

Corporate Presentation

Patrick Amstutz, CEO

May, 2023

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Molecular Partners at a Glance

WHAT WE INVENTED

- New class of therapeutics – **Designed Ankyrin Repeat Proteins or DARPins**
- DARPIn as therapeutic modality to **close the gap between small molecules and antibodies**
- 7 clinical-stage compounds, **>2500 patients treated**, manufacturing established

HOW WE APPLY IT

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

WHY INVEST






- **First tri-specific T-cell engager DARPIn** as a unique multi-specific treatment for **AML (MP0533)**
- Harnessing the power of radioactivity by applying it to cancers through **Radio DARPIn Therapies**
- More to come as we are **building additional compounds, including DARPIn SWITCH**

AND

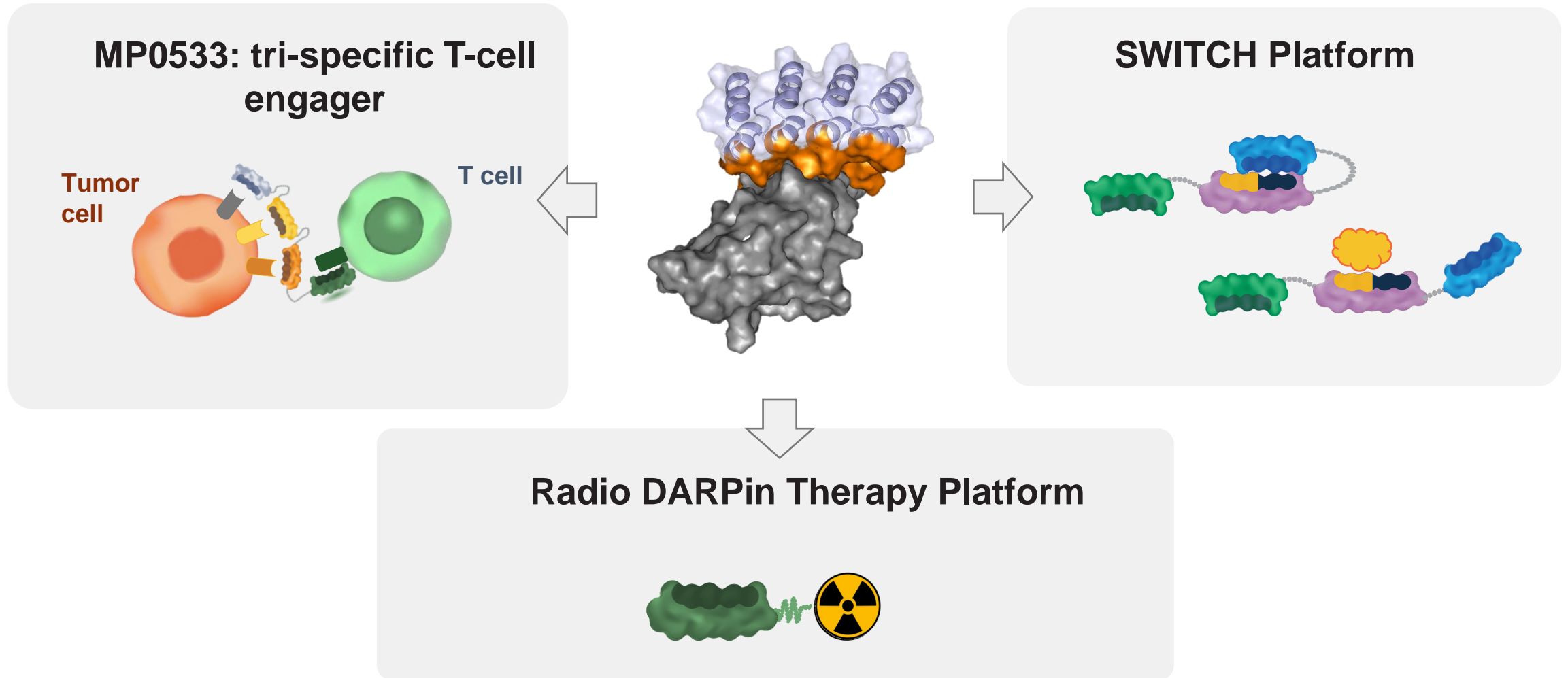
- We are well capitalized with **cash of ~ CHF 250 million*** into 2026

Pipeline

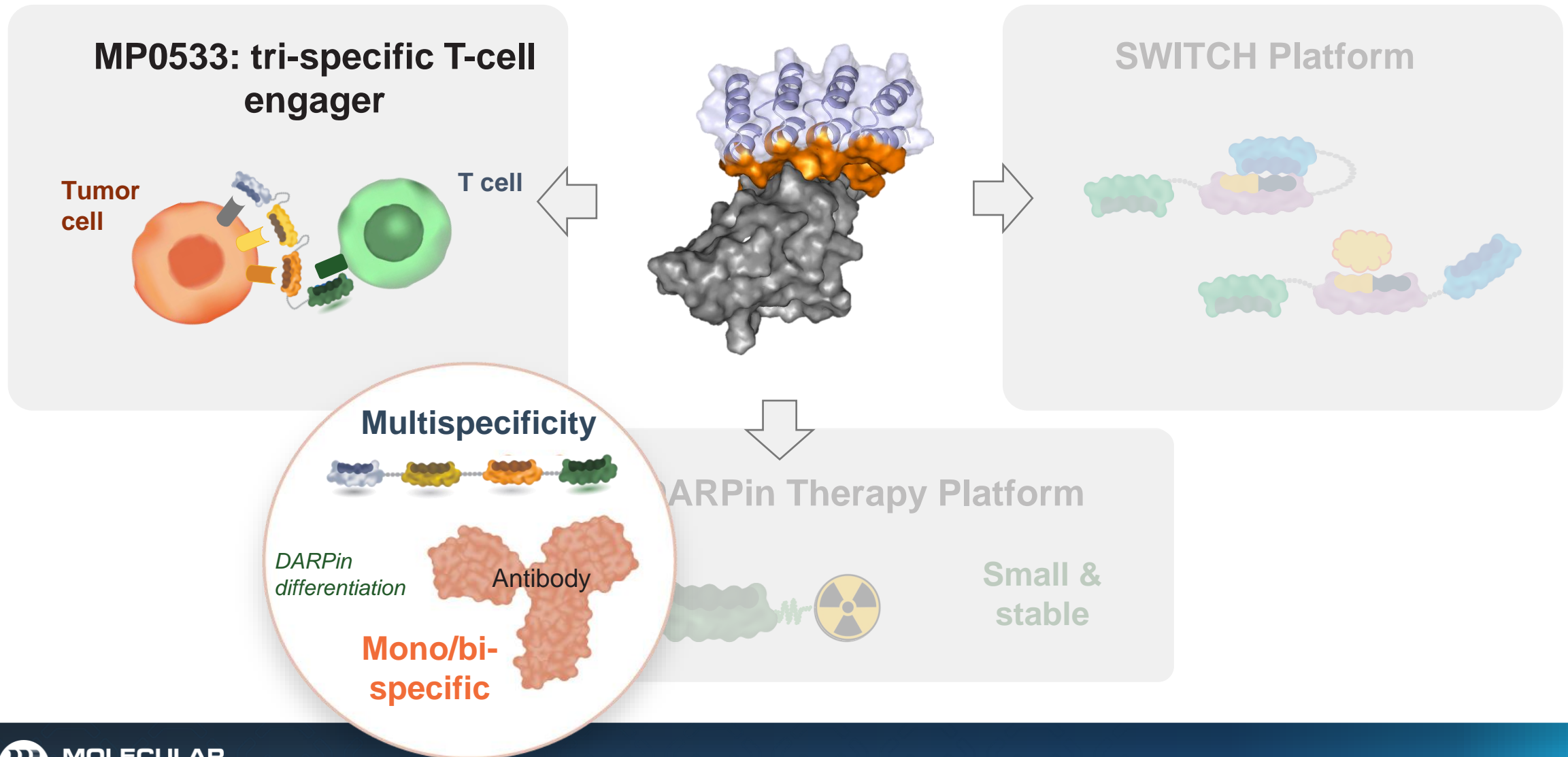
Oncology
 Discovery Oncology
 Virology
 Ophthalmology

CANDIDATE	RESEARCH	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	RIGHTS
MP0317 FAP x CD40	Solid Tumors					
MP0533 CD33+CD70+CD123 x CD3	AML					
Radio DARPIn Therapy Platform	DLL3 2 nd target ongoing	<i>In-house programs</i>				
	Solid Tumors	<i>Partnered programs</i>				
Virology						
Immune Cell Engagers						
Abicipar¹ VEGF	Wet AMD					
Ensovibep² Sars-Cov-2	Covid					

