# Corporate Presentation

## Full-Year 2023 Earnings Call

March 15, 2024

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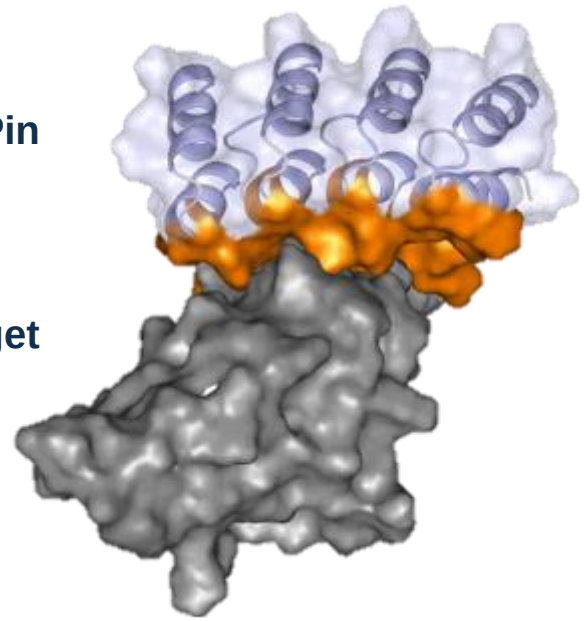
# Agenda & Speakers

| Welcome & Introduction | Highlights 2023 Outlook 2024 | Financial Overview | MP0533 & AML | cKIT & Switch-DARPin | DLL3 & Radio-DARPin |
|---|---|---|---|---|---|
|  |  |  |  |  |  |
| **Seth Lewis**<br>SVP IR & Strategy | **Patrick Amstutz**<br>CEO | **Robert Hendriks**<br>SVP Finance | **Philippe Legenne**<br>Acting CMO | **Anne Goubier**<br>SVP Research & Early Development | **Daniel Steiner**<br>SVP Research & Technology |

# The 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 solutions** for a defined medical problems not addressable by antibody designs
- Demonstrate **true patient value** with **early clinical readouts**
- Combine our **capabilities with world-class partners** to deliver innovative therapeutics

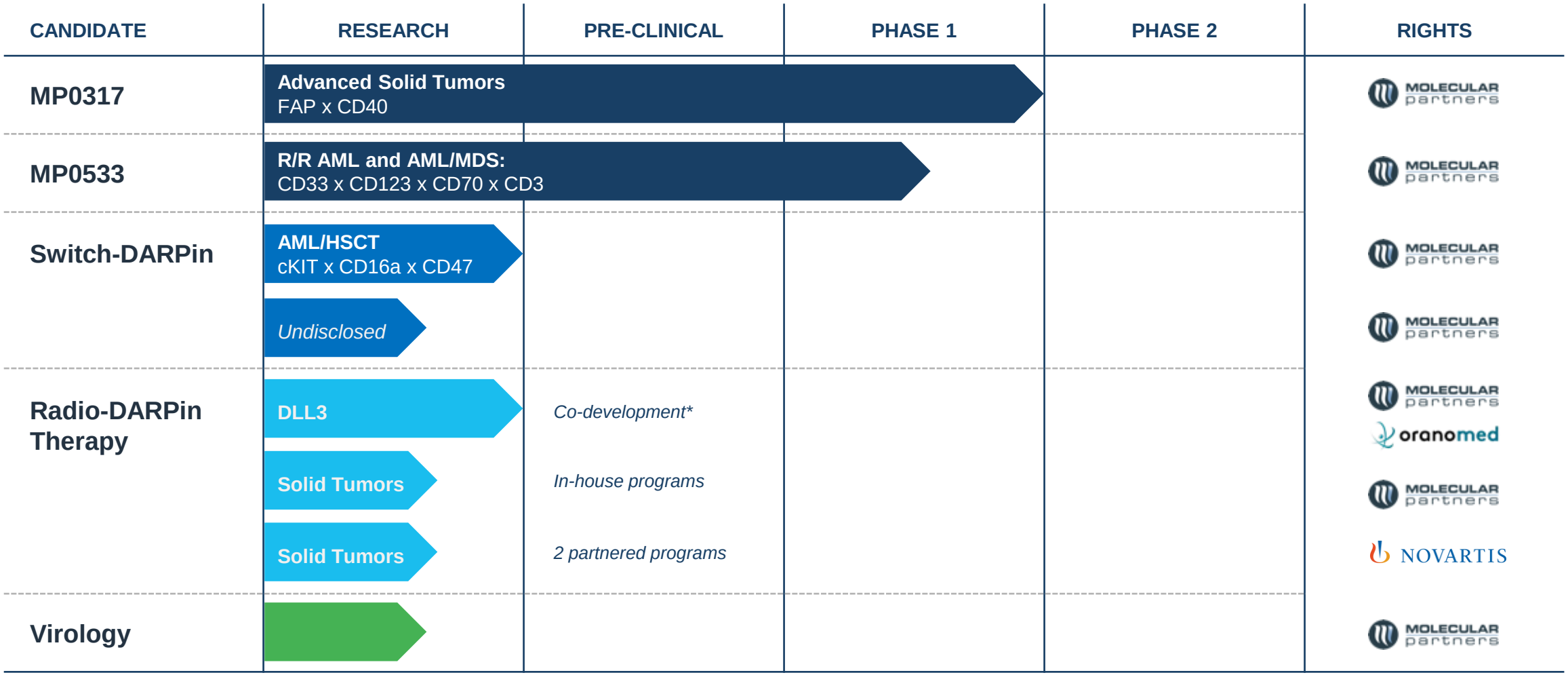
# 2023 Highlights

| | |
|---|---|
| **MP0533** | • Novel **tetra-specific T cell engager** for R/R AML and high-risk MDS/AML patients<br>• **ASH 2023: encouraging initial clinical data** with acceptable safety and initial activity<br>• Phase 1/2a study with dose-escalation well on track; **dosing patients in DR 6** ongoing |
| **Switch-DARPin & cKIT** | • Demonstrated **proof-of-concept** for **Switch-DARPin platform** at PEGS 2023<br>• 1st program, **cKIT x CD16a x SWITCH-CD47;** targeted **conditioning regimen** for HSCT in AML & beyond |
| **Radio-DARPin Therapy** | • Successful RDT platform optimization to **reduce kidney accumulation** and **increase tumor uptake**<br>• **Collaboration agreement with Orano Med** to co-develop RDTs with up to three targets, including DLL3<br>• Novartis collaboration progressing according to plan on two targets |
| **MP0317** | • Bi-specific CD40 agonist targeting FAP for tumor-localized immune activation with **favorable safety profile** confirmed tumor-localized CD40 activation leading to **remodeling of TME** in patients |
| **Operations** | • Strong financial position with CHF ~187 M in cash as of Dec. 31, 2023<br>• **Capitalized well into 2026** |



AML, acute myeloid leukemia; ASH, American Society of Hematology; DLL3, Delta-like ligand 3; DR, dose-regimen; EANM, European Association of Nuclear Medicine; FAP, fibroblast activation protein; MDS, myelodysplastic syndrome; RDT, Radio-DARPin Therapy; R/R, relapsed/refractory; SITC, Society for Immunotherapy of Cancer; TME, tumor microenvironment.

# Pipeline




*The co-development agreement with Orano Med includes up to 3 potential oncology targets including DLL3.
AML, acute myeloid leukemia; DLL3, Delta-like ligand 3; HSCT, hematopoietic stem cell transplant;
MDS, myelodysplastic syndrome; R/R, relapsed/refractory.

# Financial Overview

# Key Figures FY2023

| *(CHF million, except per share and FTE data)* | ***FY 2023*** | *FY 2022* | ***change*** |
|---|---|---|---|
| **Revenues** | **7.0** | **189.6** | **(182.6)** |
| **Total operating expenses**[1] | **(68.1)** | **(73.0)** | **4.9** |
| **Operating result** | **(61.1)** | **116.6** | **(177.7)** |
| **Net financial result** | **(0.9)** | **1.2** | **(2.1)** |
| **Net result** | **(62.0)** | **117.8** | **(179.8)** |
| **Basic net result per share (in CHF)** | **(1.89)** | **3.63** | **(5.52)** |
| **Net cash from / (used in) operations** | **(59.0)** | **118.6** | **(177.6)** |
| **Cash balance (incl. s.t. deposits) as of Dec 31** [2] | **186.9** | **249.1** | **(62.2)** |
| **Number of FTE's as of Dec 31** | **167.5** | **175.3** | **(7.8)** |

[1] Thereof non-cash costs of CHF 8.1 m in FY2023 and CHF 8.6 m in FY2022
[2] Including CHF 119.6m short-term time deposits (2022: 161.2m)
Note: Rounding differences may occur

# Financial Guidance* for 2024

- Total expenses of CHF 70-80 million,
  of which around CHF 8 million non-cash effective costs

- ~**CHF 187 million** cash & cash equivalents (incl. short-term time deposits)
  ensure comfortable **funding well into 2026**
  (excl. any potential payments from R&D partnerships)

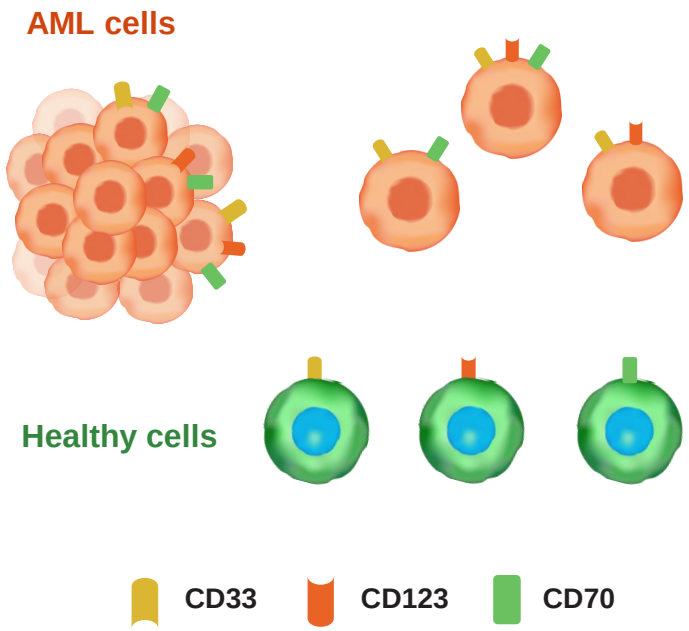
* Guidance subject to progress and changes of pipeline

# MP0533

Tetra-specific T cell Engager for AML

# MP0533: Avidity-Driven Selectivity for Cancer Cells in AML

**PROBLEM**: AML-associated antigens are also expressed on healthy cells




**AML remains a deadly disease** and persistence of **LSCs** drives relapse

**AML cell population is heterogeneous**:

- Individual AML blasts and LSCs lack a clean target
- AML cells can be differentiated from healthy cells (e.g. HSCs) by their **co-expression of specific targets** (e.g. CD33, CD123, CD70)

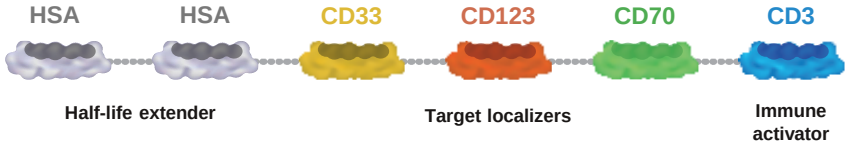


AML, acute myeloid leukemia; HSC, hematopoietic stem cell; HSA, human serum albumin; LSC, leukemic stem cells.

