presented at ASCO 2023

- MP0317 dose-escalation: enrolling at the highest planned dose (10 mg/kg)
- **Favorable safety profile**; one DLT observed (not confirmed)

The study is registered at ClinicalTrials.gov (NCT05098405).
PD, pharmacodynamics, PK, pharmacokinetics; Q1W, weekly dosing; Q3W, every-3-weeks dosing.

FAP-localized Enrichment of DCs Confirmed in Tumor Biopsy Imaging

PRIOR TO TREATMENT

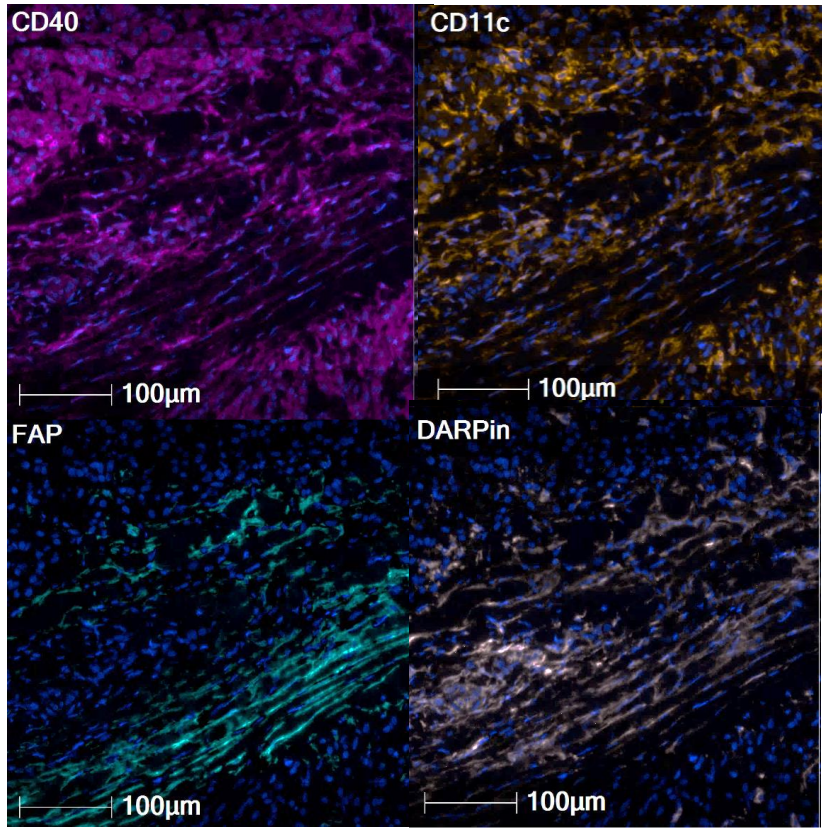


Minimal DC presence in FAP-positive tumor area

DC infiltration

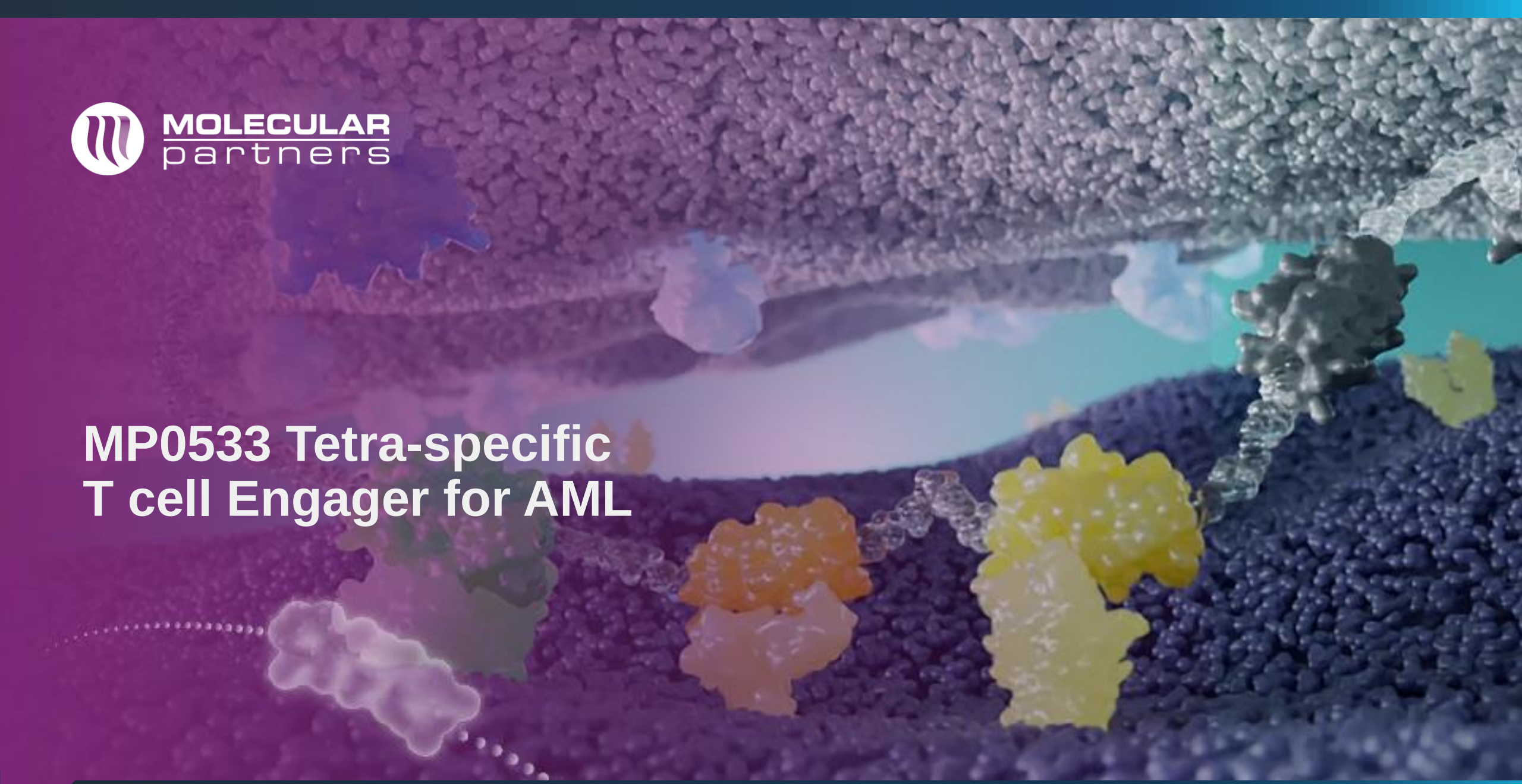
MP0317

CYCLE 2 DAY 8