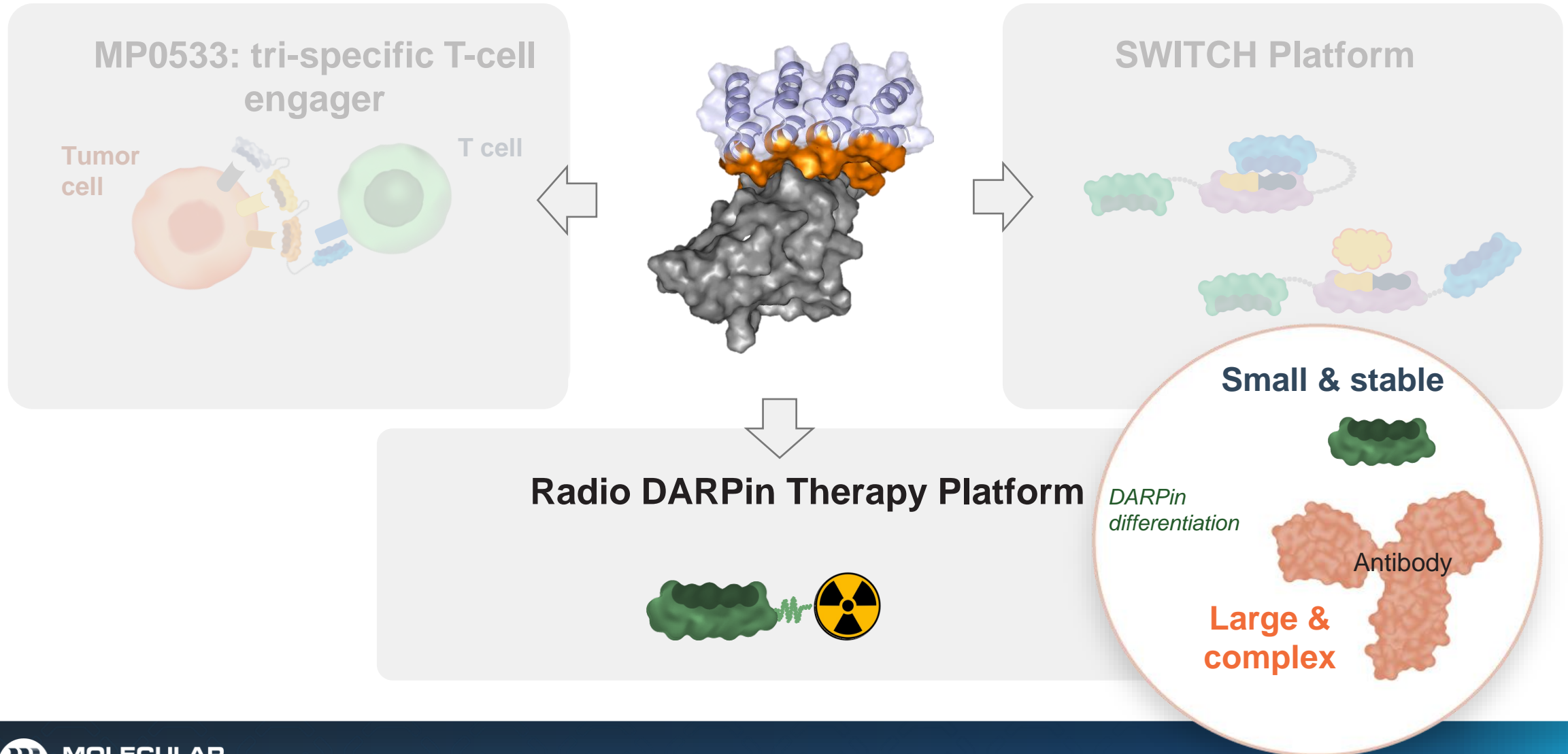
Future of DARPin Therapy Framework



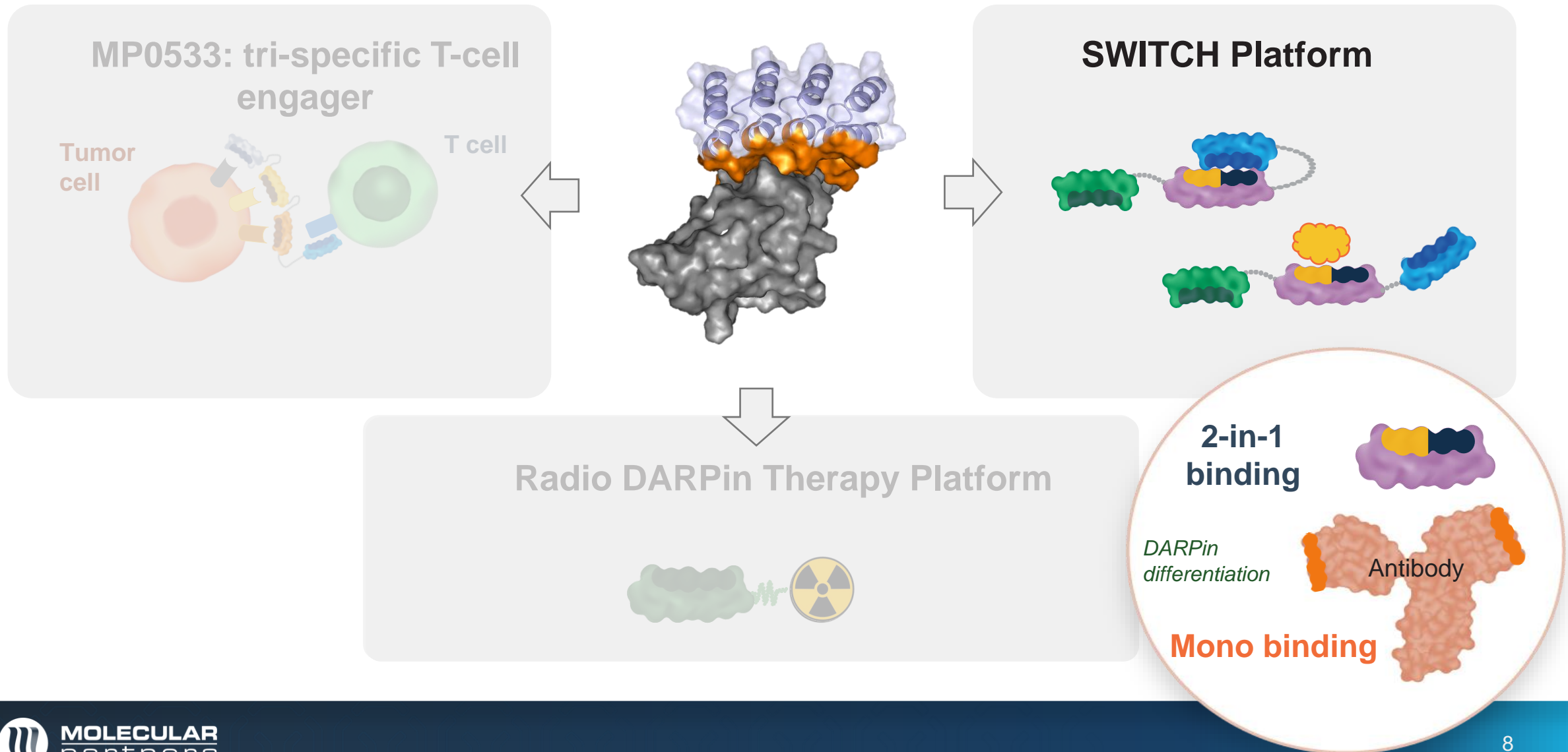
Future of DARPin Therapy Framework – Multi-DARPin



Future of DARPin Therapy Framework - RDT



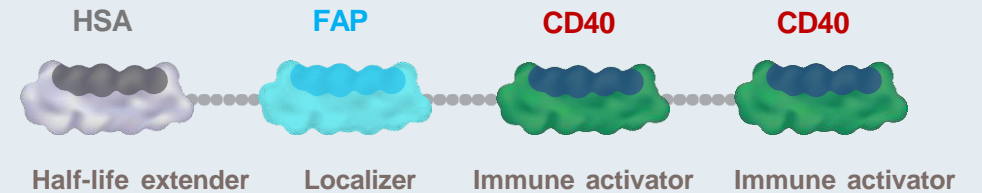
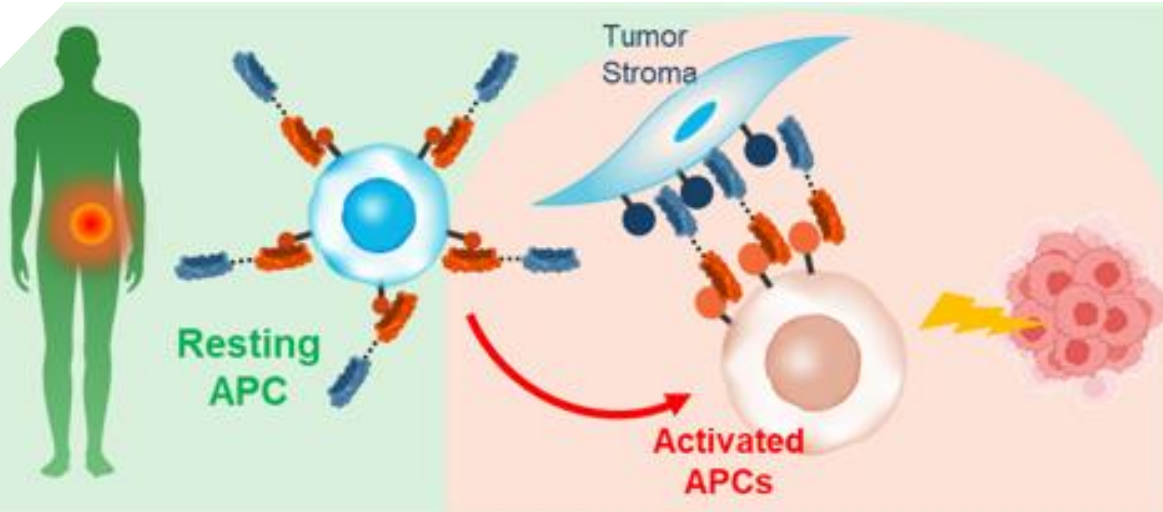
Future of DARPin Therapy Framework - SWITCH



MP0317 - Tumor-localized immunotherapy

Clinical update

MP0317: A Phase 1 Localized CD40 Agonist



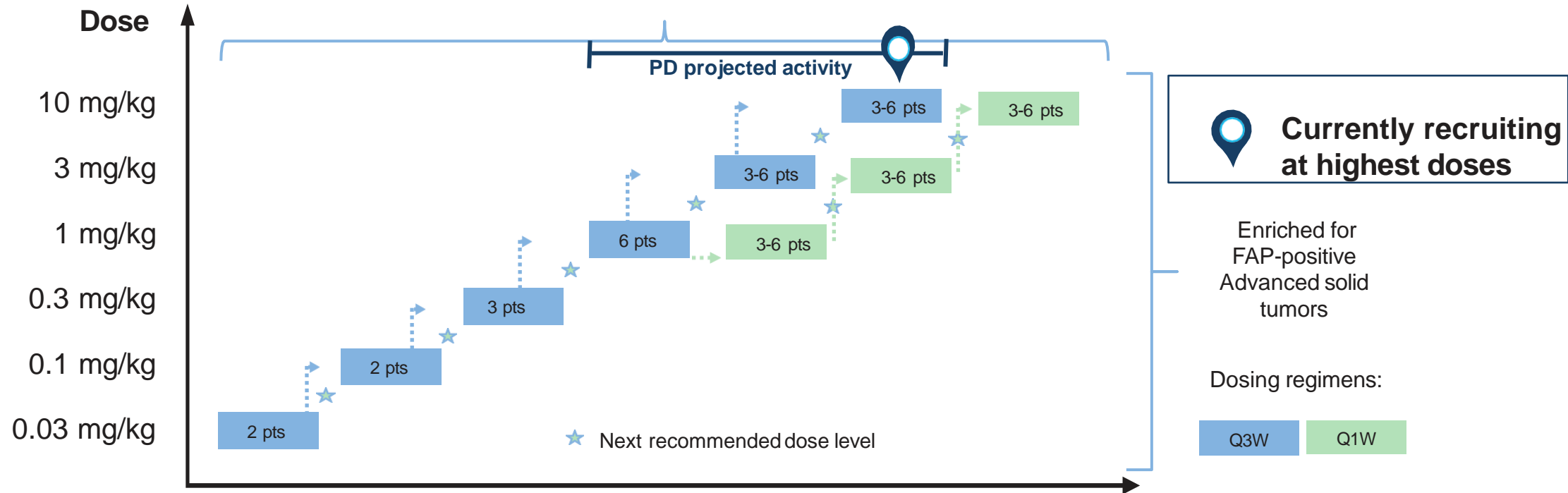
FAP: Expressed on fibroblasts in tumor stroma, local cluster