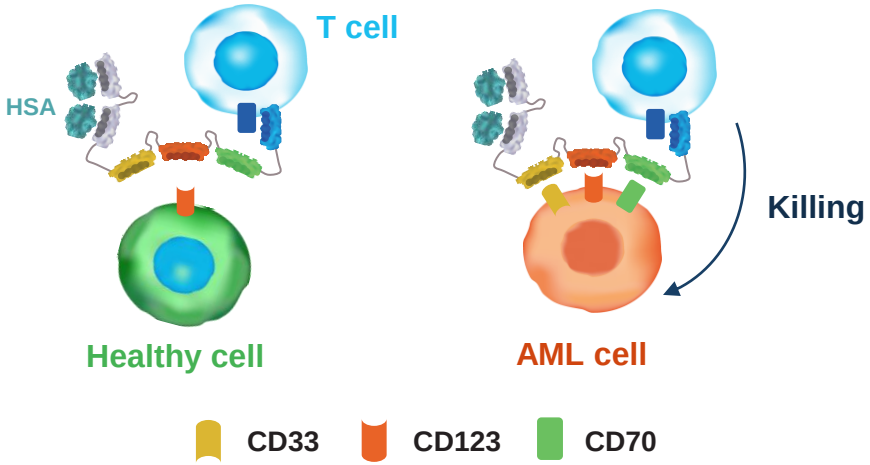
# MP0533: Avidity-Driven Selectivity for Cancer Cells in AML

**SOLUTION:** MP0533 induces T cell-mediated killing of cells co-expressing TAAs

**MP0533 design:**




**MP0533 MoA:**




MP0533 is designed to induce **T cell-mediated killing preferentially when 2 or 3 target antigens** (CD33, CD123, CD70) **are co-expressed**

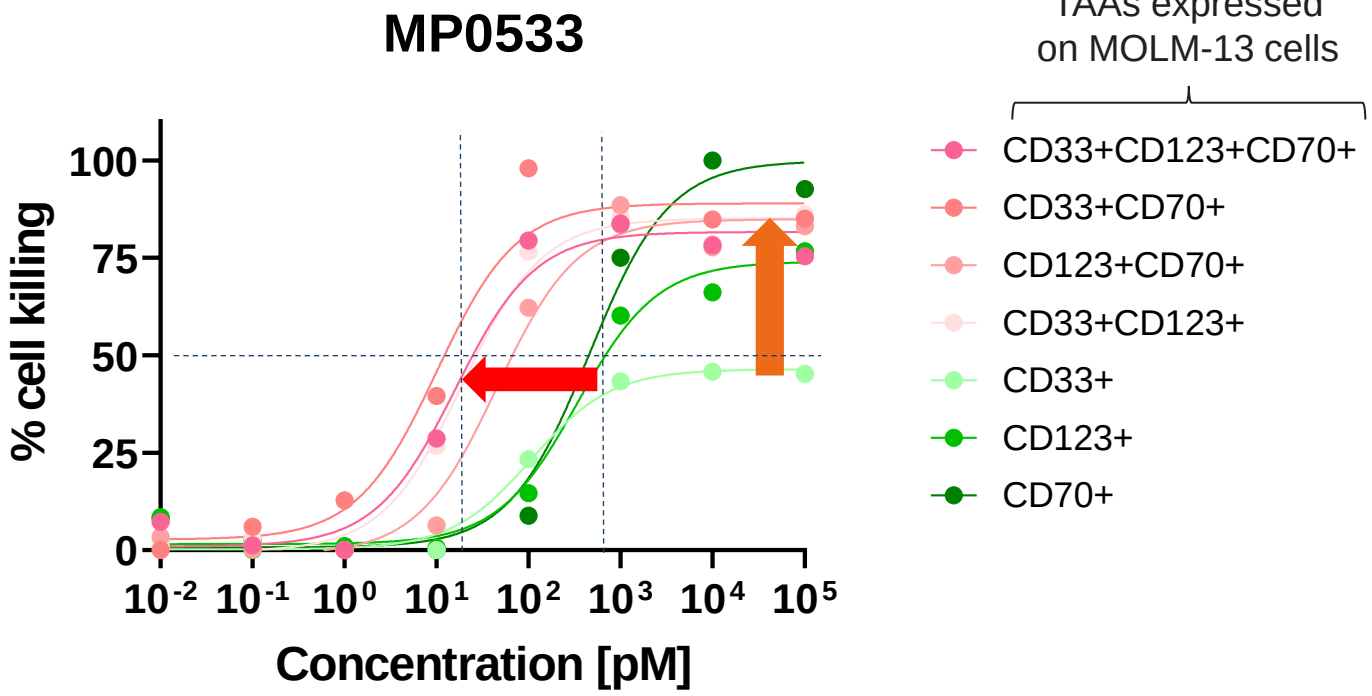
MP0533 is hypothesized to preserve healthy cells, hence **opening a therapeutic window**

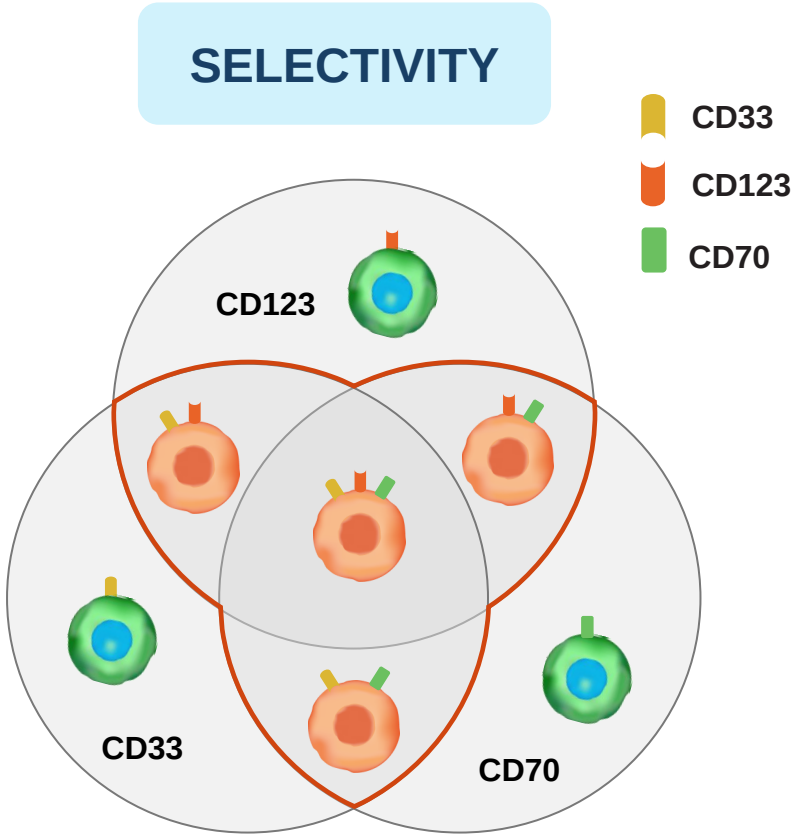
MP0533 has the potential to kill all AML cells (blasts and LSCs) despite heterogeneity, ensuring **long-term disease control**



AML, acute myeloid leukemia; HSC, hematopoietic stem cell; HSA, human serum albumin; LSC, leukemic stem cells; TAA, tumor-associated antigen.