High DC infiltration in FAP-positive tumor area in MP0317 presence

Tumor biopsy of a patient with GIST in Cohort 5b (Q1W); biopsy location: peritoneum.
DC, dendritic cell; FAP, fibroblast activation protein; GIST, gastrointestinal stromal tumor.

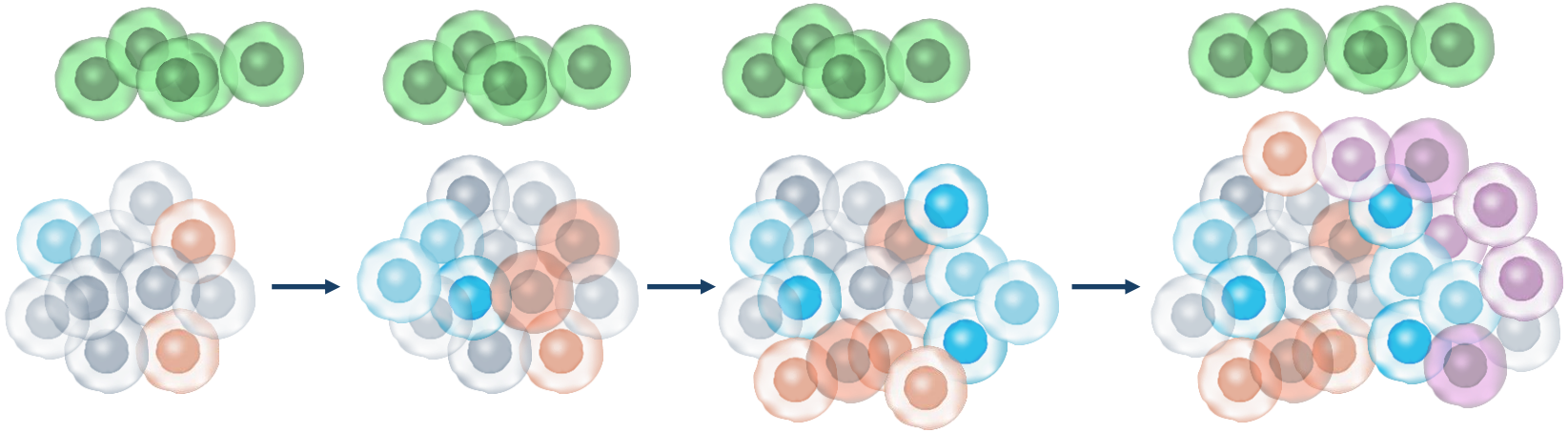


MP0533 Tetra-specific T cell Engager for AML

What Are the Main Challenges of AML?

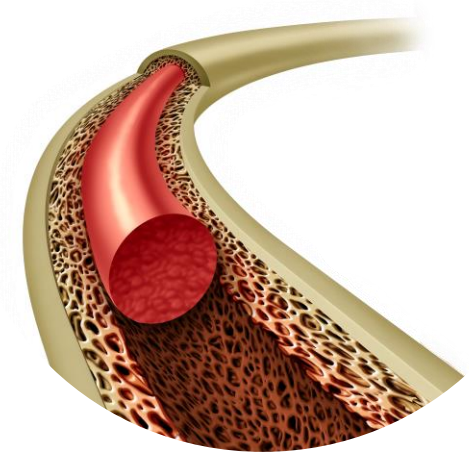
Healthy cells

AML cells



AML cell population is heterogeneous

Individual AML cells do not have a clean target – but are characterized by co-expression of targets