CD40: Expressed on APCs, activation via clustering

- **DARPin design goal:** Solve systemic toxicity of CD40 agonists by localizing immune activation to tumor
- **Outcomes:** Preliminary clinical data supports systemic safety and tumor localization; initial signs of local immune activation
- **Next milestones:**
 - **H1 23:** Partnering for combination trials
 - **External Validation Potential:** Roche's CD40 x FAP (RG6189 / RO7300490) combination trial with PDL-1 (280 pts)

MP0317-CP101 Clinical Trial Update

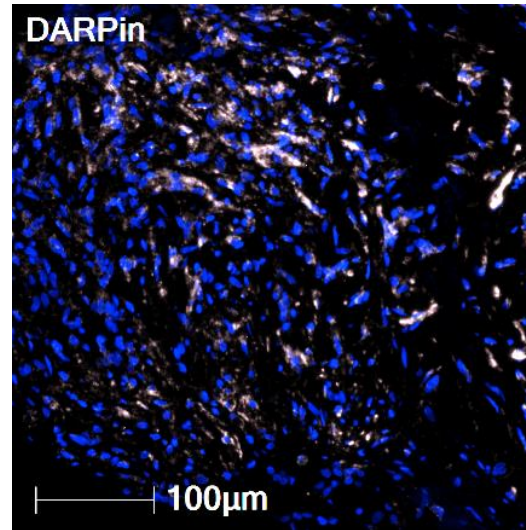
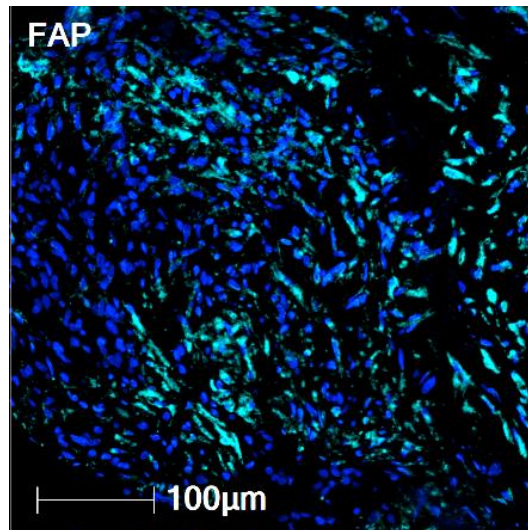
Dose-Escalation MP0317 Monotherapy



- Dose escalation ongoing at 10 mg/kg – the highest dose
- No dose-limiting toxicities to date
- Expected PD activity from 1 mg/kg
- Dosing regimen flexibility

MP0317 Co-localizes and Occupies FAP in Tumor

MP0317 and FAP co-localize in tumor



DAPI ●

MP0317 ●

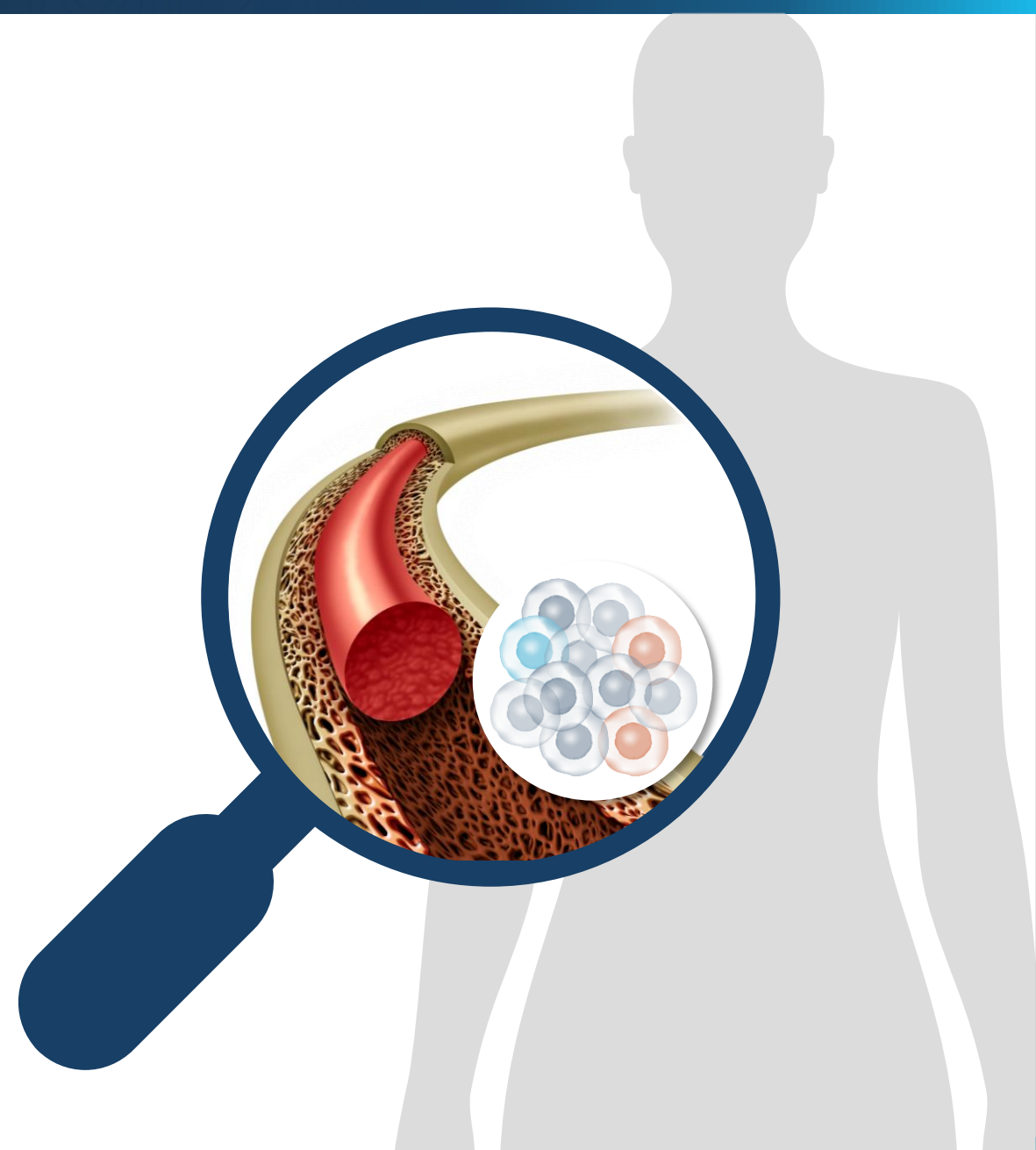
FAP ●

- Representative multiplex-immunofluorescence for subject 03-003, a cervical cancer patient dosed at 0.3 mg/kg
- 26 % of FAP is occupied by MP0317
- Tumor biopsy specimen

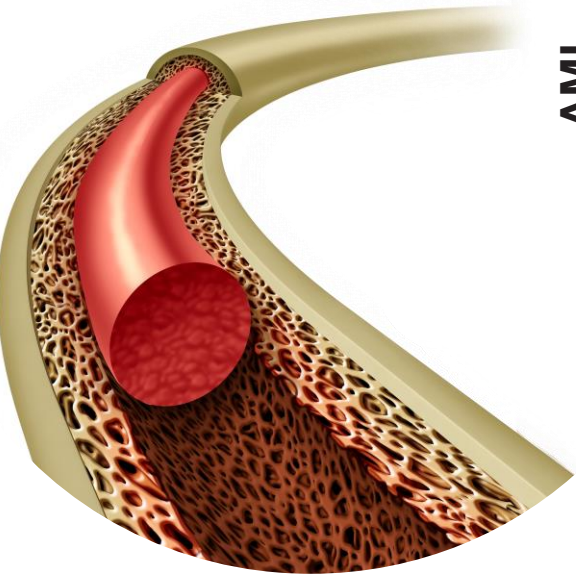
MP0533 - Multi-specific DARPin for AML

What is AML?

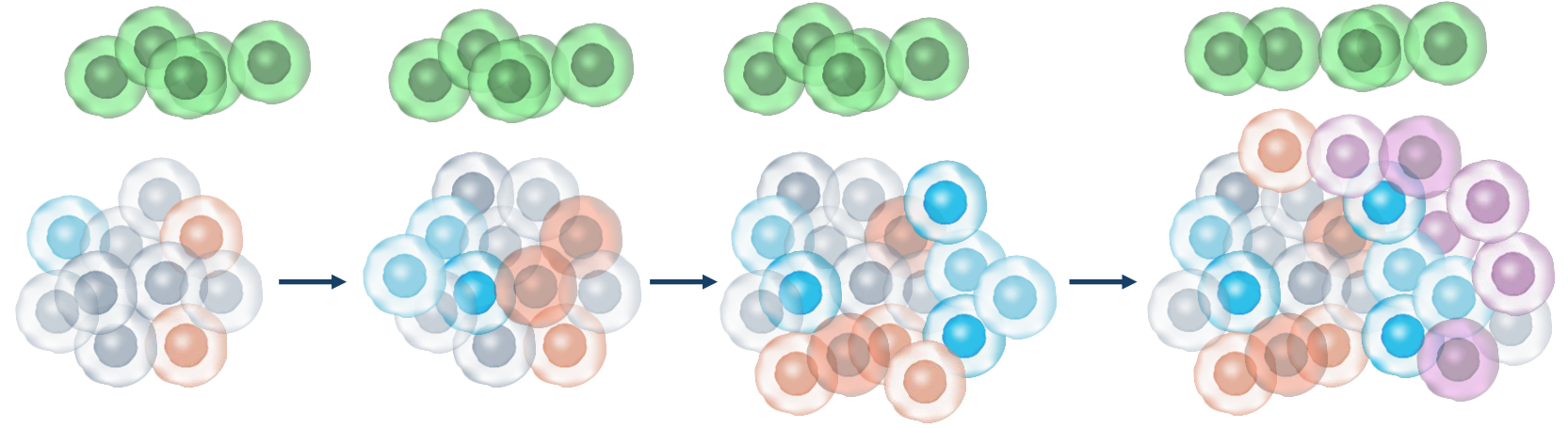
- **Acute myeloid leukemia (AML)** is the **most common leukemia among the adult population** and accounts for about 80% of all cases.
- With recent advancements in the management guidelines, the **cure rates have increased up to 15% in patients older than 60 years** and about 40% in patients below 60 years of age. **But it remains the most fatal type of leukemia.**
- According to **the American Cancer Society (ACS)**, in 2022, AML was commonly found in elderly people with an average age at diagnosis being 68, and survival remained remarkably low. It affected approximately 60,650 people in 2022 and **caused 24000 deaths.**
- The global market for AML therapeutics in 2021 was estimated at sales of USD1.3 billion. Overall, Credit Suisse* estimates that there may be **\$12.7 billion in potential revenue from the AML market in 2032, implying a potential 2021-2032 CAGR of 23%.**



What Are the Main Challenges of AML?