# MP0533 Induces Specific Killing of AML Cells Expressing Two or Three TAAs



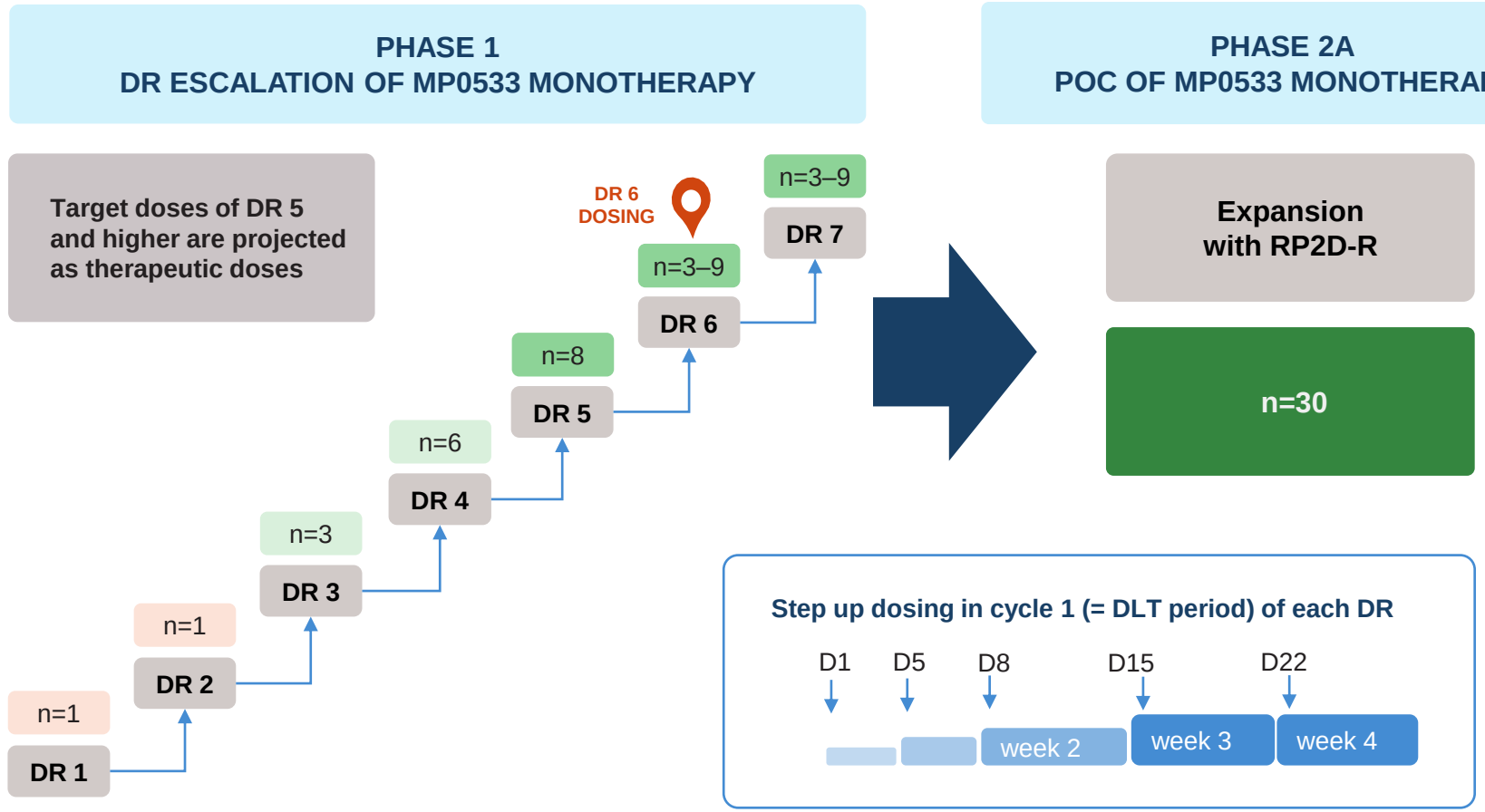




*Bianchi et al, manuscript tentatively accepted in Feb 2024 for publication*

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

## STUDY DESIGN

- FIH, multicenter, single-arm, open-label, Phase 1/2a study of MP0533 monotherapy (NCT05673057)
- Objectives: Safety/tolerability, PK/PD, and preliminary activity
- Eligible patients: Adults with R/R AML or MDS/AML
- Centers: 9 sites initiated across Europe




**Study currently dosing patients in DR 6, plans to present data in H1 2024**

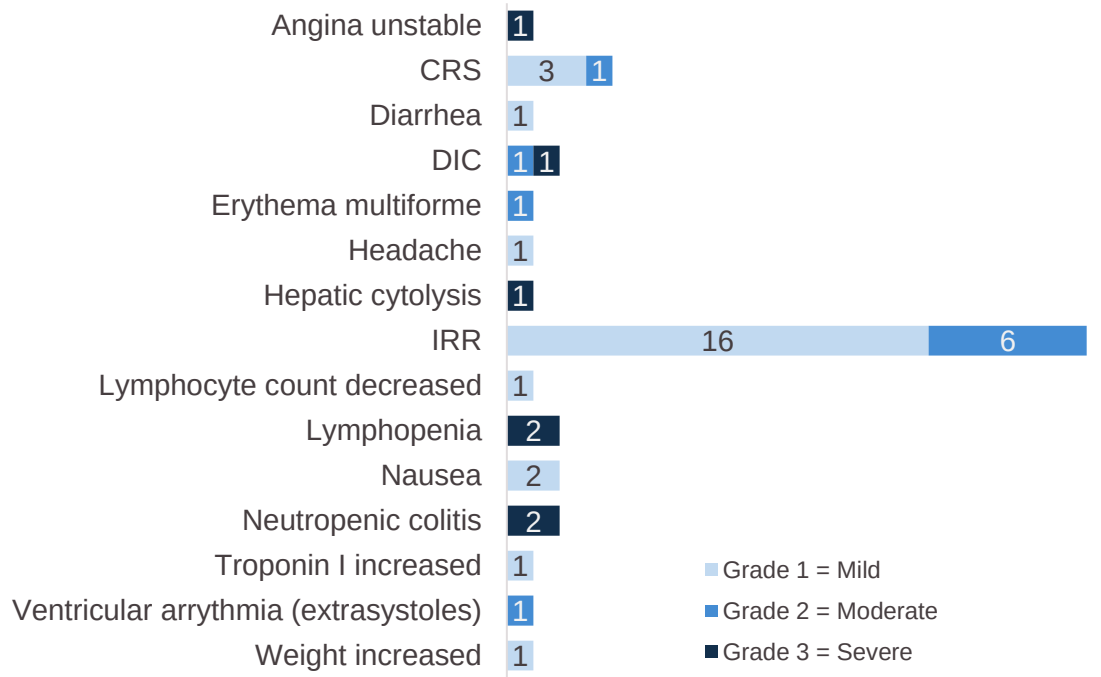
AML, acute myeloid leukemia; D, treatment cycle day; DLT, dose-limiting toxicity; DR, dose regimen; MDS, myelodysplastic syndrome; n, number of patients; PD, pharmacodynamic; PK, pharmacokinetics; POC, proof of concept; RP2D-R, recommended phase 2 DR; R/R, relapsed/refractory.

# MP0533 - Patient Characteristics and Safety Profile

| PATIENT CHARACTERISTICS | DR COHORTS 1–4 (n=11) |
|---|---|
| **Sex, n (%)** | |
| Female / male | 5 (45) / 6 (55) |
| **Age** | |
| Mean / Median (range) | 66 / 75 (26–81) |
| **ECOG PS, n (%)** | |
| 0 / 1 / 2 | 4 (36) / 5 (46) / 2 (18) |
| **Hematologic malignancy, n (%)** | |
| AML / MDS/AML | 9 (82) / 2 (18) |
| **ELN risk category, n (%)** | |
| Intermediate / adverse | 1 (9) / 10 (91)* |
| **No. of prior systemic treatment lines, n (%)** | |
| 1 / 2 / 3 | 4 (36) / 5 (46) / 2 (18) |

*TP53 mutated: 3 (27%)

**MP0533-RELATED TEAEs (n=43 reported)**




**Acceptable safety profile for MP0533 reported for DR 1–4 (11 patients):**

- Overall, AE profile consistent with AML and elderly/heavily pretreated patients with many comorbidities
- IRR and CRS are the most frequent MP0533-related TEAEs (Grade 1–2)
- No DLTs in any of the MP0533 DRs to date



*Pabst et al, ASH 2023 poster presentation (data cut-off 24 Oct 2023)*

AE, adverse event; CRS, cytokine release syndrome; DIC, disseminated intravascular coagulation; ELN, European LeukemiaNet; IRR, infusion-related reaction; TEAE, treatment-emerging AE.

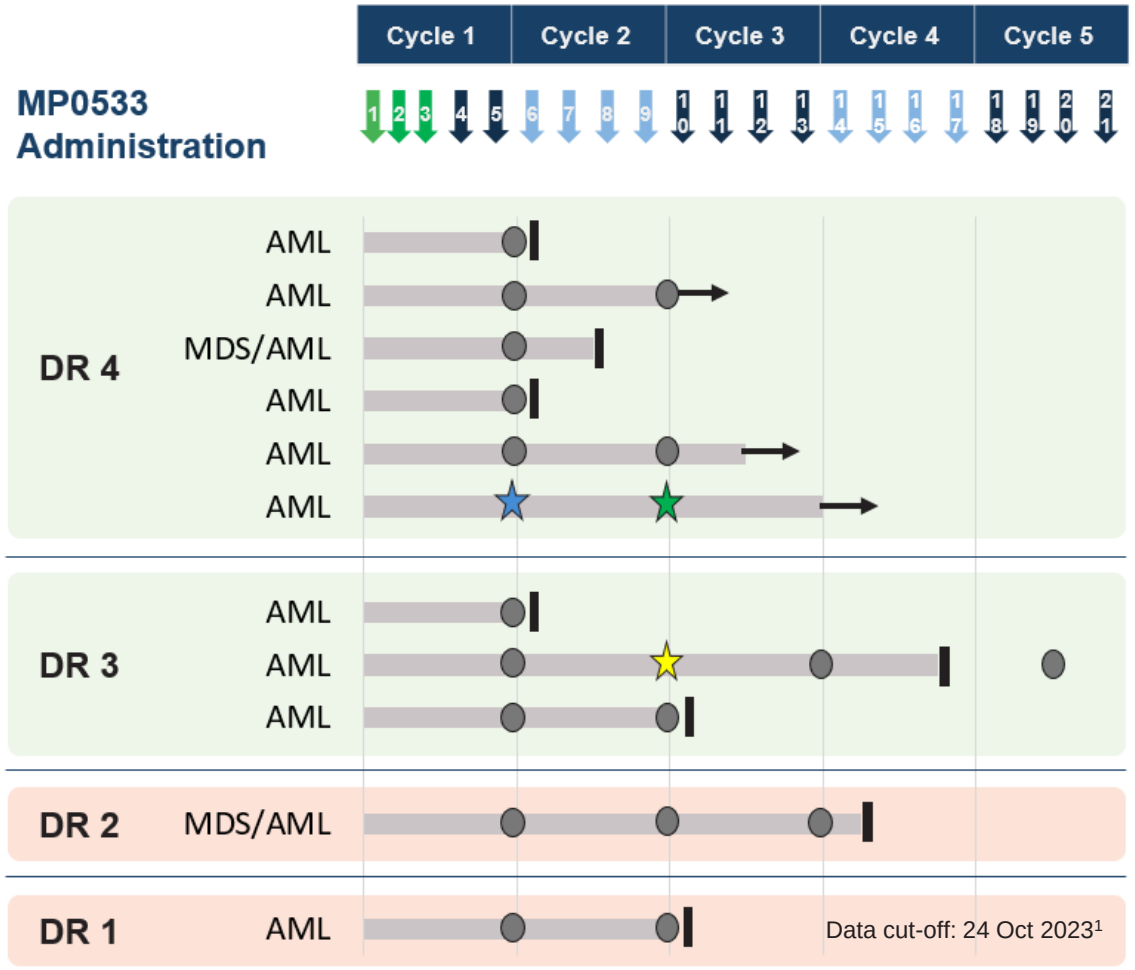
# MP0533 Treatment and Clinical Response

## Encouraging initial clinical data with two responders[1]

- CR in 1 patient at DR 4
- MLFS in 1 patient at DR 3

## Currently dosing patients in DR 6

- DR 5 and above are projected as therapeutically active doses
- Next update in H1 2024




**LEGEND**

- CR
- CRi
- MLFS
- No response

Response (2022 ELN[2]) was assessed every 4 weeks until disease progression and results are presented as indicated

- MP0533 treatment
- Treatment continuation at data cut-off
- Treatment discontinuation

Arrows at the top indicate MP0533 administration at D1, D5, D8, D15 and weekly thereafter

- Step-up dosing is presented in green arrows
- Color changes in blue arrows indicate start of a new 28-day cycle

[1]Pabst et al. ASH 2023 poster presentation; [2]Döhner et al. Blood 2022;140(12)1345-77.
CR, complete response; CRi, CR with incomplete hematologic recovery; ELN, European LeukemiaNet; MLFS, morphologic leukemia-free state.