Bone Marrow

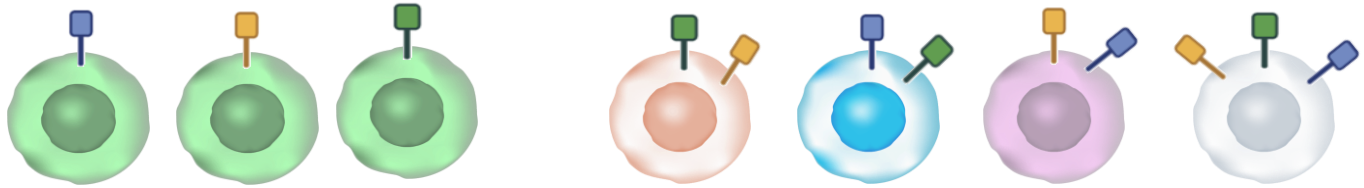
Healthy cells

AML cells/LSC

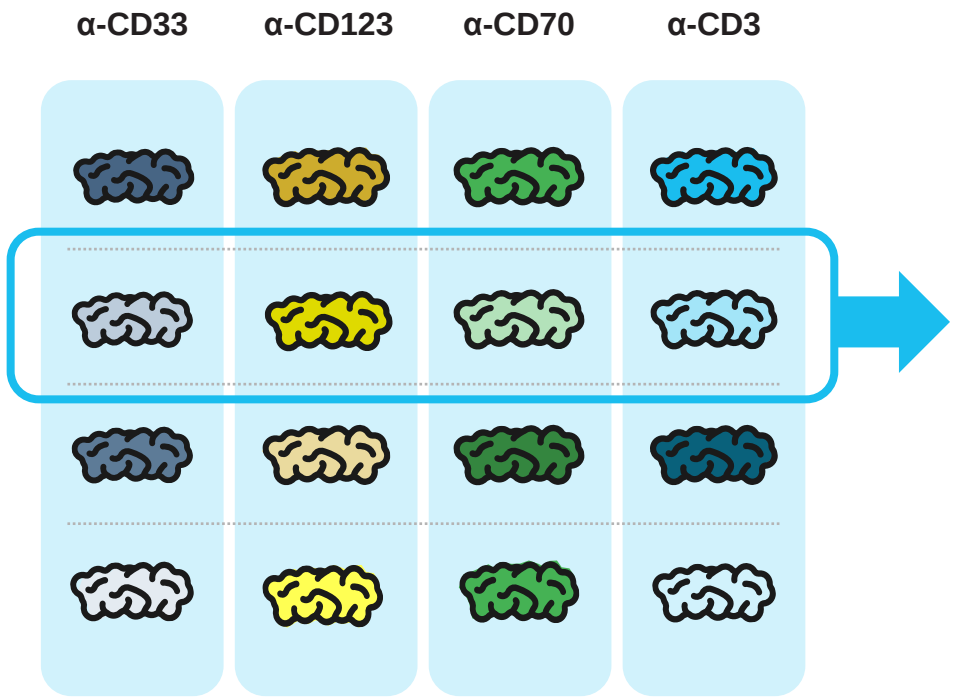
CD33

CD123

CD70

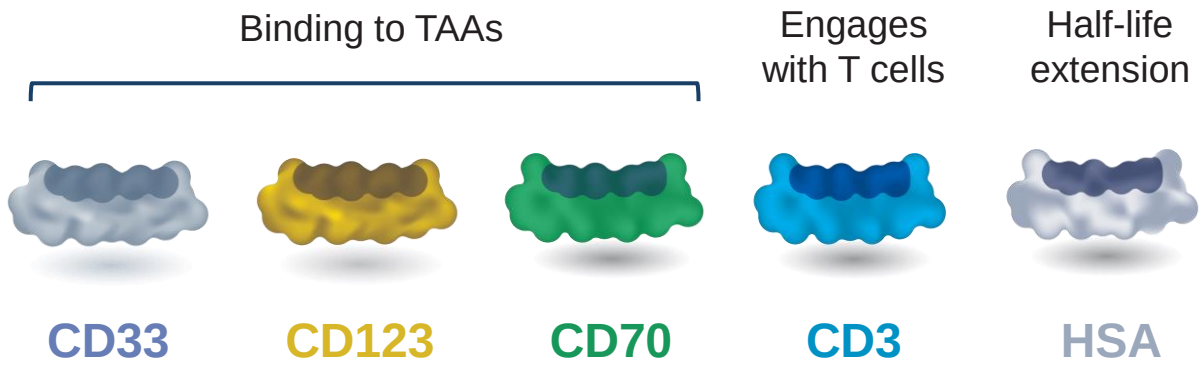


Exploiting DARPin Platform Versatility for Avidity-driven Killing Unlocking the Value of Rare Combinations