Healthy cell
AML cells



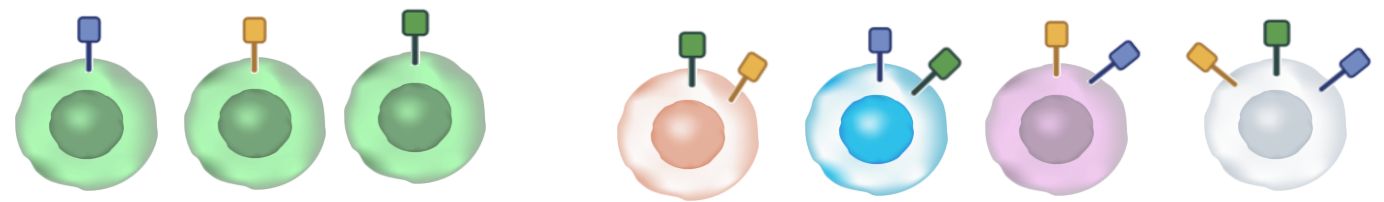
AML cell population is heterogeneous

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

Healthy cells

AML cell/ LSC

- CD33
- CD123
- CD70



CD123/CD70/CD33 co-expression differentiates LSCs and AML Blasts

Allowing for or avidity-driven specific T cell killing of LSCs and blasts

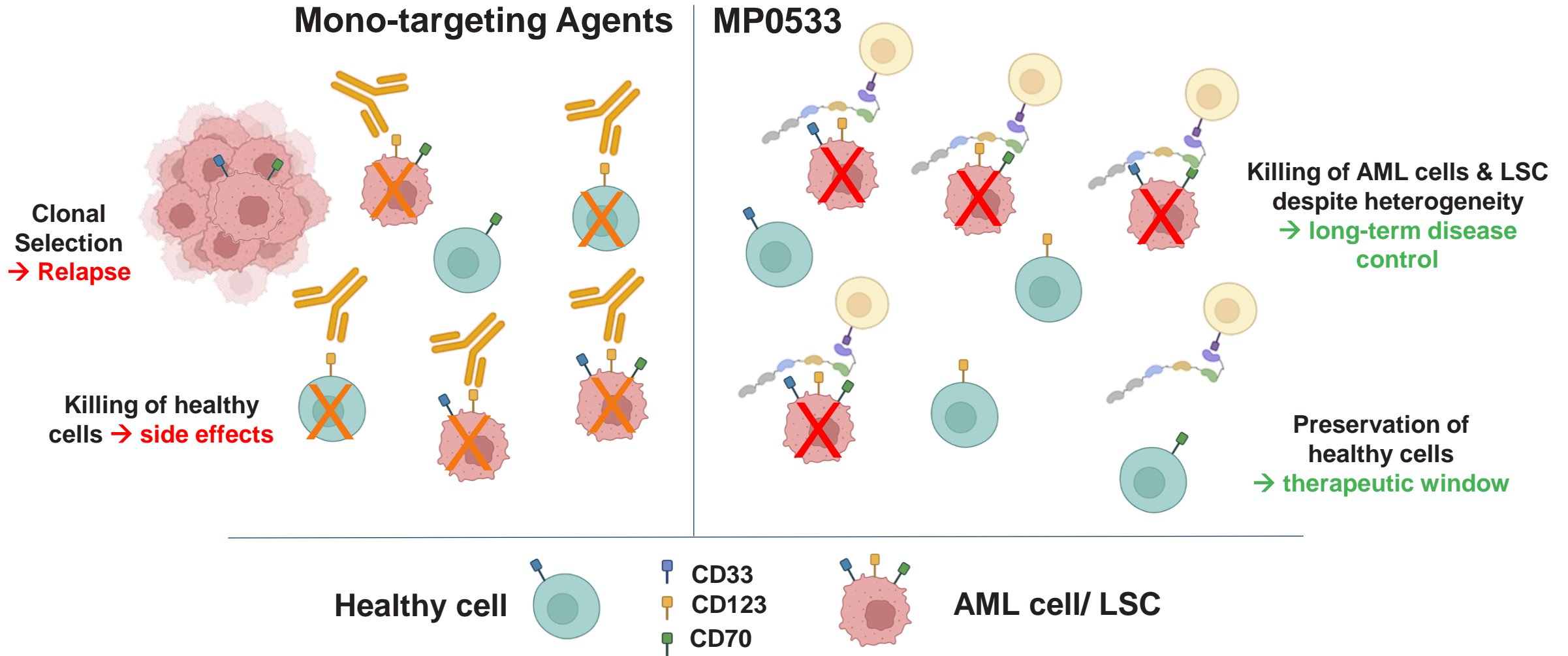
	LSCs	Blasts	HSC	Lymphocytes	Inflamed EC	Myeloid cells	pDCs	Basophiles
CD70	Low	Low	Neg /Low	Variable	Neg	Neg	Neg	Neg
CD123	High	High	Low	Neg	Medium	Low/ Medium	High	High
CD33	High	High	Medium	Neg	Neg	High/ Medium	Low	Medium
Theoretical Avidity-based killing*	Yes	Yes	Limited	No	No	Limited	Limited	Likely

* Assuming equivalent affinity for CD33, CD123 and CD70

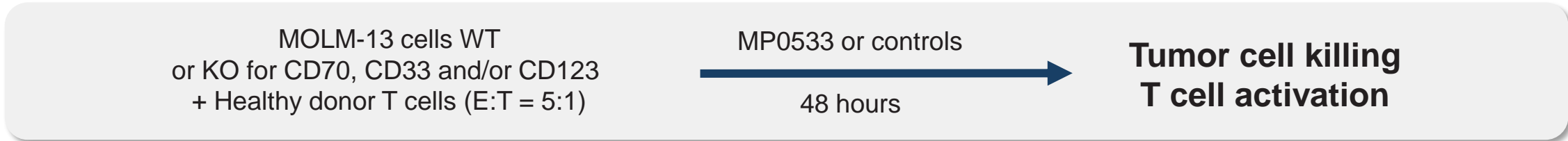
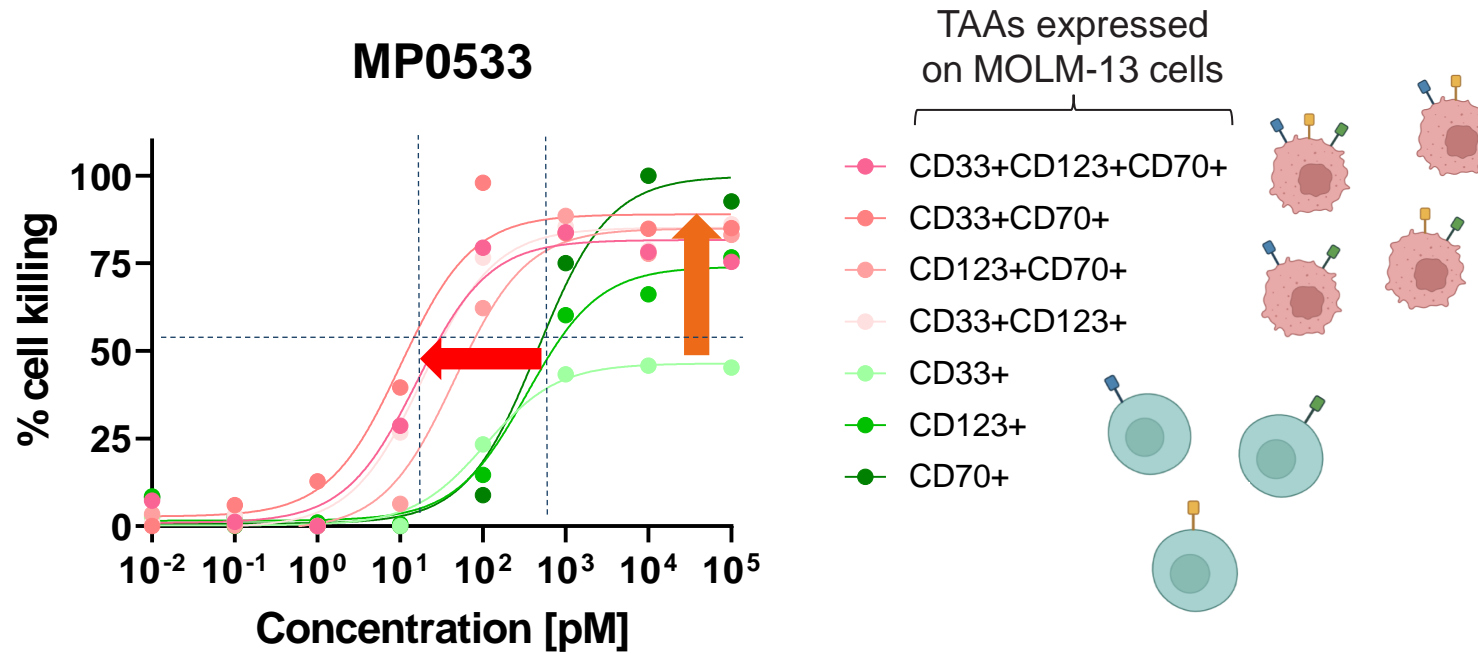
Eliminating LSC and Blast through avidity-driven selective targeting should be doable and will allow

- Treating frail patients thanks to a higher safety profile
- Increasing dose and thus deepening responses for long term control of the disease