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

## STUDY DESIGN

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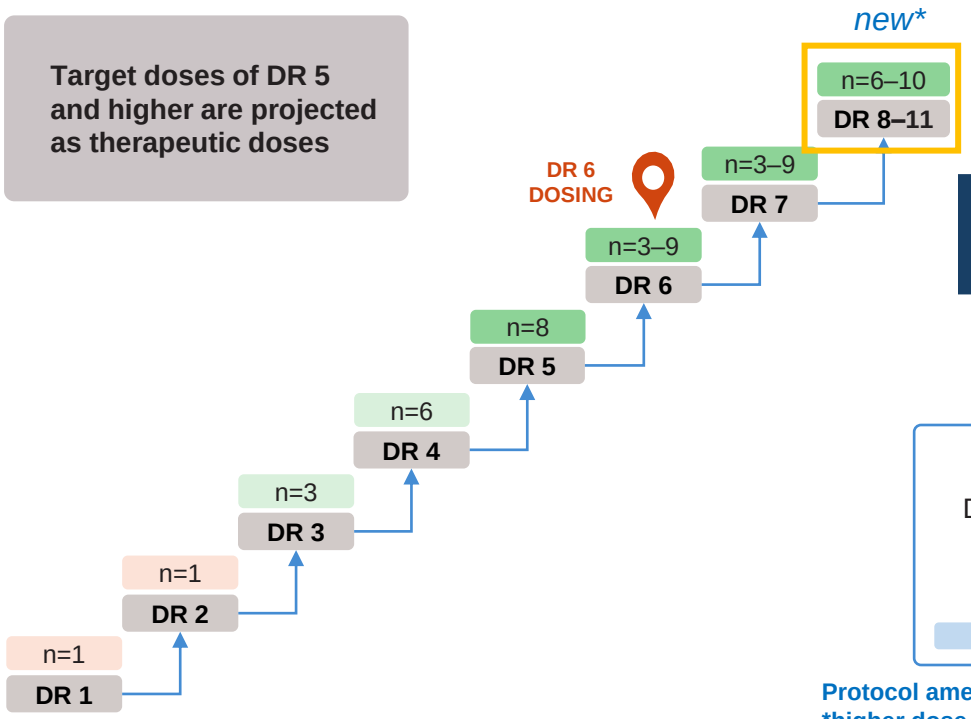
**PHASE 1**
**DR ESCALATION OF MP0533 MONOTHERAPY**

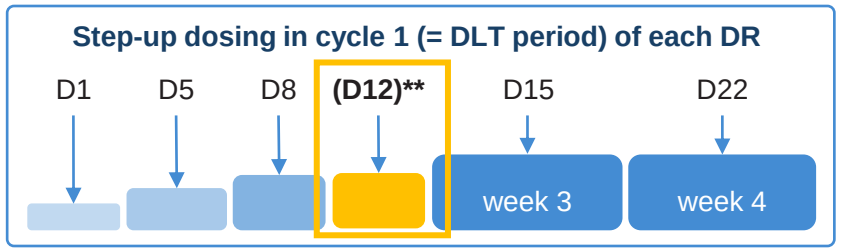
**PHASE 2A**
**POC OF MP0533 MONOTHERAPY**

**Target doses of DR 5 and higher are projected as therapeutic doses**




**Expansion with RP2D-R**

**n=30**




**Protocol amendment to include:**
***higher dose cohorts**
****optional D12* if DR 6–7 transition from step-up dose to target dose is not tolerated**

**Study currently dosing patients in DR 6, plans to present data in H1 2024**

AML, acute myeloid leukemia; D, treatment cycle day; DLT, dose-limiting toxicity; DR, dose regimen; MDS, myelodysplastic syndrome; n, number of patients; PD, pharmacodynamic; PK, pharmacokinetics; POC, proof of concept; RP2D-R, recommended phase 2 DR; R/R, relapsed/refractory.

# Switch-DARPin Platform & first program for HSCT in AML

Targeted and conditional activation of immune cells

# Next-Generation Conditioning for HSCT in AML and Beyond

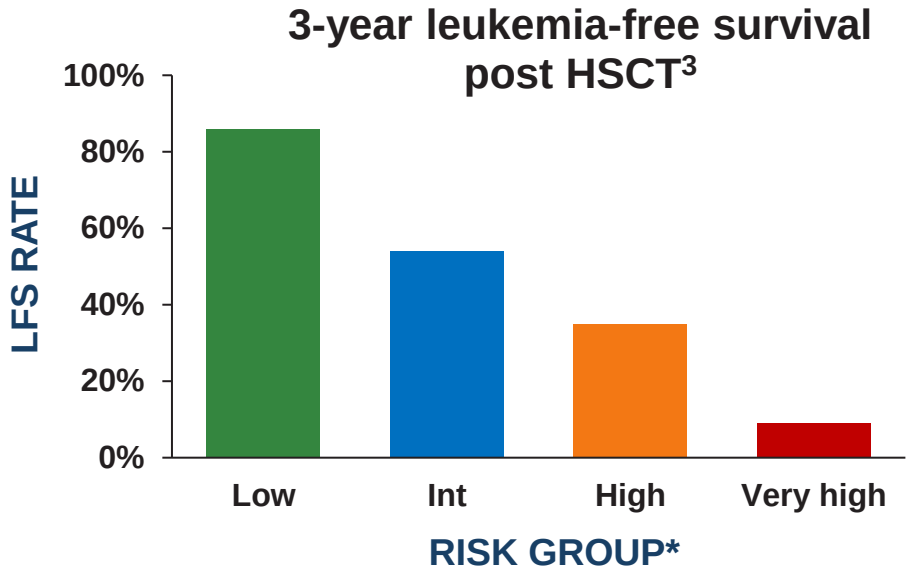
**HSCT is potentially curative for AML**, however:

**Conditioning regimens followed by HSCT do not always kill all AML cells**[1,2]

→ Many patients **relapse post HSCT**, especially AML patients with poor cytogenetic risk profile

**High-intensity conditioning regimen bears high toxicity**[1,2]

→ Many patients receive **reduced intensity conditioning with higher risk of relapse** or do not qualify for HSCT




## Opportunity for next-generation conditioning regimen

- Induce deep molecular remission to kill all AML clones, including in patients with poor cytogenetic risk profile
- Limit toxicity to allow access to HSCT for more AML patients, including elderly or frail patients
- Beyond AML: broaden applicability of HSCT for other diseases (e.g., genetic diseases) by improving safety of conditioning regimen



1.Jethava et al. Bone Marrow Transplant 2017;52:1504-11; 2. Döhner et al. Blood 2022;140:1345-77; 3. Moses Murdock et al. Blood 2022;139:3546-57.
*Risk groups defined based on different variables, including age, cytogenetic risk profile, type of and response to conditioning.
AML, acute myeloid leukemia; HSCT, hematopoietic stem cell transplantation; Int, intermediate; LFS, leukemia-free survival.

# Next-Generation Conditioning for HSCT in AML

**Target cKIT to eliminate HSCs/LSCs**

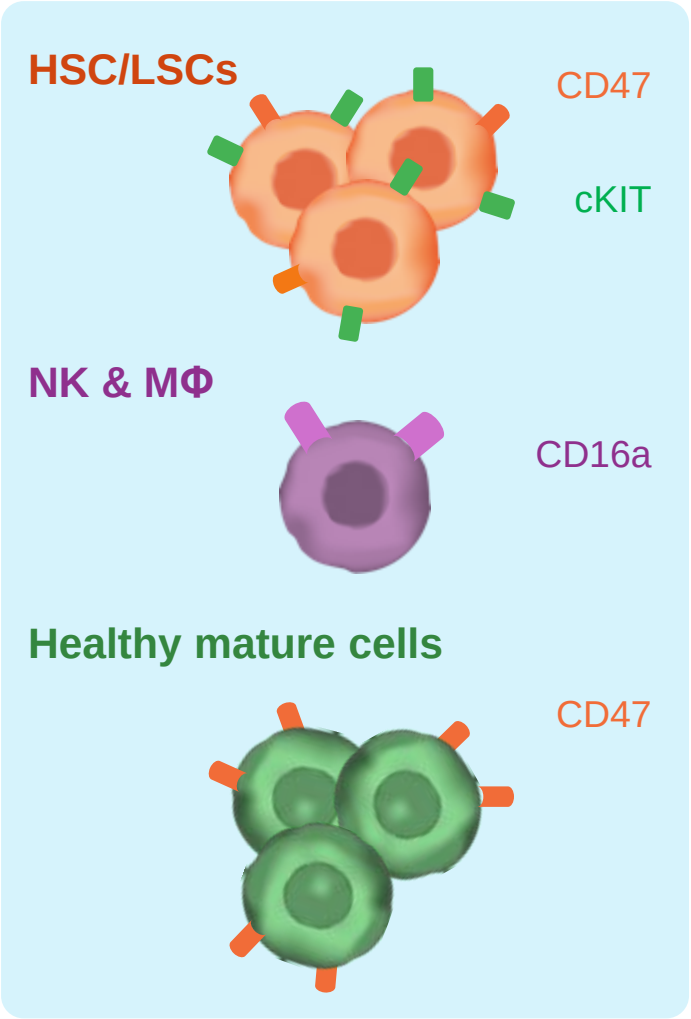
- cKIT is critical for stem cell maintenance and renewal[1, 2]
- Simple antagonists (mAbs) to cKIT are not potent enough

**Engage NK cells and macrophages (MΦ) via CD16a to kill HSCs/LSCs**

- Effective and safe approach
- NK and MΦ activity is limited by CD47 expression on HSC/LSCs[3]

**Conditionally block CD47 on LSCs/HSCs to boost NK cell and MΦ killing activity**

- CD47 is widely expressed as "do-not-eat-me signal" and prevents killing of cells, including HSCs/LSCs[1,3]
- Swich MoA allows conditional local blocking of CD47 on HSCs/LSCs






1. Valent et al. Int J Mol Sci 2019; 2. Rev in Kent et al. molecular pathways 2008; 3.Chhabra, Weissman and Shizuru, STM 2016.
HSC, hematopoietic stem cell; LSC, leukemic stem cell; mAb, monoclonal antibody; MoA, mode of action; MΦ, macrophage.