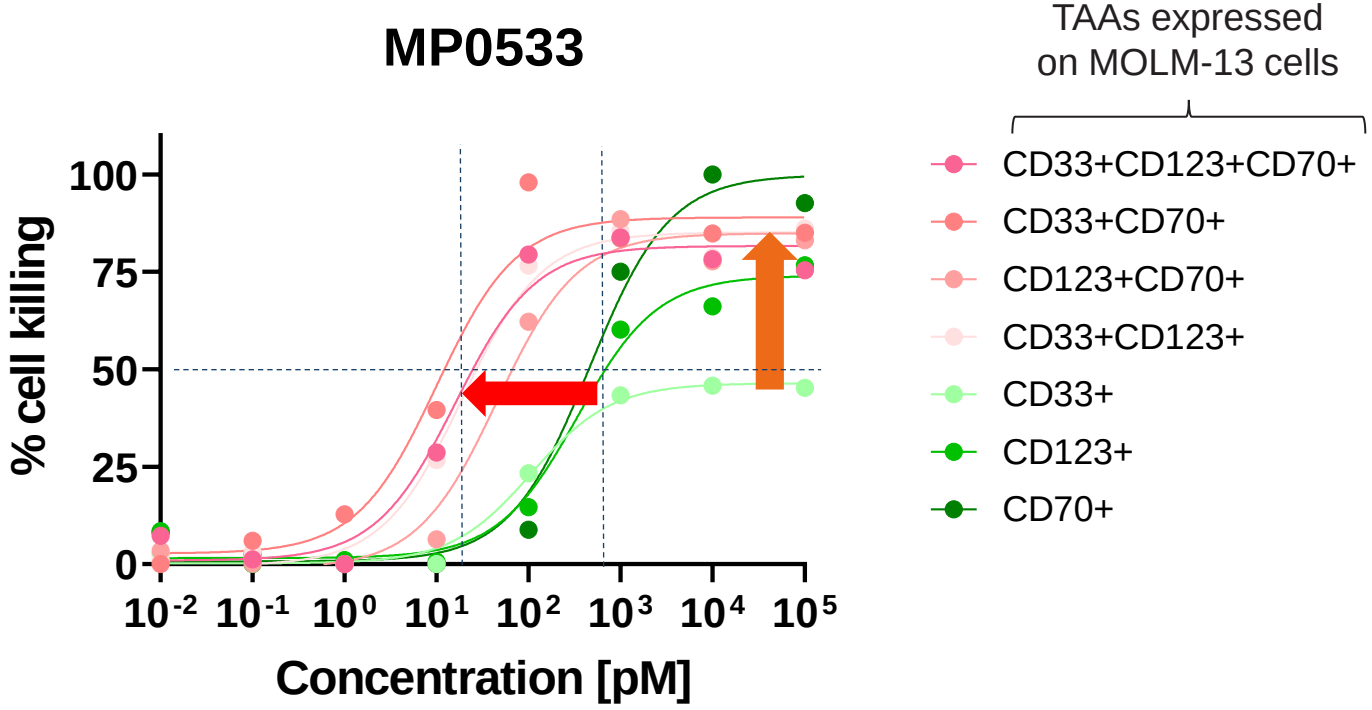
Tested > 8000 combinations

Each binding domain and each linker was optimized for affinity and steric fit

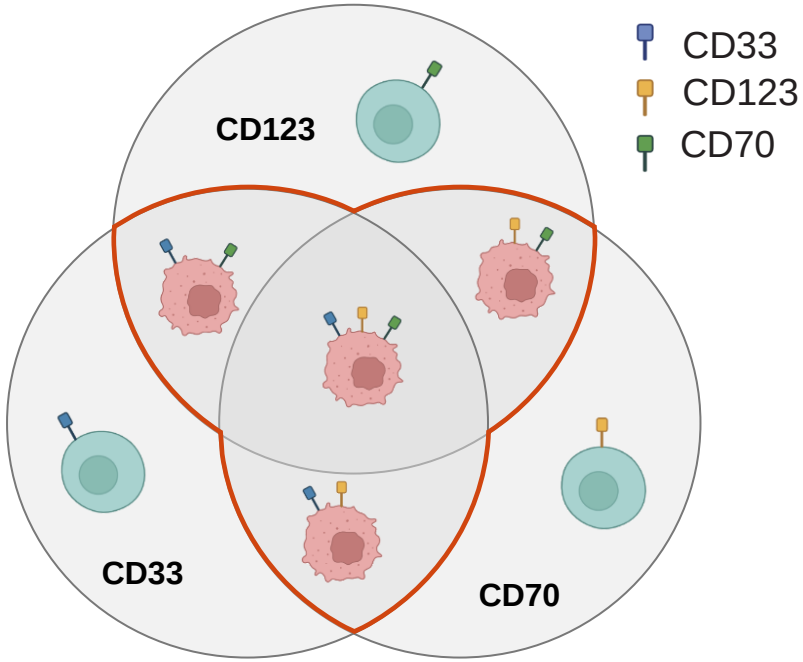


HSA, human serum albumin; TAA, tumor-associated antigen.

MP0533 Induces Specific Killing of AML Cells Expressing 2 or 3 TAAs



SELECTIVITY



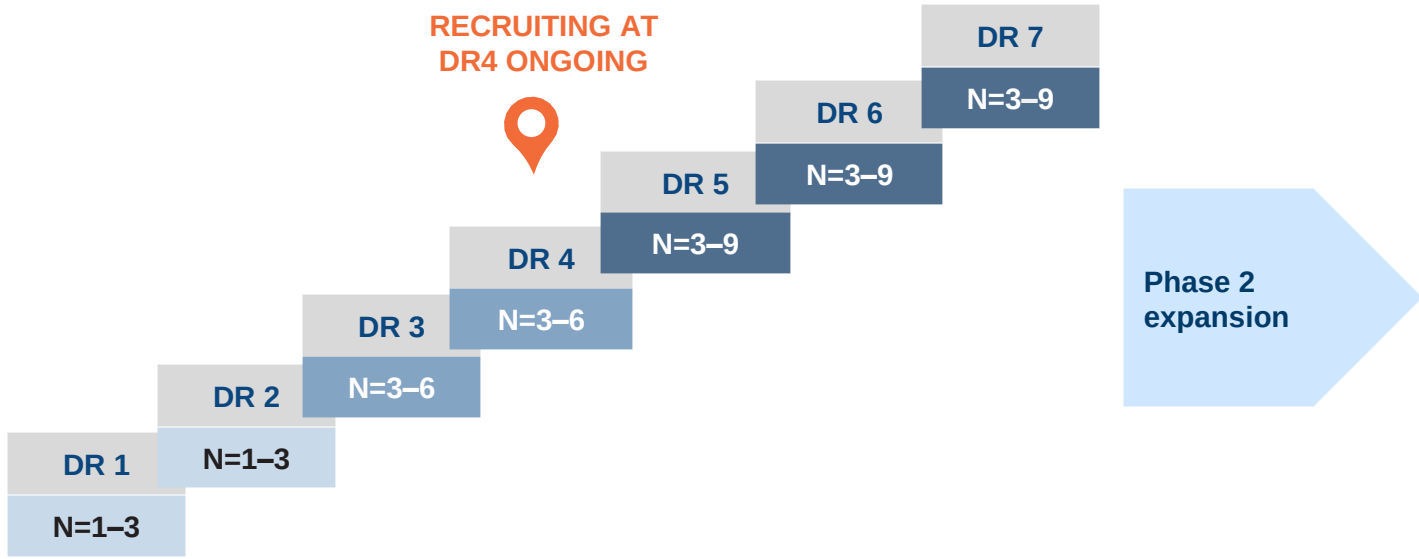
TAA, tumor-associated antigen.