Avidity-guided selectivity for cancer cells in AML

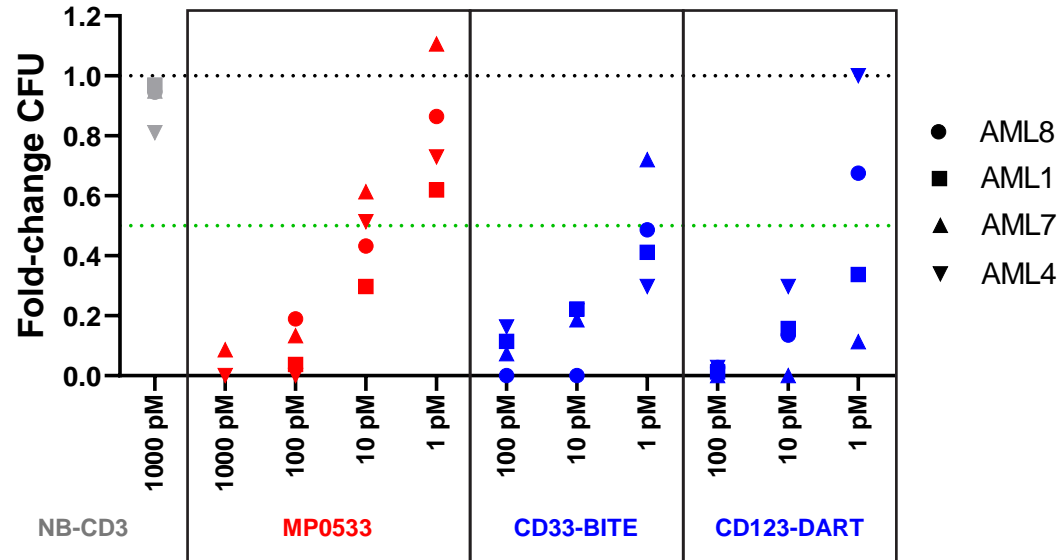


MP0533 Induces Specific Killing of AML Cells Expressing 2 or 3 TAAs

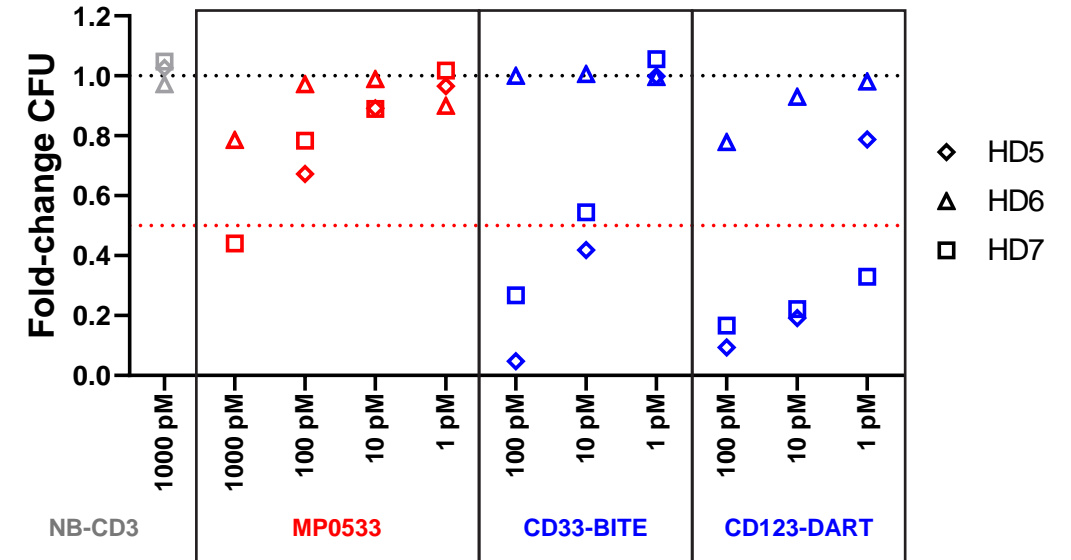


Preclinical data strongly supportive of target profile

Allogeneic killing of AML CD34+ LSC



Allogeneic killing of healthy donor CD34+ HSC



Efficacy

Safety

As presented at ASH 2022

Phase I Dose Escalation Trial in R/R AML patients

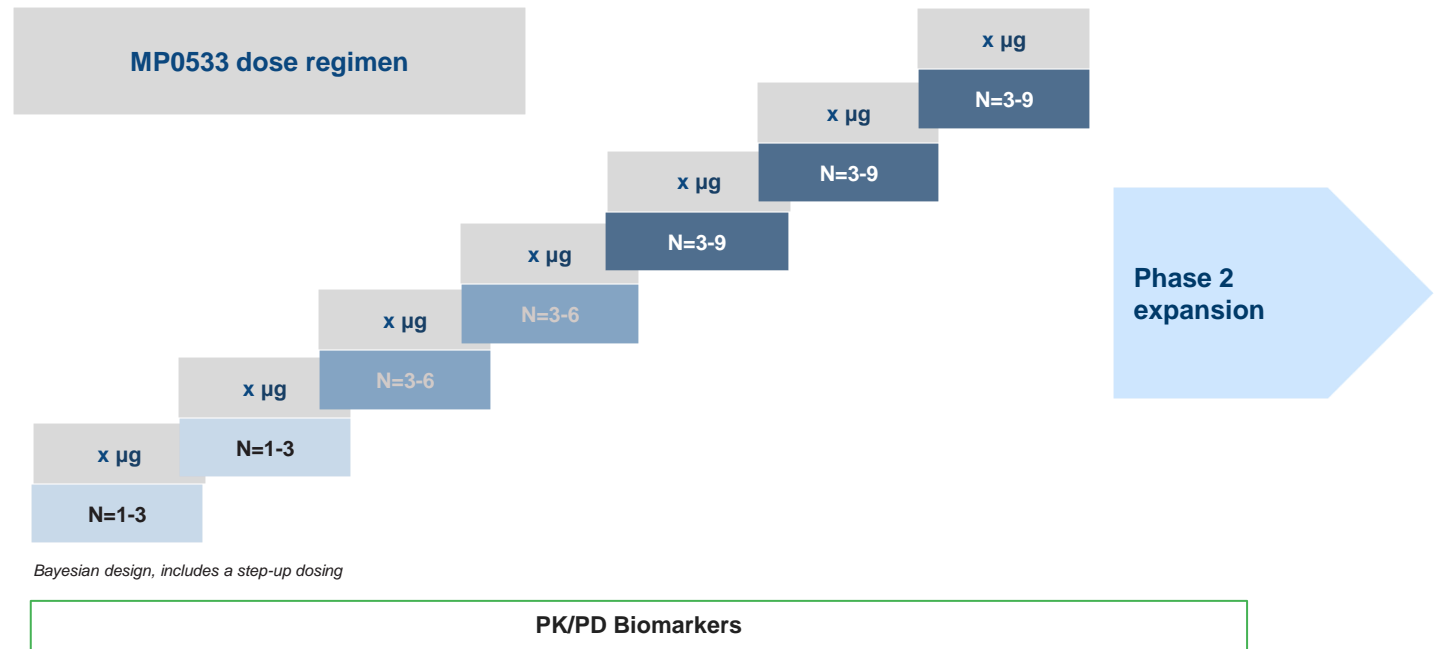
Patient population: AML or MDS/AML relapsed/refractory to HMA, induction CT or allogeneic HSCT

N= 20-45 patients

Endpoints:

- DLTs, Safety, Tolerability
- **Efficacy**, effect on LSCs, PK, T-cell Activation, Cytokine Release

Centers: 5 sites open/initiating (Switzerland/ The Netherlands)



Study Open and Recruiting

Abbreviations: CT = chemotherapy; DLT = Dose limiting toxicity; HMA = hypomethylating agent; HSCT = human stem cell transplantation; N = number of patients

The MP0533 Advantage in AML

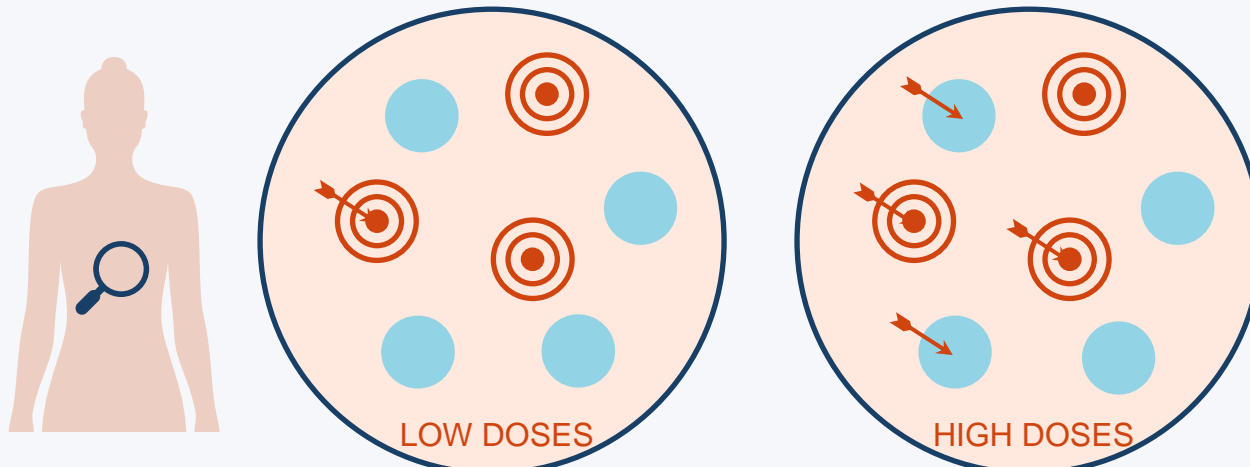
OTHER TARGETED DRUGS

LOW DOSES

- ✗ Do not kill sufficient tumor cells at low doses
- ✗ Tumor regrows and is treatment resistant
- ✓ Less harm to healthy cells

HIGH DOSES

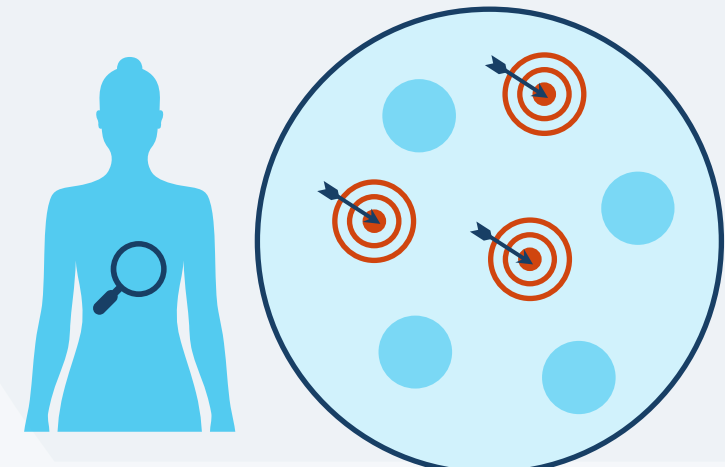
- ✓ More tumor cells are killed
- ✗ Are still not specific enough to fully clear the 'seed' tumor cells
- ✗ Harm healthy cells



MP0533 DARPin

Specific and exhaustive targeting of 'seed' tumor cells with minimal impact on healthy cells

- ✓ Tumor cells are killed --> AML treatment
- ✓ 'Seed' tumor cells are killed --> no relapse
- ✓ Less harm to healthy cells including at high doses



Radio DARPin Therapy Platform

Field that carries high hope in the fight of cancer

DARPin differentiation: small size, high affinity and stability

Unlocking the Potential of Radiopharmaceuticals



Radiation therapy kills cancer cells and has been used for decades. But it's not precise, as it also kills healthy cells and patients can only receive so much radiation.



Radiopharmaceuticals (also called radioligands) are an exciting new drug class that delivers radiation selectively to the tumor, overcoming the limitations of 'standard' radiation therapy.