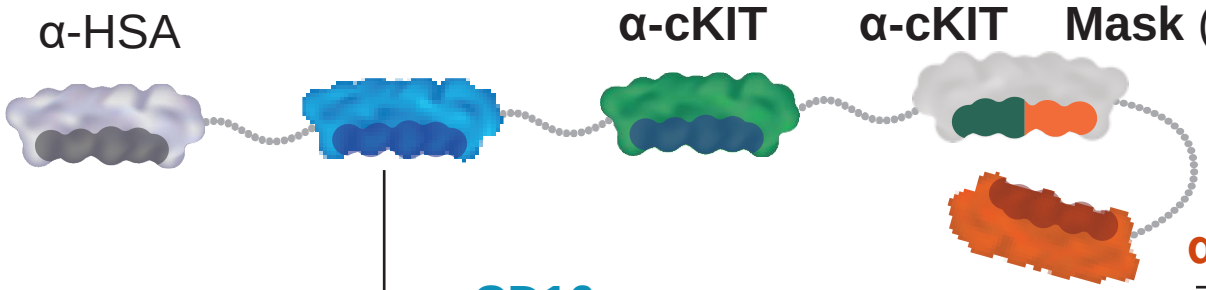
# cKIT x CD16a x CD47 Switch-DARPin

## Our solution for a safe conditioning regimen and long-term disease control

### cKIT (CD117)

**HSC marker essential for HSC maintenance and renewal**

- **Challenge:** optimal HSC depletion requires both cKIT blocking AND potent immune cell mediated killing
- cKIT-CD16a-CD47 Switch-DARPin proposed to demonstrate full activity




### Switch-DARPin

**Prevents peripheral CD47 blockade**

- Higher safety
- Expected better biodistribution
- Allows use of Fc-engaging modalities

### α-CD16a

Innate immune cell engager

**CD16a effector function**

- ADCC and ADCP induction
- No impact of inhibitory Fc
- Reduced CRS (compared to TCE)

### α-CD47

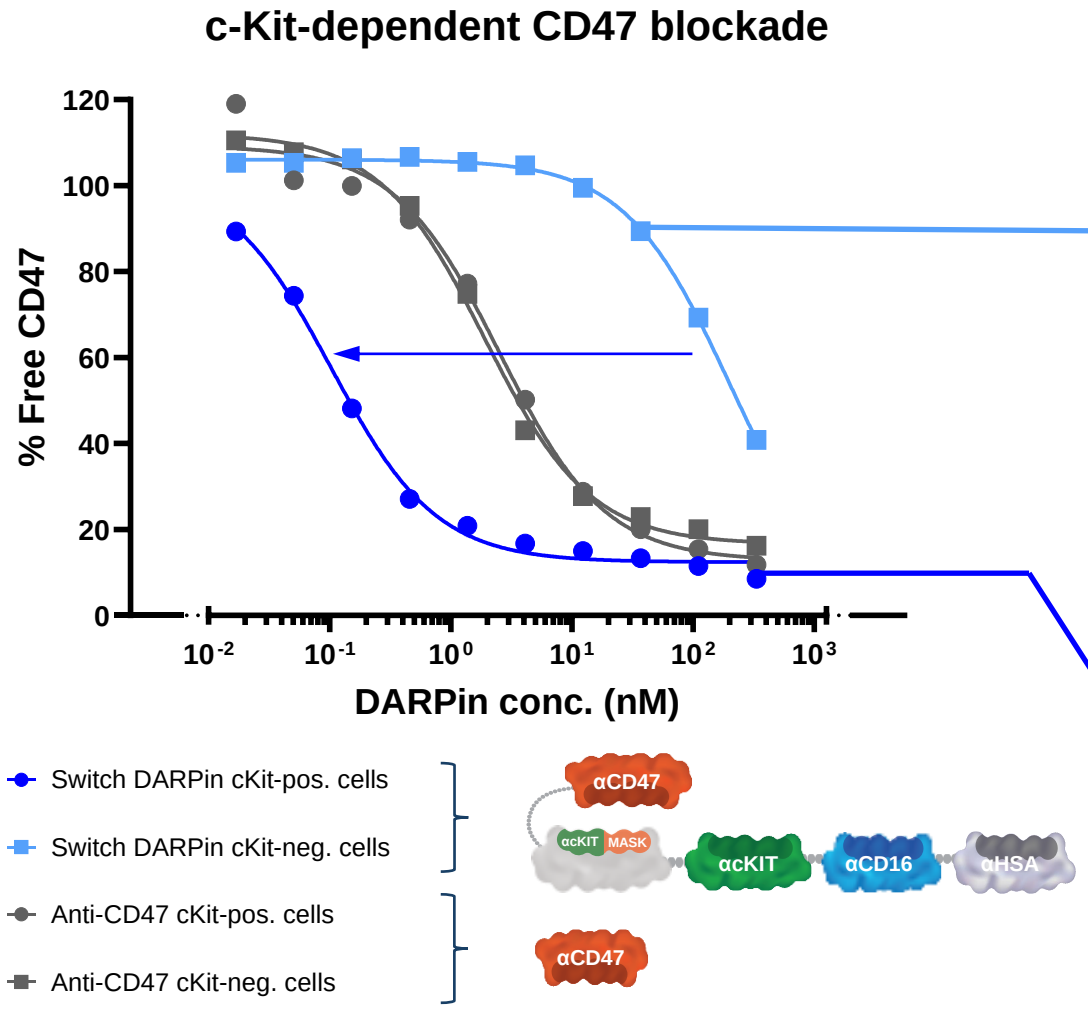
**CD47 innate checkpoint blockade**

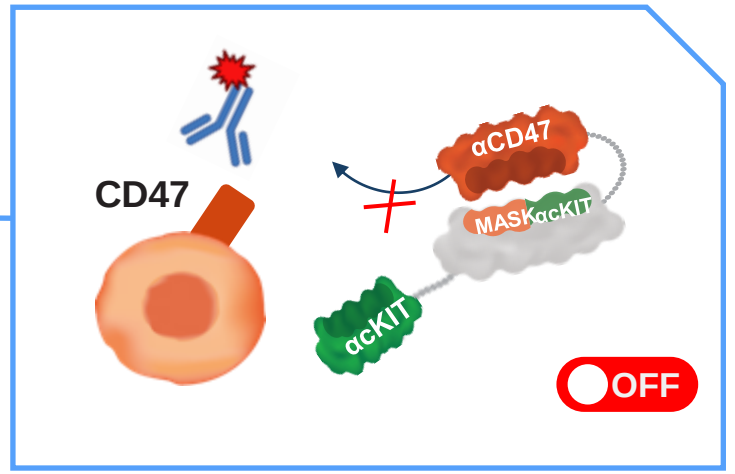
- Block "do-not-eat-me" signal = enhances phagocytosis
- High expression on HSC = target for ADCC and ADCP



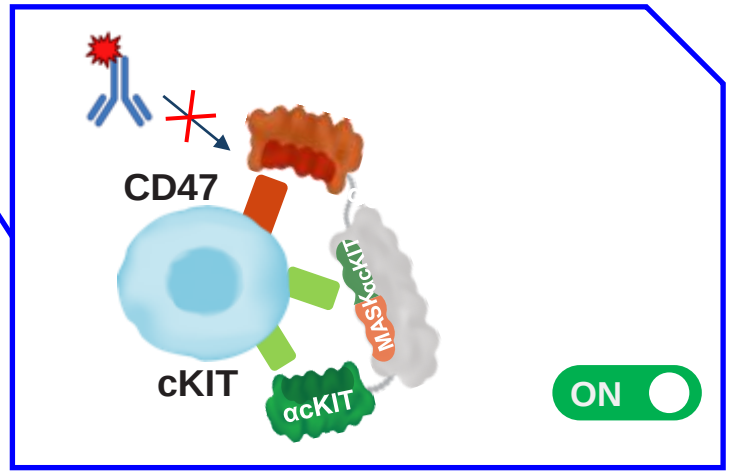
ADCC, antibody-dependent cell-mediated cytotoxicity; ADCP, antibody-dependent cellular phagocytosis; CRS, cytokine release syndrome; TCE, T-cell engager