MP0533 Phase 1 Dose-escalation Trial in R/R AML patients

Patient population
AML or MDS/AML R/R to HMA, induction CT or allogenic HSCT
N=20–45 patients

Endpoints
DLTs, safety, tolerability
antileukemic activity
PK, T-cell activation, cytokine release

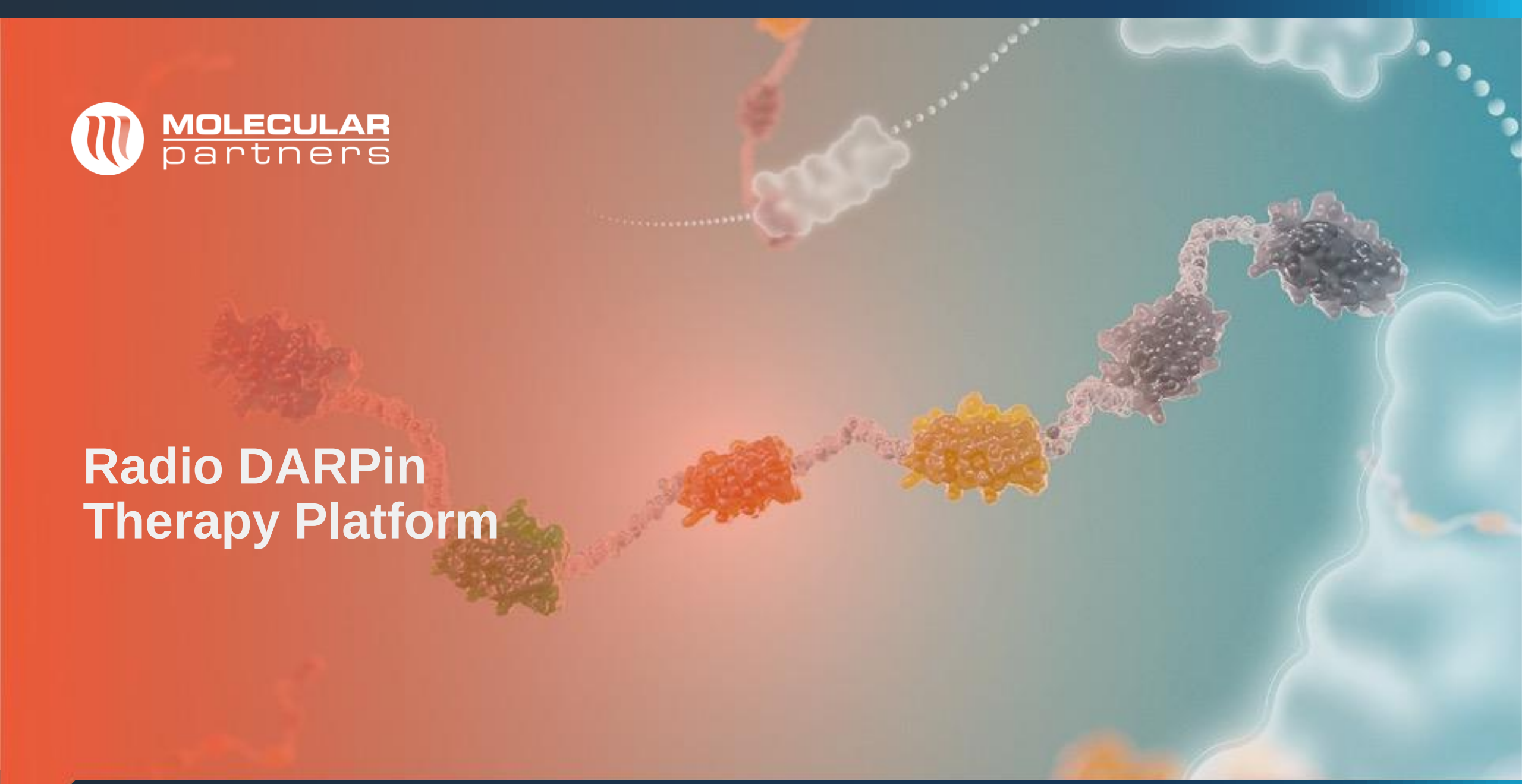
Centers
7 sites open across Europe (NCT05673057)



Bayesian design, includes a step-up dosing

Study open and recruiting, initial results expected in Q4 2023

AML, acute myeloid leukemia; CT, chemotherapy; DLT, dose-limiting toxicity; HMA, hypomethylating agent; HSCT, hematopoietic stem cell transplantation; N, number of patients; PK, pharmacokinetics; R/R, relapsed/refractory.



Radio DARPin Therapy Platform

Precision Oncology by Targeted Radioligand Therapy

Effective radioligands deliver a sufficiently large dose of radioactivity to the tumor for cell killing, while sparing healthy tissues

Ligand:
Specific targeting of tumor cells

Therapeutic radioisotope:
DNA damage to kill tumor cells

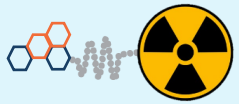
PET/CT scan pictures adapted from Sathekge M, Bruchertseifer F, Knoesen O et al. 225Ac-PSMA-617 in chemotherapy-naive patients with advanced prostate cancer: a pilot study. Eur J Nucl Med Mol Imaging 46, 129–138 (2019). https://doi.org/10.1007/s00259-018-4167-0.