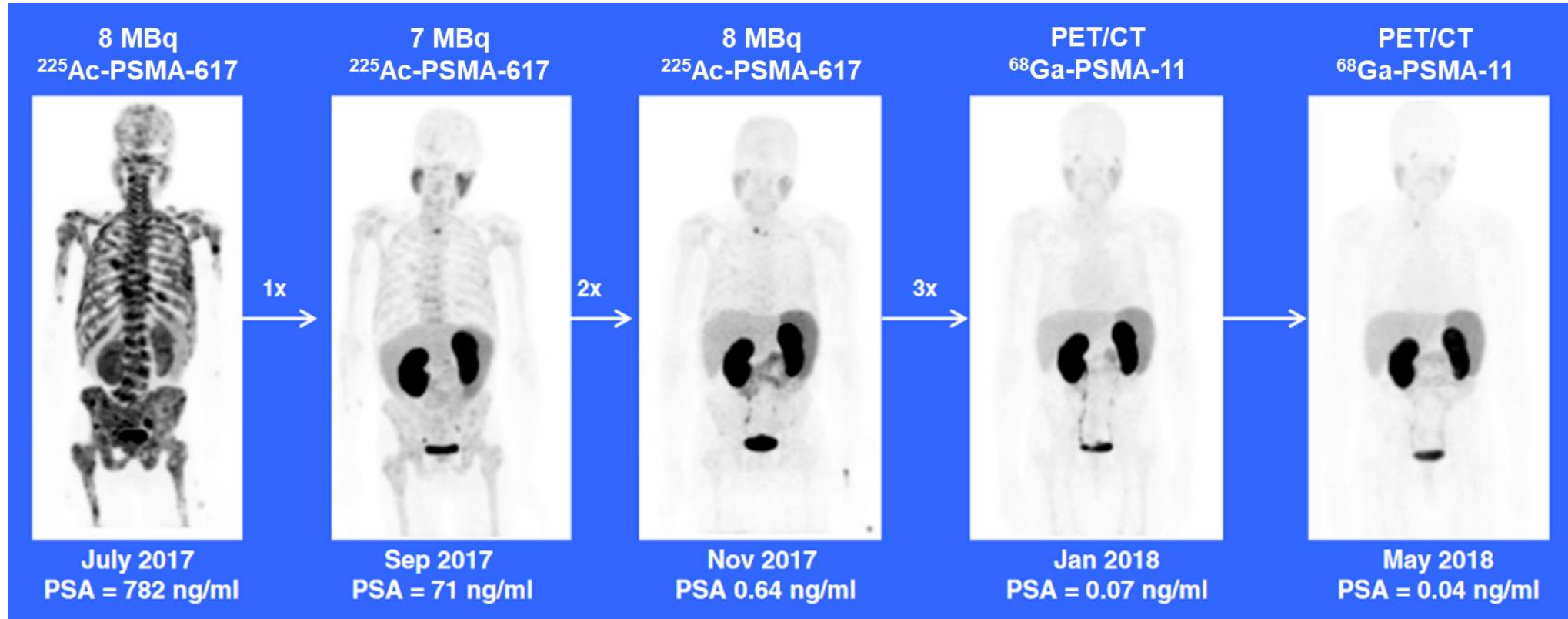


One key challenge for this new drug class is ensuring that the radiation does not damage healthy tissues, like the kidneys (ligand) and bone marrow (monoclonal antibody).



DARPins are uniquely positioned to overcome these challenges and unlock the potential of radiotherapy.

The Anti-Cancer Potential of Radio DARPin Therapy



Example: Treatment of a naïve prostate cancer patient with extensive bone metastasis at primary diagnosis with $^{225}\text{Ac-PSMA-617}$
→ Complete remission after 3 cycles of treatment (symptom free at 11-month follow up)

Sathekge et al., *Eur J Nucl Med Mol Imaging*, 2019

Radiotherapy Remains Fast-growing Opportunity but Innovation is Held Back by Limited Target Universe

11 PUBLIC COMPANIES

Novartis
Bayer
Actinium
Perspective
Clarity
Fusion
Johnson & Johnson
Lantheus Holdings
POINT
Plus
Telix

18 INDICATIONS

GEP-NETs
SCLC, GBM
mCRPC
mCNPC
GRPR+ Tumors
Solid Tumors
BMT Conditioning
Cell/Gene Tx Cond.
AML
NET
Melanoma
NB, NET
HNSCC, Bladder
NTSR1+ Tumors
GBM / LM
RCC
GBM
BM Conditioning

3 TARGETS

The vast majority of programs are focused on only three targets

24
PHASE 1/2

9
PIVOTAL

4
MARKET

The global radiopharmaceuticals market size was valued at USD 4.38 Billion in 2021 and is projected to reach USD 11.93 Billion by 2030, growing at a CAGR of 11.76% from 2023 to 2030.*

Ongoing 2nd Round Evaluation for *de-novo* Targets

TARGET PROPERTIES

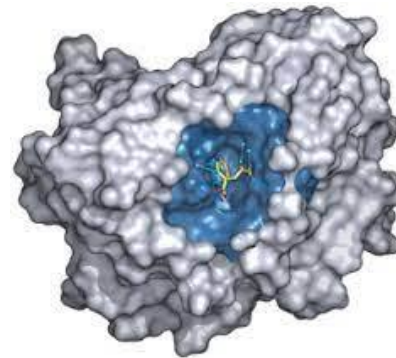
- Expressed at the cell surface and bindable
- Expression limited to tumours
- Or high differential expression between tumours and healthy tissues
- Initial signals of clinical relevance
- Relevant medical indications

RLTs



Most effective for

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



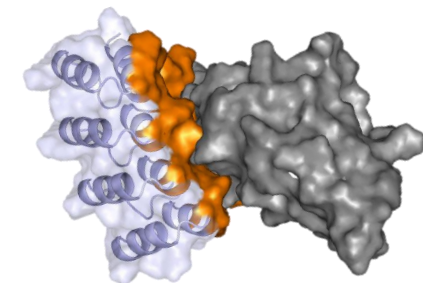
Example targets, PSMA...

RDTs



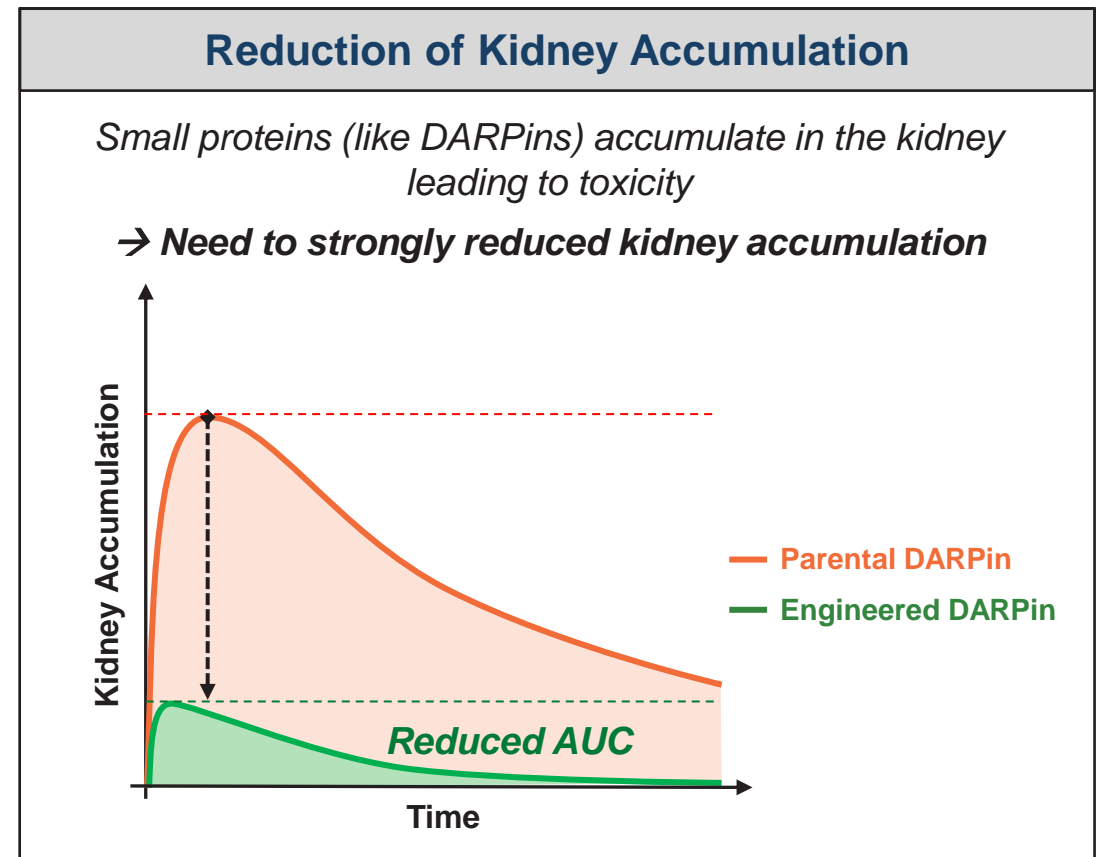
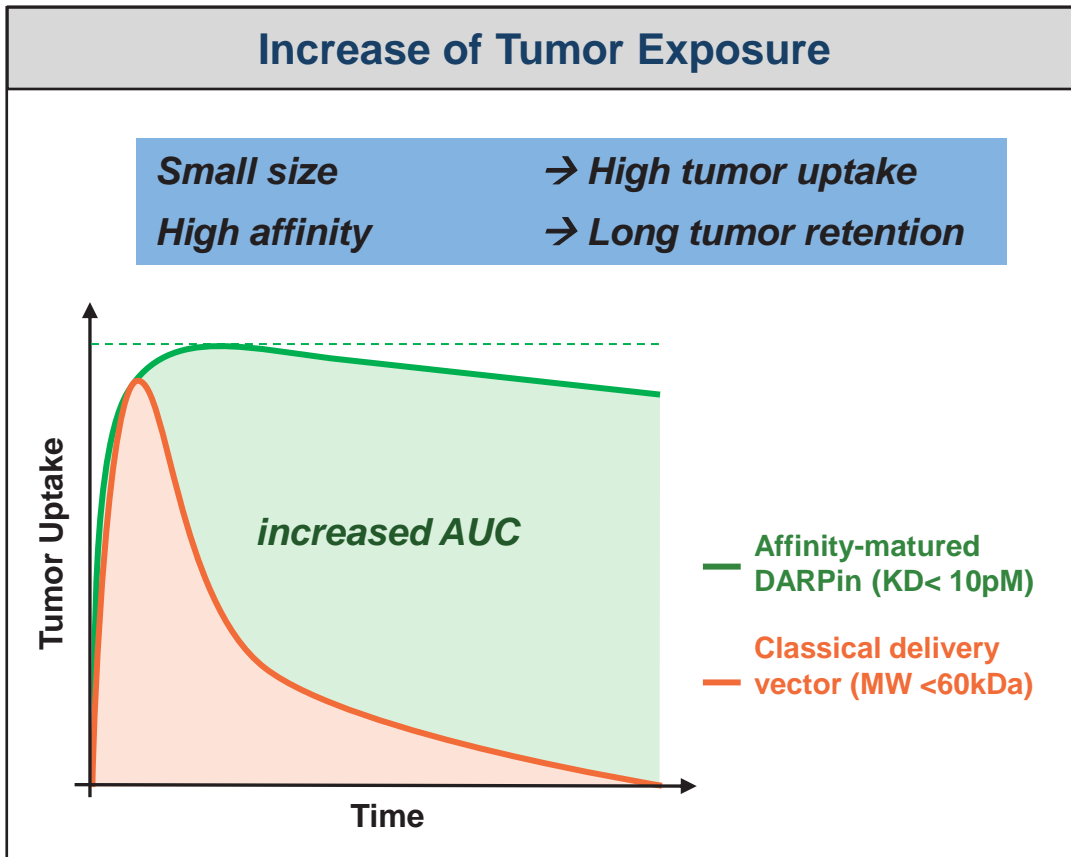
Most effective for