# Switch-DARPin POC - CD47 is Blocked Only on cKIT Positive Cells




**cKIT Negative cells**
Switch is OFF
**CD47 is NOT blocked**



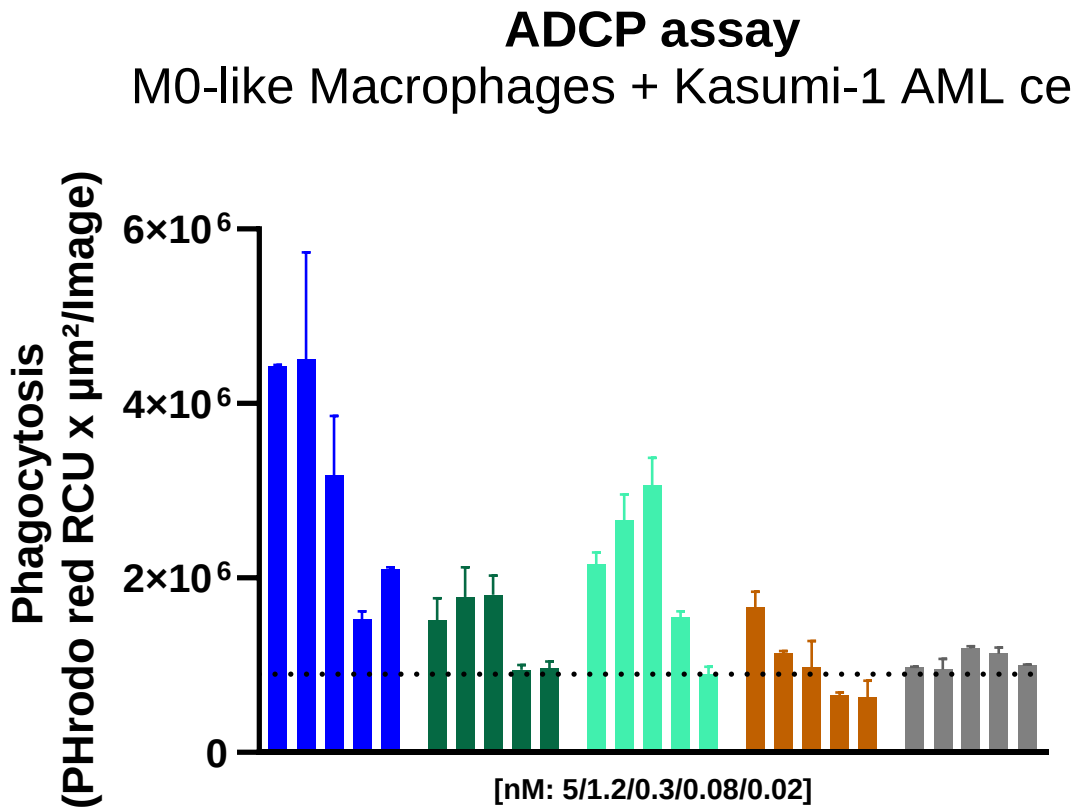

**cKIT Positive cells**
Switch is ON
**CD47 is Blocked**

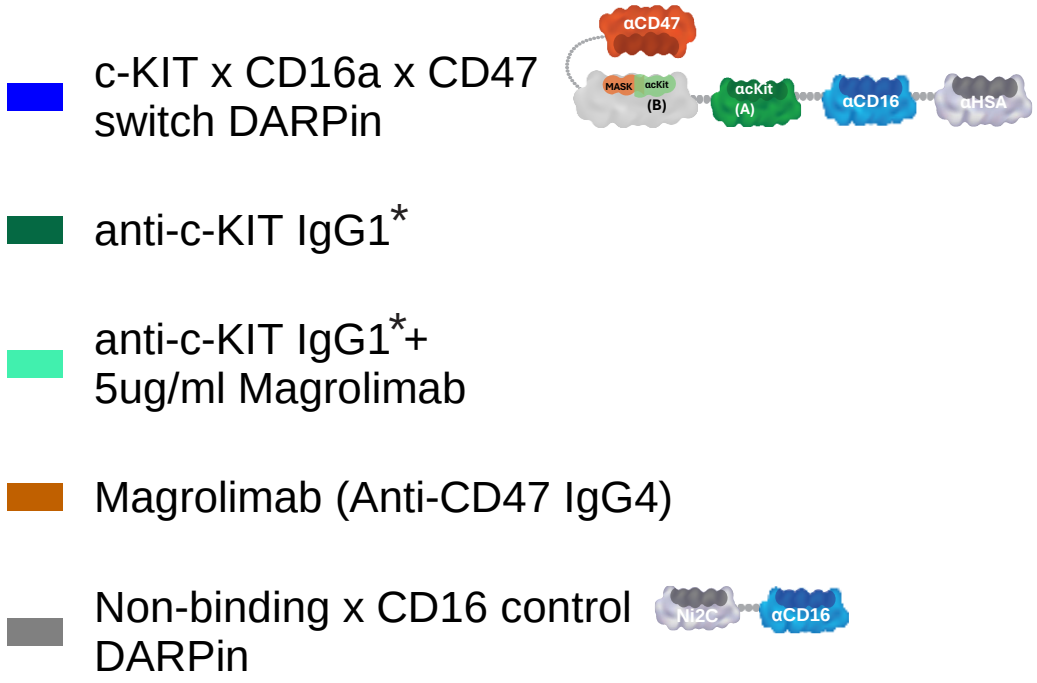
anti-CD47
detection agent



POC, proof-of-concept;

# c-KIT x CD16a x CD47 Switch-DARPin shows superior ADCP activity compared to a combo of an Fc-active (IgG1) anti-cKIT Ab + Magrolimab



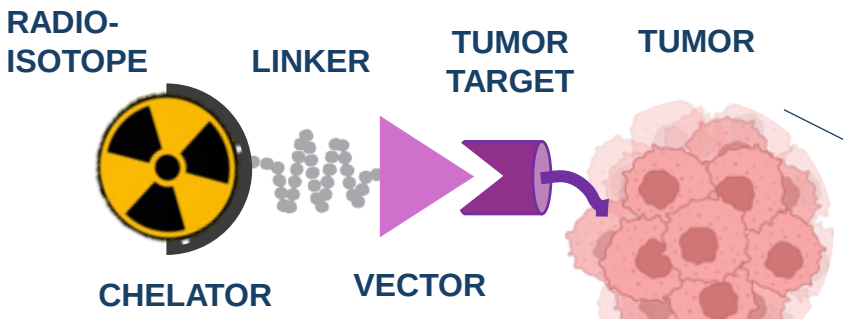



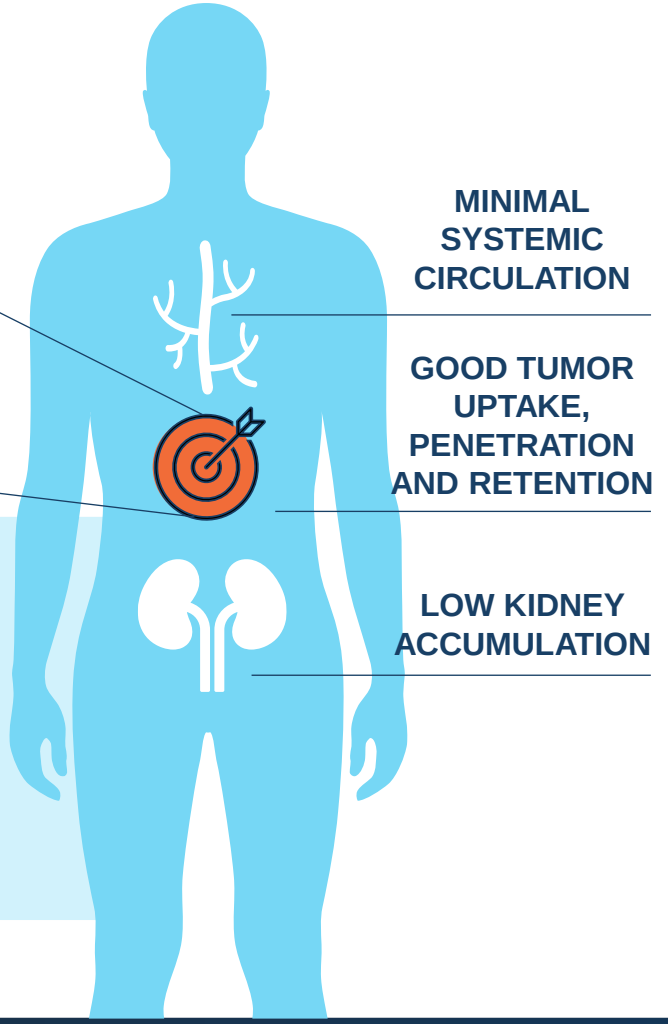

*Fc-active version of JSP-191, reproduced by MP

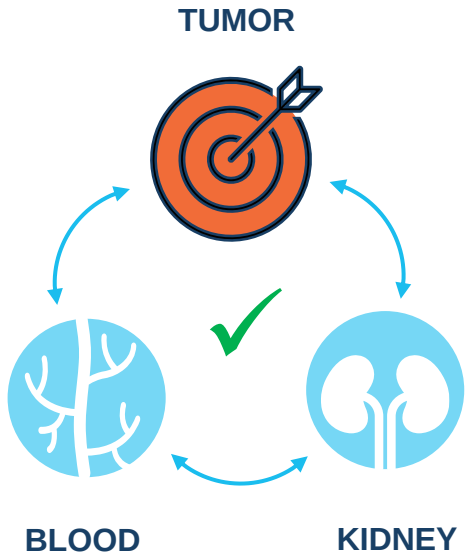
# Radio-DARPin Therapy

Platform & Pipeline

# Ideal Properties of Radiotherapy Product Candidate




**Deliver radioisotope selectively to the tumor while sparing healthy tissues**

"special focus on kidneys and bone marrow (blood), which are the most frequent dose-limiting organs"

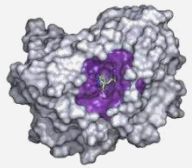
# LMW Molecules as Ideal Vectors but Limited Target Space

## LMW MOLECULES

Targets with cavity where a Low Molecular Weight (LMW) vector with high affinity and specificity can be identified

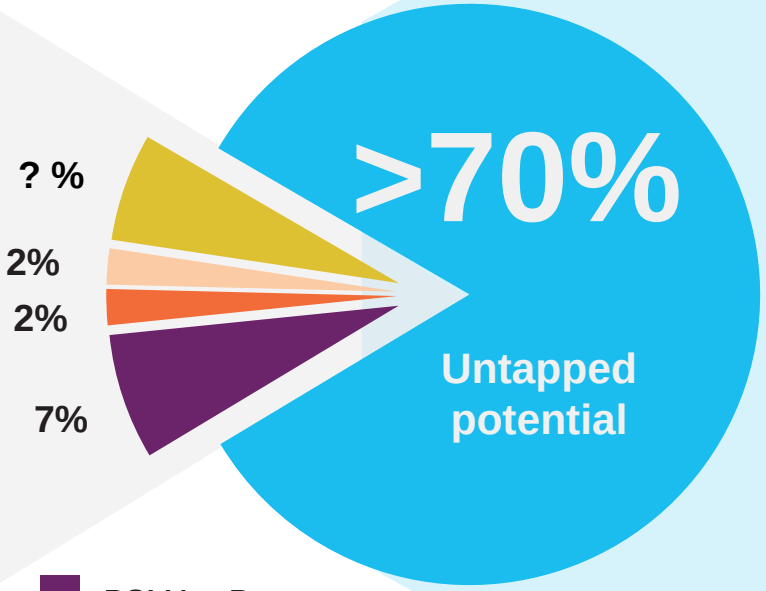
**Target Examples:**

**PSMA**
**SSTR2**



PSMA (1Z8L)

## TARGET SPACE*



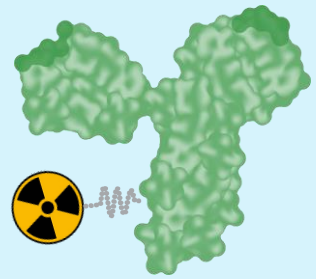

- PSMA + Prostate
- SSTR2 + NETs
- SSTR2 expansion
- Potential other LMW suitable targets**
- Other tumor targets & cancers