Radio DARPin Therapeutics (RDTs): Platform to Expand the Targetable Space in Nuclear Oncology

IDEAL RADIO PLATFORM PROPERTIES

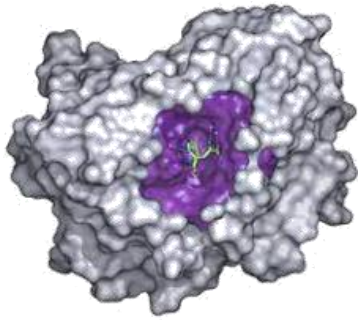
- High affinity
- High specificity
- Short systemic half-life
- Low kidney uptake
- **Broad target range**

RLTs



Most effective for

Targets where a small molecule ligand with high affinity & specificity can be generated or is available

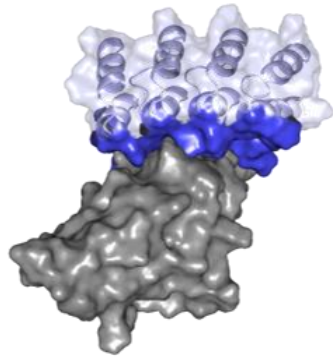


Example targets: PSMA…

RDTs

Most effective for

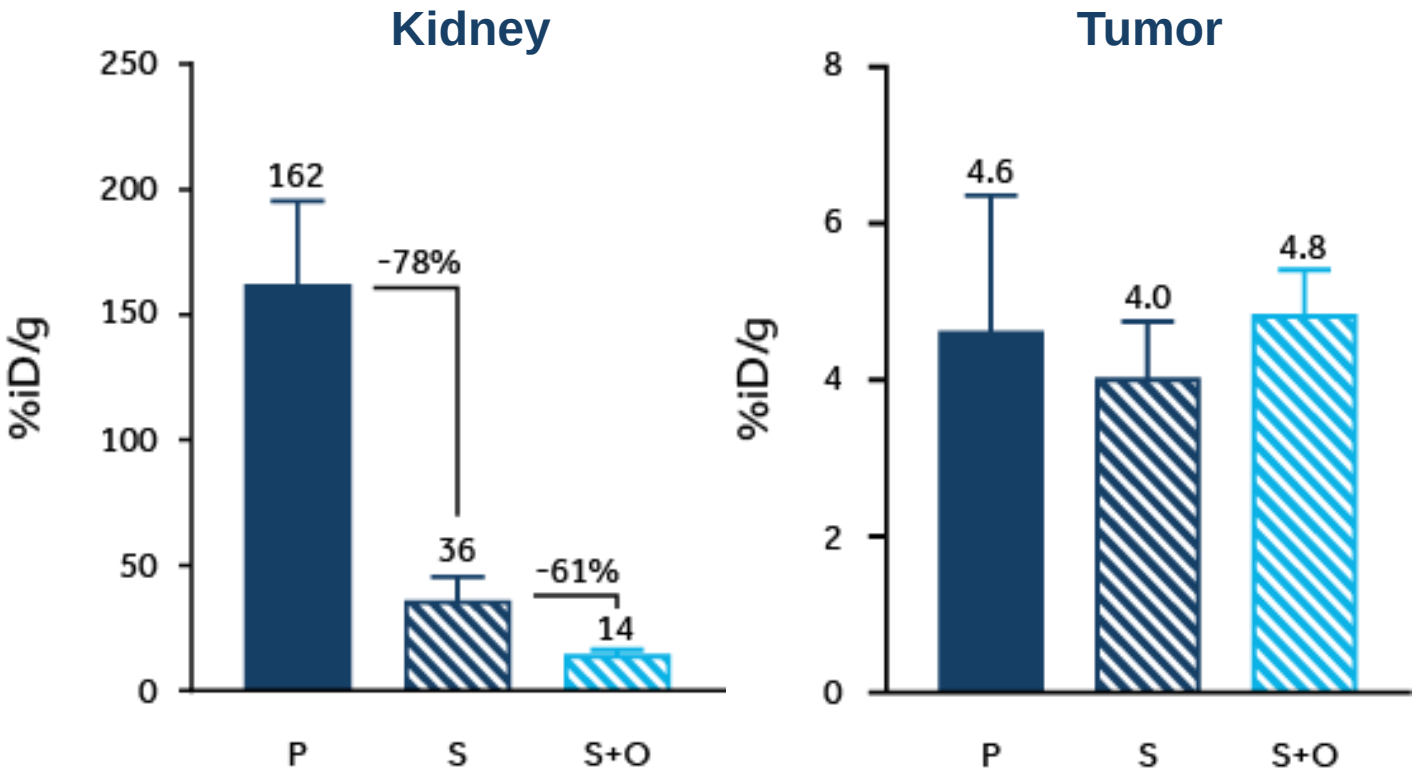
Targets that are challenging for peptides or small molecules (for desired specificity & affinity)



Example targets: Her2, DLL3, …

PSMA: PSB 1Z8L; CD33: PDB 5IHB.
DLL3, delta-like ligand 3; Her2, human epidermal growth factor receptor 2; PSMA, prostate-specific membrane antigen; RDT, radio-DARPin therapy; RLT, radio-ligand therapy.