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



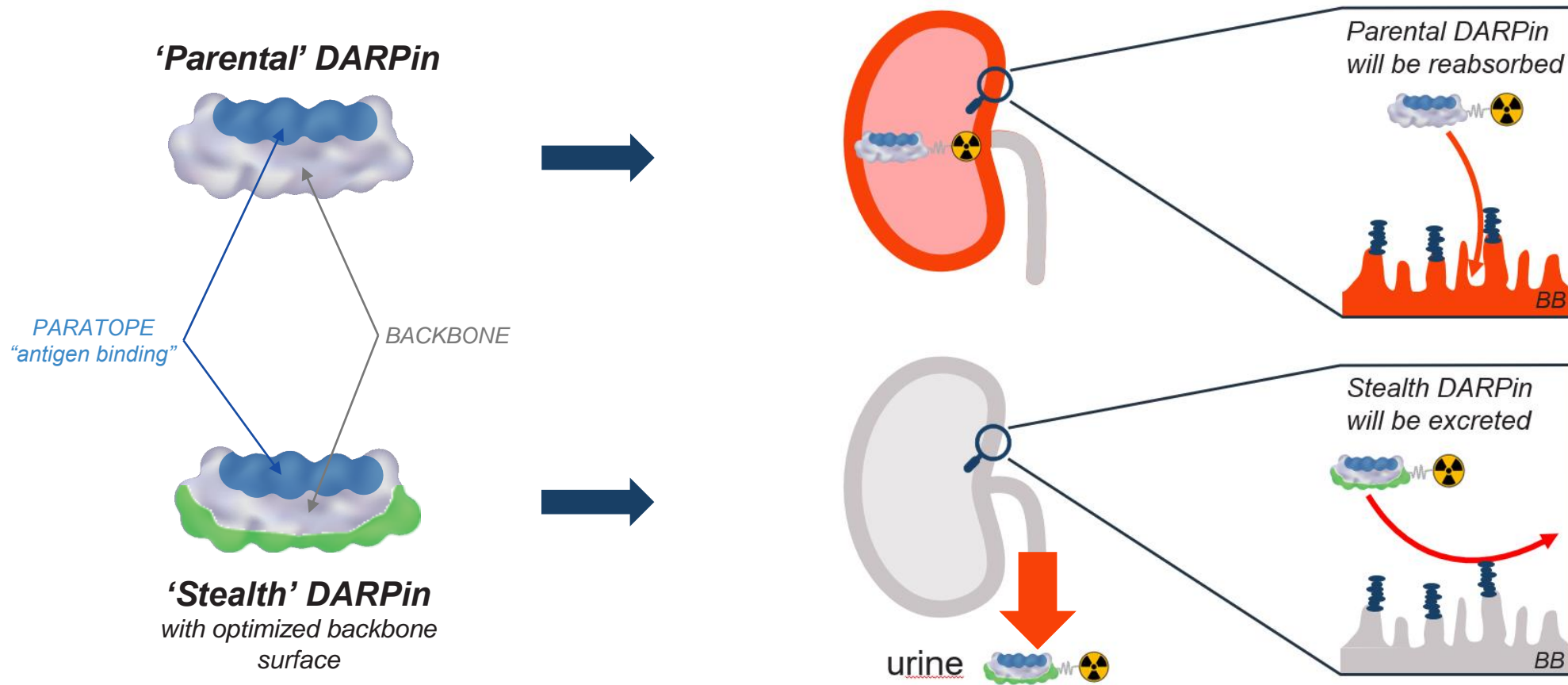
Example targets, Her2, DLL3, ...

Main Challenge: Reaching Tumor: Kidney Ratio > 1



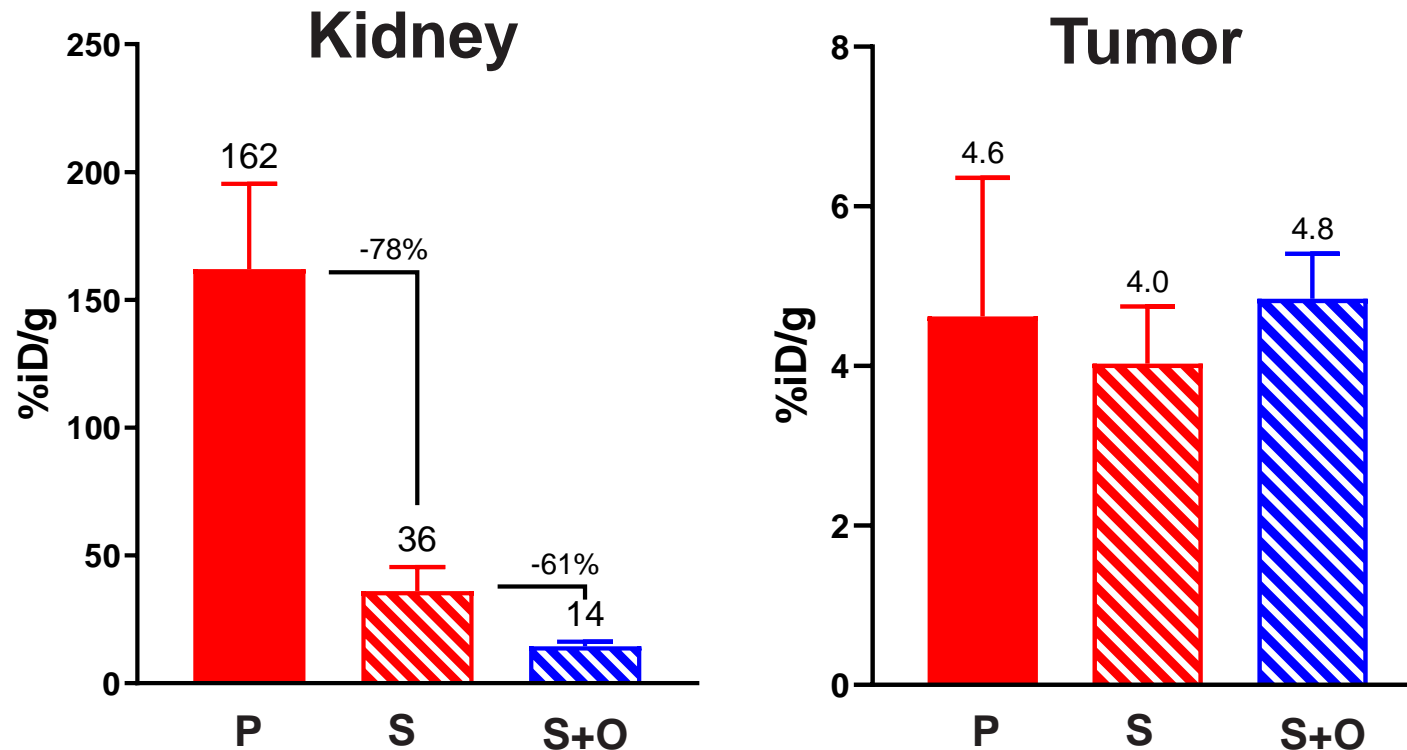
Avoiding Kidney Accumulation with Radio DARPin Therapy







Optimizing the backbone surface greatly increases DARPin excretion over reabsorption in the kidney



BB: Brush border of proximal tubular cells in the kidney with megalin/cubulin receptor complex

Stealth Kidney Accumulation is Further Reduced Combining with Orthogonal Approach while Maintaining high Tumor Uptake



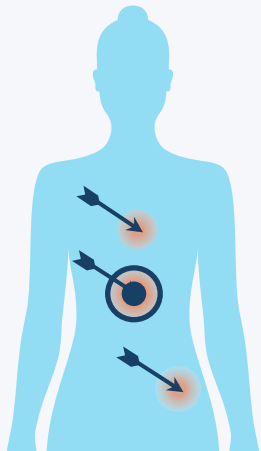
After 4 hours timepoint	T/K*
P: Parental 	 1/35
S: Stealth 	 1/9
S+O: Stealth + Orthogonal 	 1/3

*tumor to kidney ratio

The Radio DARPin Therapy Advantage

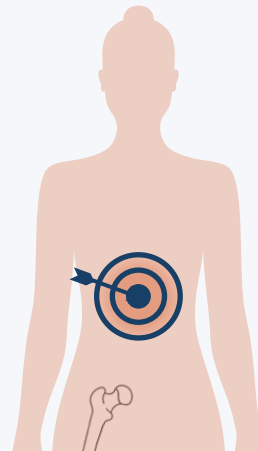
LIGANDS & PEPTIDES

- ✓ Fast entry and exit from the body to limit exposure of healthy tissue (kidney often limiting for peptides)
- ✗ Nature of binding limits the number of potential targets (affinity and selectivity)



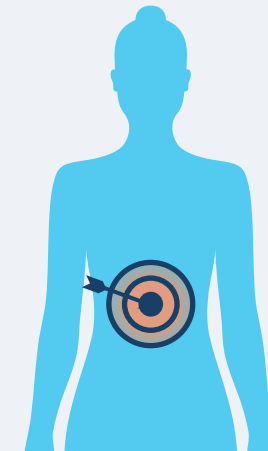
MONOCLONAL ANTIBODIES

- ✗ Stay in the body too long, exposing bone marrow to radiation
- ✓ Proven class of binding proteins for broad range of tumor targets



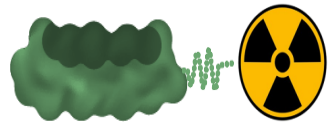
DARPins

- ✓ Fast entry and exit from the body to limit exposure of healthy tissue (engineering for low kidney radiation)
- ✓ Proven class of binding proteins for broad range of tumor targets



Radio DARPin Therapeutics Pipeline

Novartis Collaboration



Collaboration with leader in RLT leader



- \$20m upfront
- Up to \$560m in potential milestones
- Up to double-digit royalties