## PROTEIN - PROTEIN BINDERS

Proven class for high affinity & specificity binding of protein surfaces of broad range of tumor targets

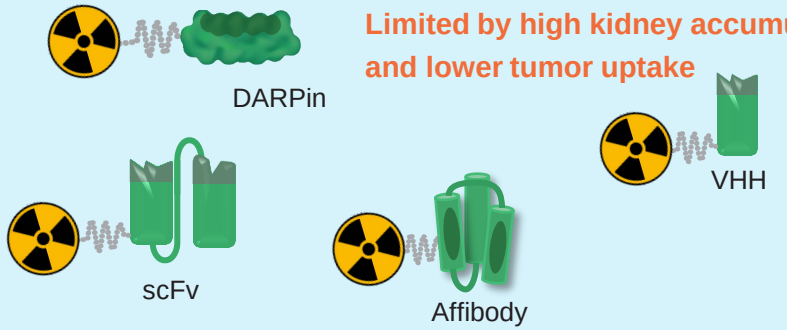
### ANTIBODIES

**Limited by low tumor penetration and too long systemic half-life leading to exposure of bone marrow to radiation**



### SMALL PROTEINS

**Limited by high kidney accumulation and lower tumor uptake**



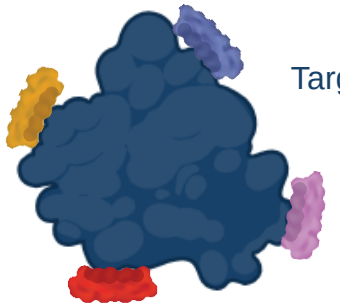


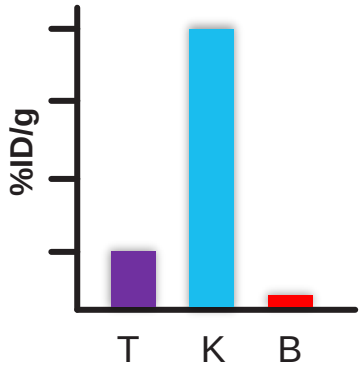

* Source: Guggenheim Securities Report 2023
** e.g. FAP, CAIX, FOLR1, NTSR1, Eph2A, GPC3, MC2R, GRPR, ITGB6
LMW, low molecular weight; NET, neuroendocrine tumor

# The Engineering Strategy for RDT Candidates

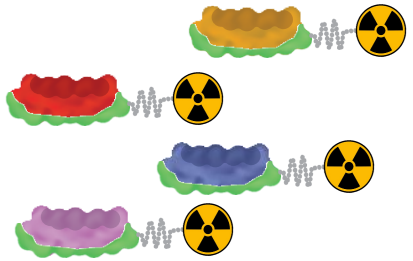
**T**: Tumor
**K**: Kidney
**B**: Blood

## 1 STARTING POINT
**Diverse DARPins with high affinity**

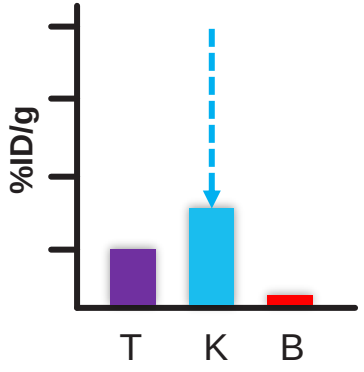



## 2 STEALTH DESIGN
**Reducing uptake in kidney**

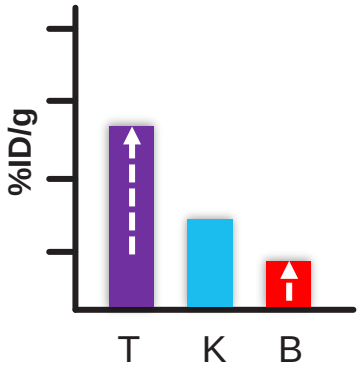


*Identify candidates with <25% ID/g in kidney*



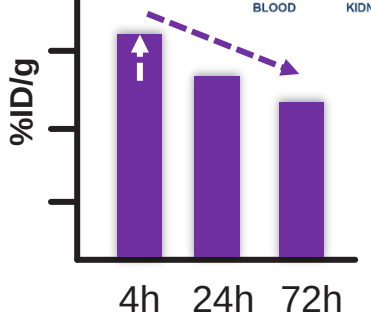

## 3 TUMOR LOADING
**Tuning half-life in circulation**


*Increase tumor uptake while keeping systemic $t_{1/2}$ low*



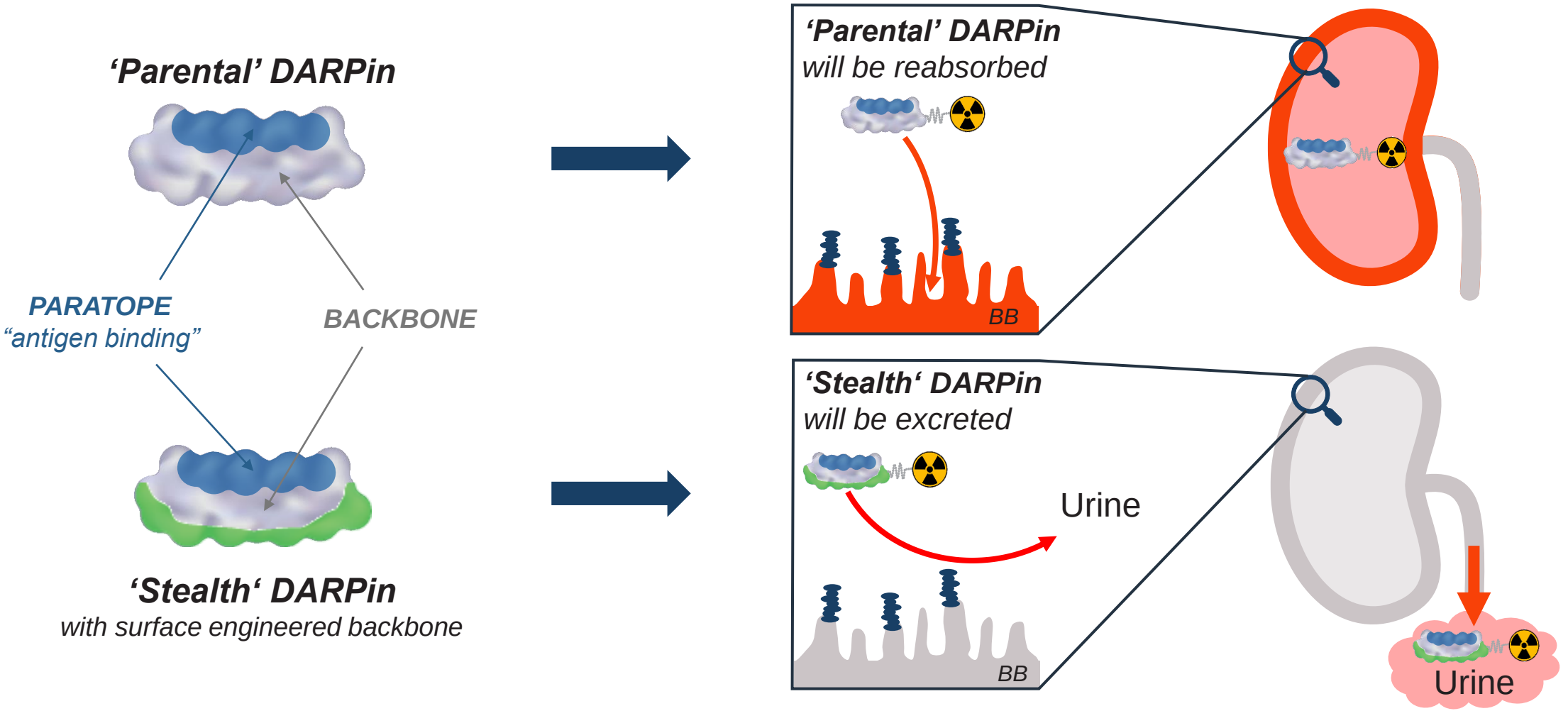

## 4 TUMOR RETENTION
**Affinity maturation**


*If needed, improve affinity to further increase tumor uptake and optimize tumor retention*