Surface Engineered Radio-DARPins Show Strongly Reduced Kidney Update

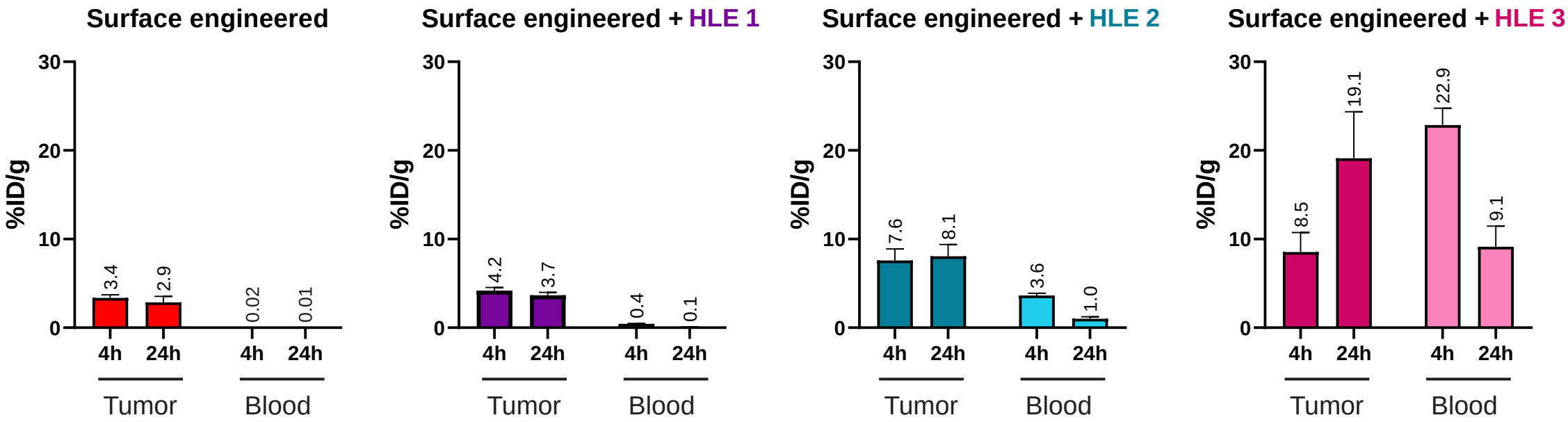


After 4 hour timepoint	T/K*
P: Parental	1/35
S: Surface Engineered	1/9
S+O: Surf. Eng. + Orthogonal + O**	1/3

*tumor to kidney ratio

**Orthogonal = MP proprietary kidney blocking or saturating agent

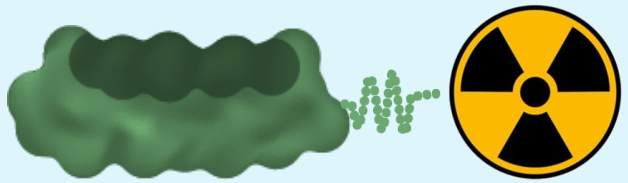
Systemic Half-life Extension (HLE) Increases Tumor Uptake



- Serum albumin binding results in increased blood levels that correlate with higher tumor uptake
- **HLE toolbox with different "strengths" allows RDT properties tailored to specific needs & payloads**

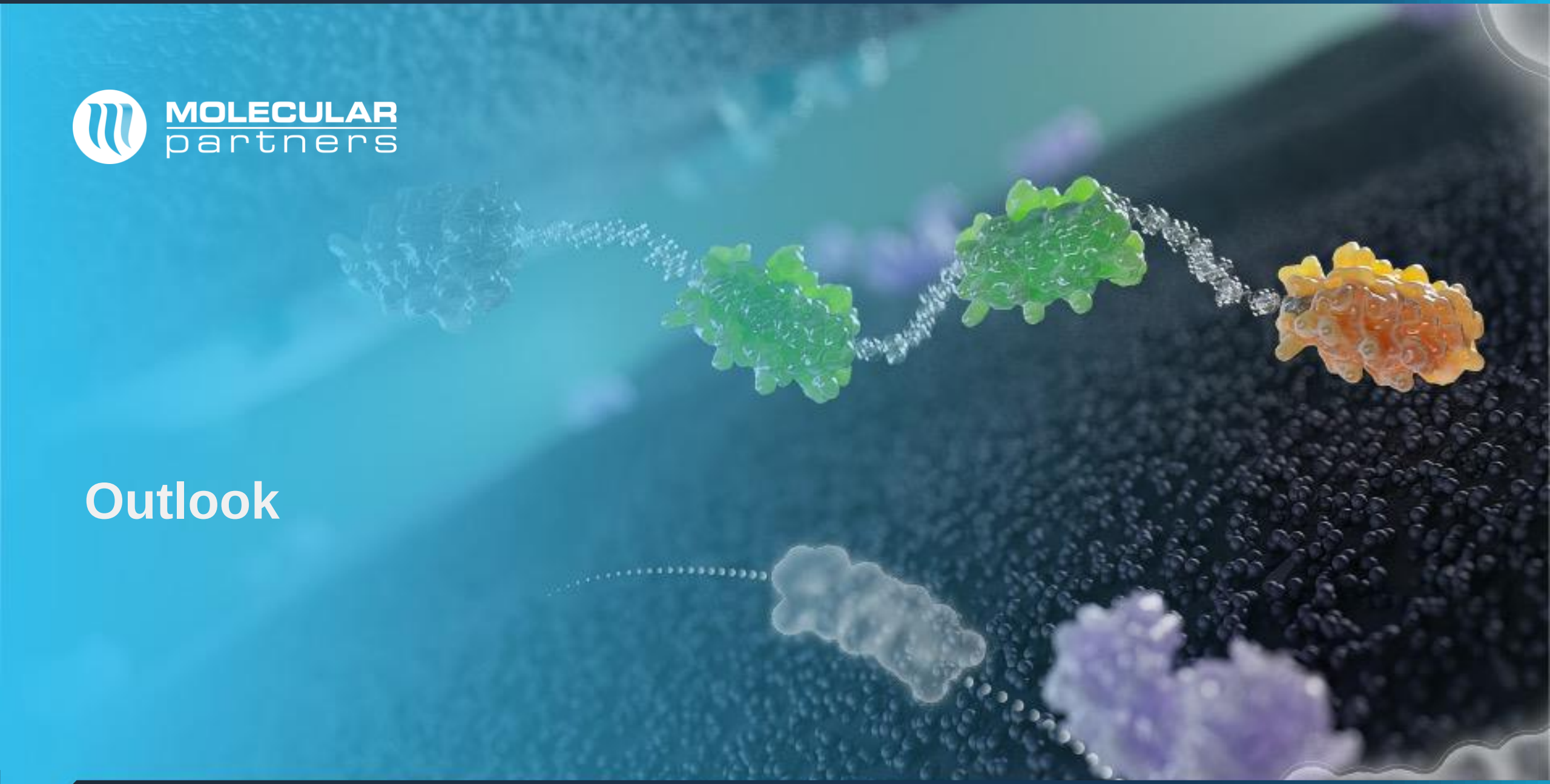
Collaborating with World Leader in Radio-Oncology