Exclusive for two tumor antigens

Molecular Partners portfolio



DLL3 selected as 1st in-house target



2nd target ongoing and further targets in evaluation



Ongoing discussions with radionuclide providers

Outlook

Key Milestones in 2023

MP0533	<ul style="list-style-type: none">• Initial clinical results of Phase 1 trial in AML, safety and initial efficacy (Q4 2023)• Additional preclinical work to support further development
MP0317	<ul style="list-style-type: none">• Completion of patient recruitment in the dose escalation of Phase 1 trial (H1 2023)• Initiation of partnering discussions
Radio DARPIn Therapy (RDT) Platform	<ul style="list-style-type: none">• Advancement of platform and candidates to be presented at scientific conferences• Further reduction of kidney uptake of RDT compounds• Selection of additional targets and corresponding candidates• Establish collaborations with radionuclide companies
Further Opportunities for DARPins	<ul style="list-style-type: none">• Establish SWITCH DARPIn platforms – immune cell engagers• Update on Virology projects

~CHF 250 million cash & cash equivalents (incl. short-term time deposits) ensure funding into 2026*

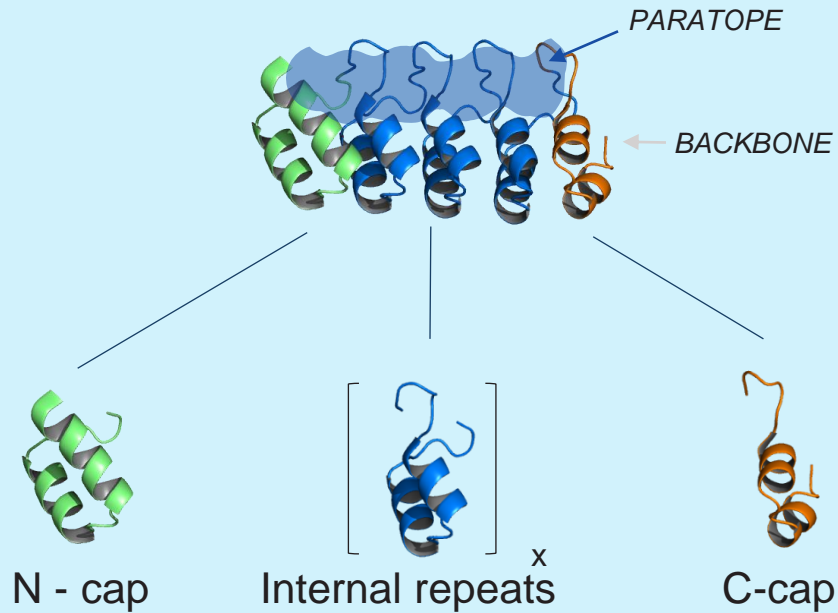
Additional Opportunities

- DARPin SWITCH

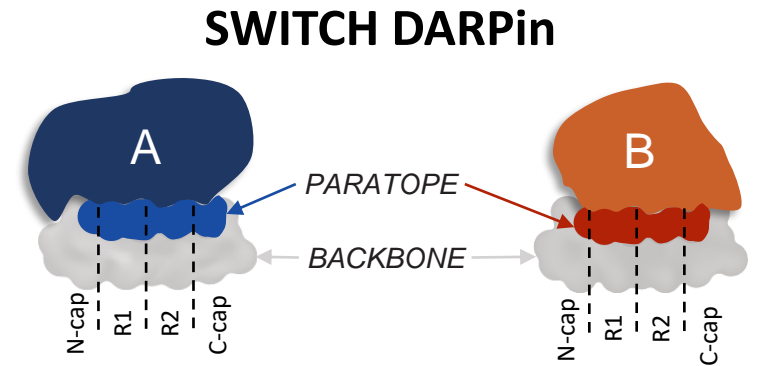
SWITCH DARPin

Binding Two different Targets with One DARPin in an Exclusive Way

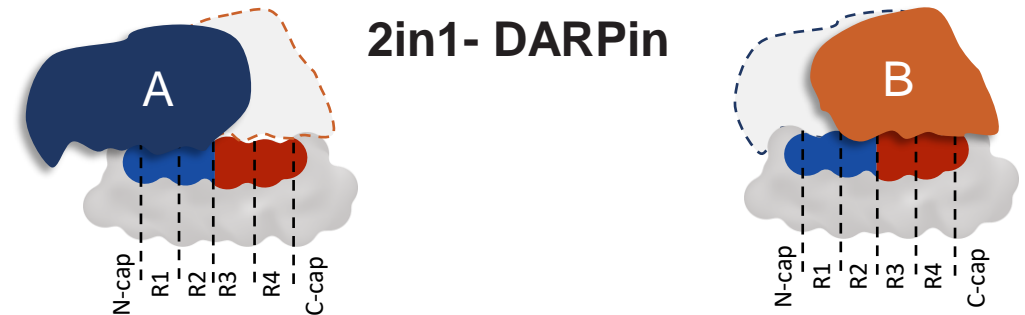
DARPinS are made of self-compatible repeats



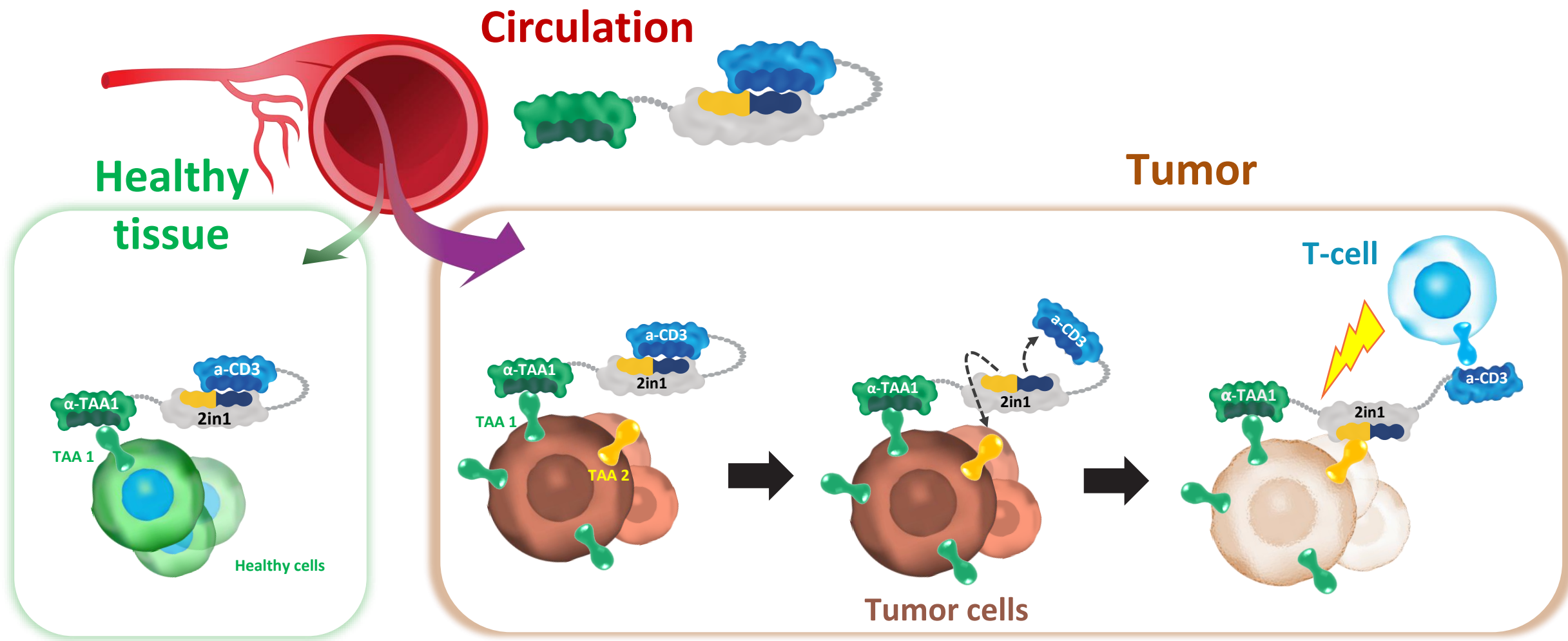
Mono-DARPinS



Fusion of paratopes into one DARPin domain



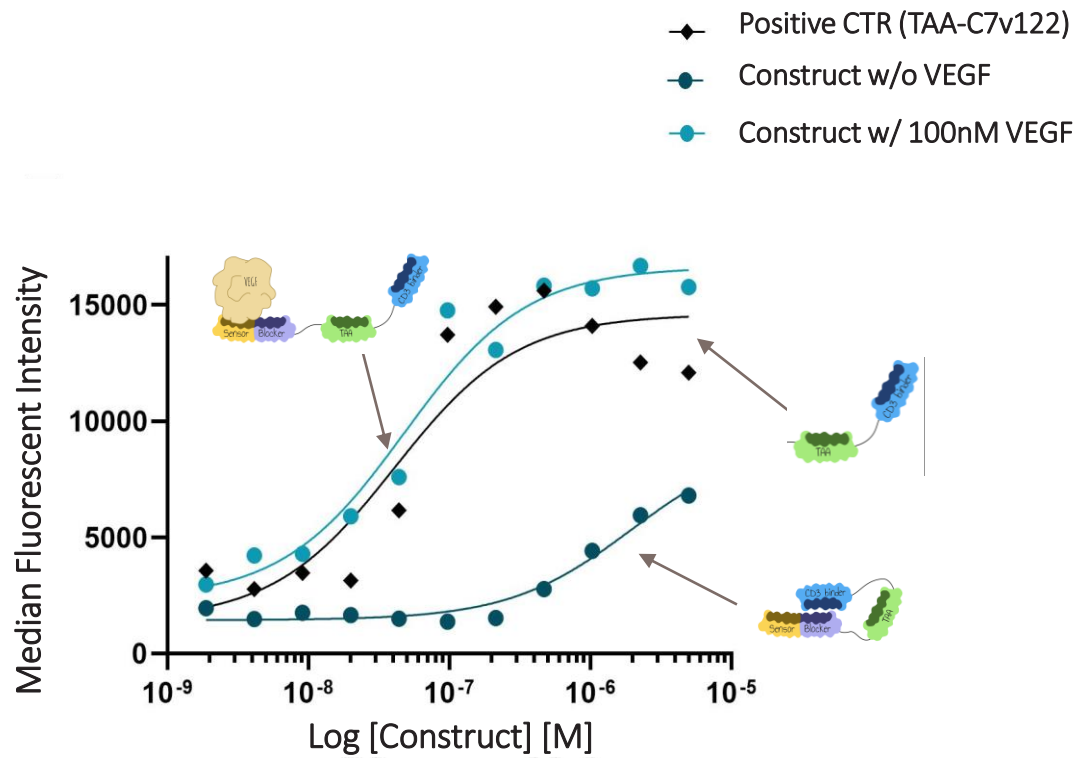
SWITCH DARPin: "Smart Biologics" of Potent Effectors



TME: tumor microenvironment; TAA: tumor-associated antigen

Soluble VEGF Can Trigger Dose-Dependent Opening of SWITCH-Drug in T-cell Activation Assay

T-cell binding



T-cell activation