NOVARTIS



- $20m up front
- Up to $560m in potential milestones
- Up to double-digit royalties
- Exclusive for two tumor antigens

Outlook

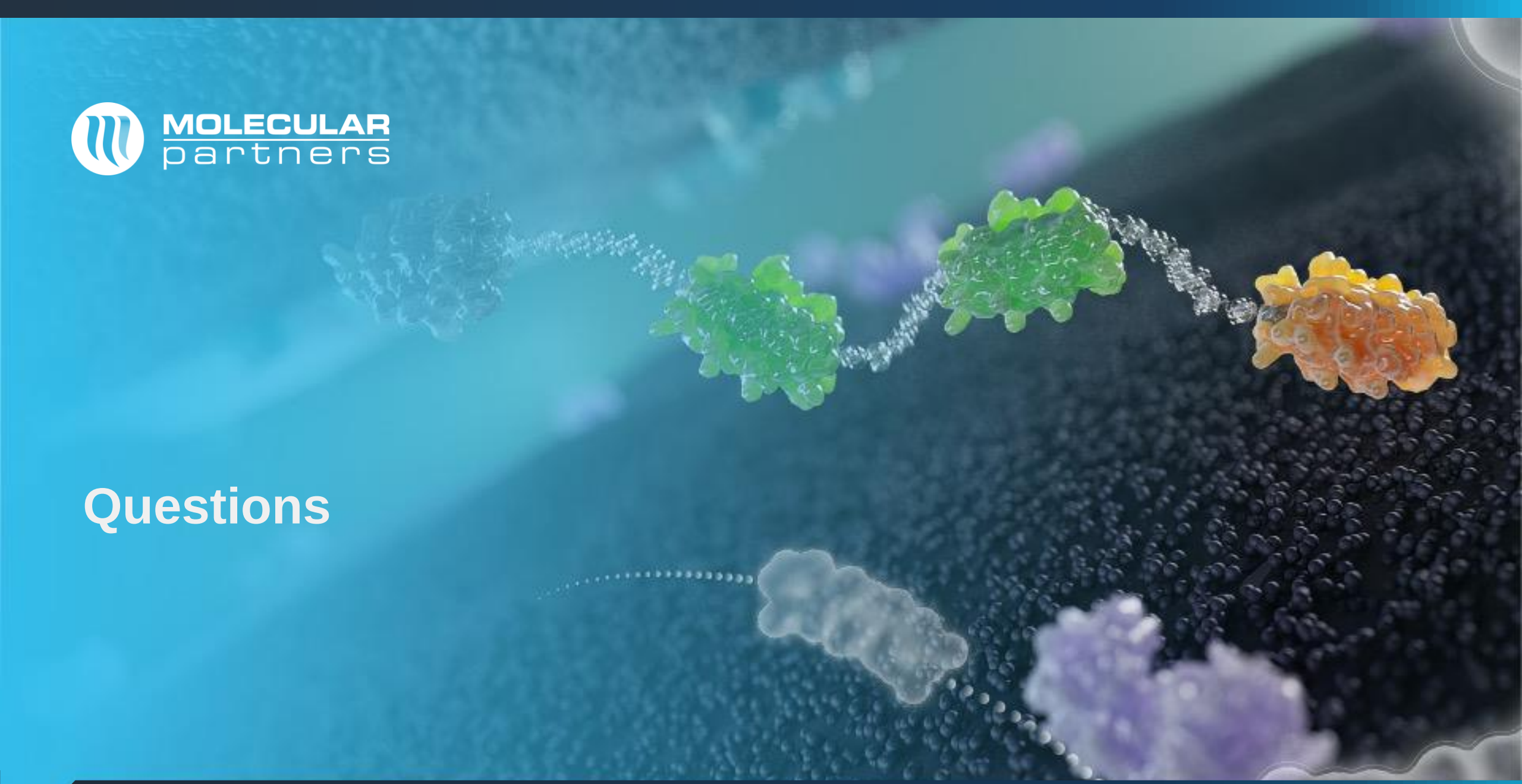


Outlook & Upcoming Milestones

MP0533	• **Initial Phase 1 results in R/R AML in Q4 2023**, additional data in H1 2024 • Clinical expansion in Europe and preparation of potential US IND application
MP0317	• Additional Phase 1 proof-of-mechanism and safety data at **SITC 2023** • Partnering for clinical development in combination settings
Radio DARPin Therapy Platform	• Build on advances in reduced kidney accumulation, **focus on tumor accumulation** • Evaluation of additional targets • Establish collaborations with radionuclide companies
Next Opportunities for DARPins	• **Leverage DARPin platform** for next-generation immune cell engagers • Continue to establish Switch DARPin platform

CHF ~218 million cash (incl. short-term time deposits) ensures **funding well into 2026***

*As of June 30, 2023.
AML, acute myeloid leukemia; IND, investigational new drug;
R/R, relapsed/refractory; SITC, Society for Immunotherapy of Cancers (Nov 1–5, 2023).



Questions