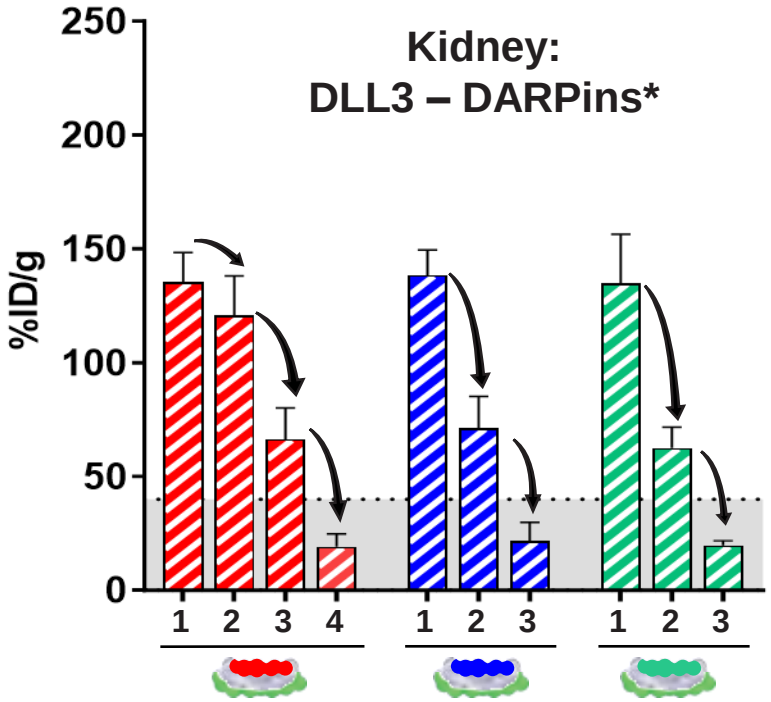



# Surface Engineering to Reduce Kidney Accumulation

## Enabled by the robust architecture of DARPin scaffold



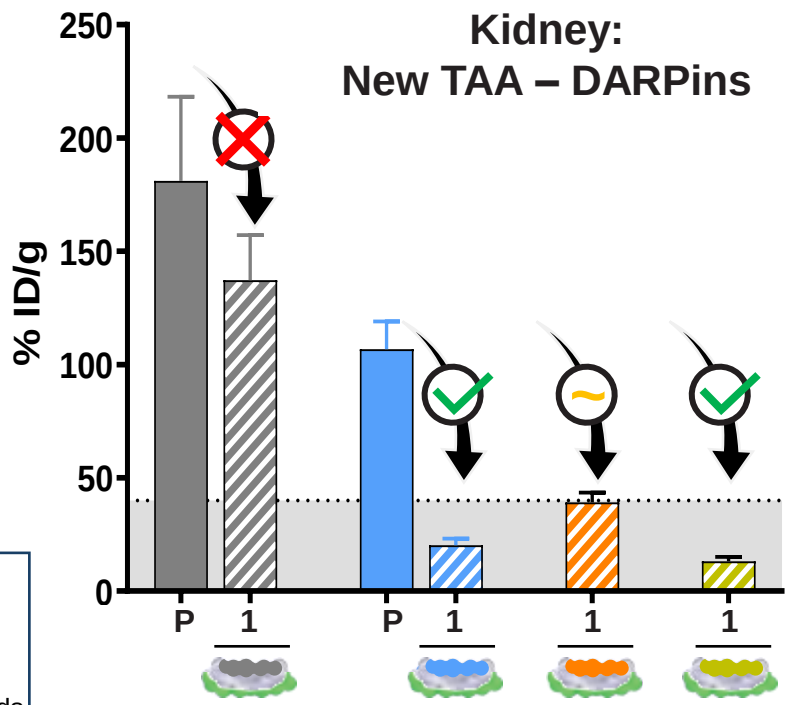
# Evolution of Surface Engineering for RDT Engine




Integration of learnings across different TAAs and **>140 engineered DARPins**

**P:** Parental

**1-4:** Surface Eng. Rounds




**AT PROGRAM START**: Iterative rounds of DARPin surface engineering and *in-vivo* testing needed to reach low kidney accumulation

**TODAY: A <u>single</u> round of DARPin surface engineering** to reach low kidney values for many DARPin binders

** Kidney value of best surface variant per engineering round displayed in graph: 4h timepoint in wt or tumor-bearing mice; DARPins conjugated to different chelators and labelled with different radioisotopes*

# Systemic Half-life Extension (HLE) Increases Tumor Uptake

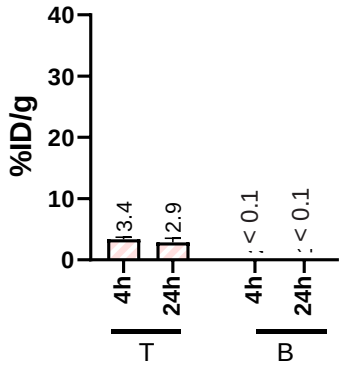
## Establishing a HLE toolbox with different “strengths & properties” to tailor to specific needs

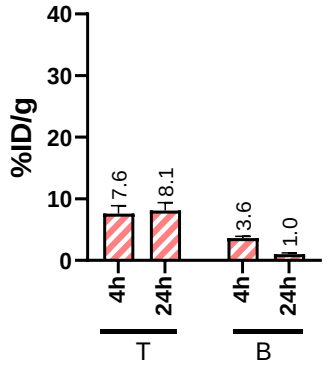

**Stealth DARPin (no HLE)**
Tumor up to 6% ID/g

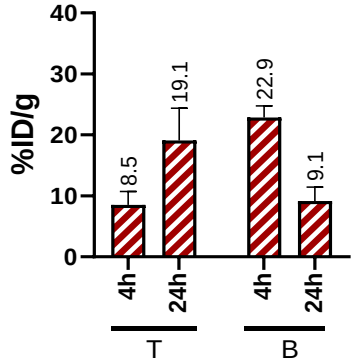
**Stealth DARPin + HLEs**
Very low blood level increase
Tumor up to 10% ID/g

**Stealth DARPin + HLEs**
Low to medium blood level increase
Tumor up to 30% ID/g

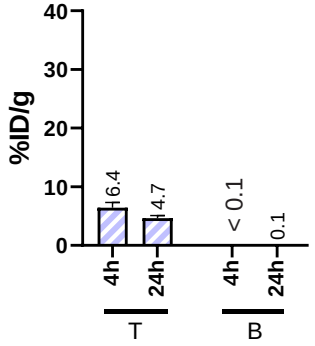
**Her2 DARPin**

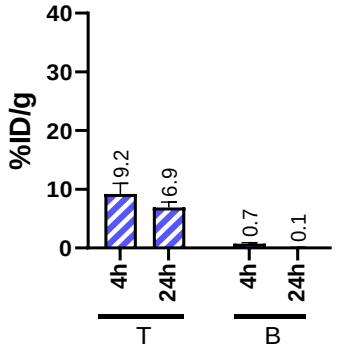


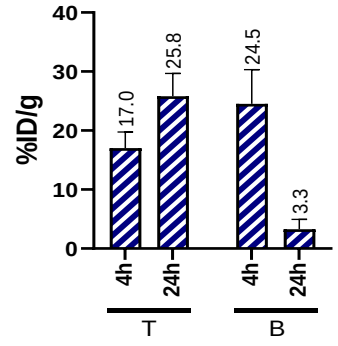



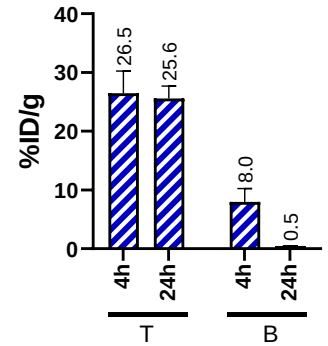




**DLL3 DARPin**




**T**: Tumor; **B**: Blood

*Her2 and DLL3 DARPins conjugated to different chelators, labelled with different radioisotopes; and tested in different mouse tumor models; αSA: HLE moieties binging to serum albumin*

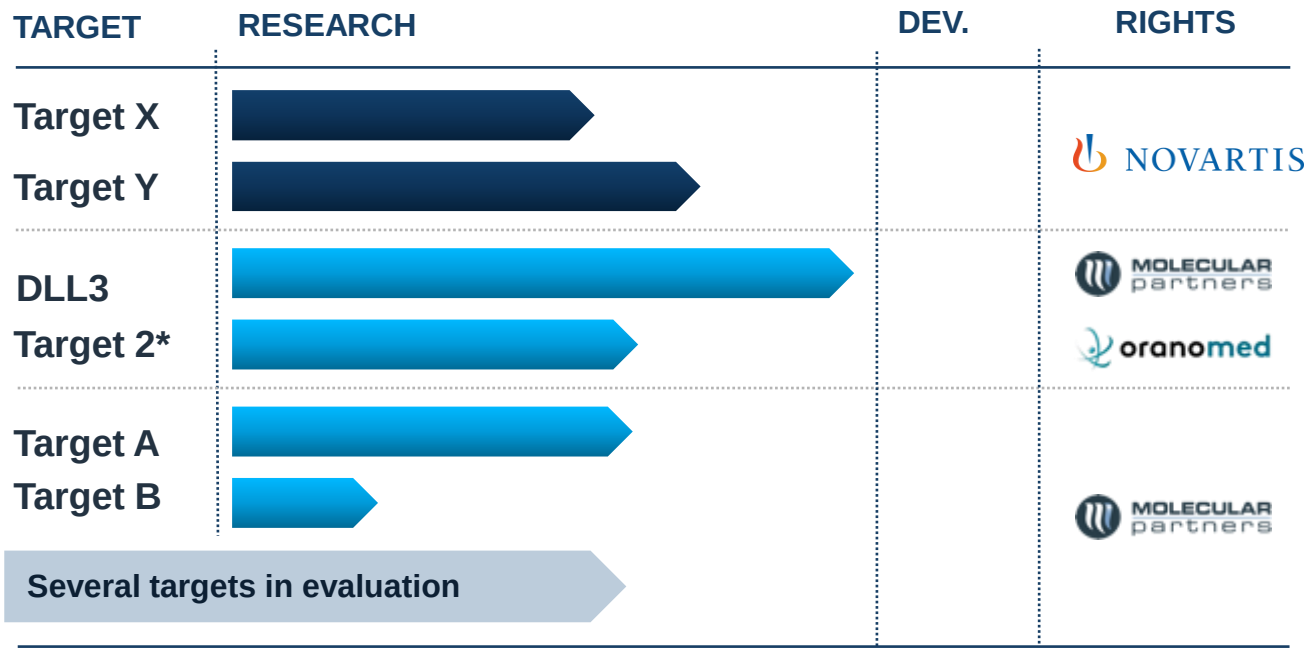
# RDT Engine & Pipeline

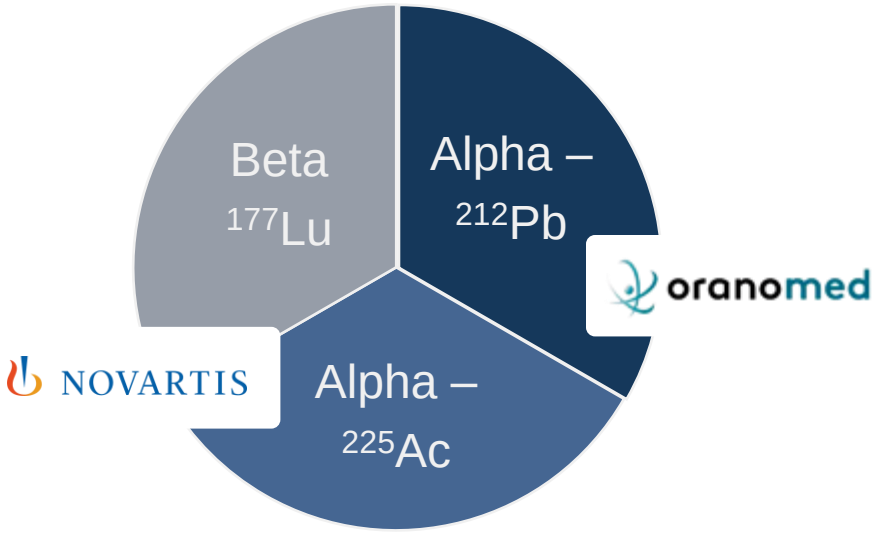
**Leverage Radio DARPin Engine & build pipeline**

- Tailor candidate properties to specific target needs and radioisotope

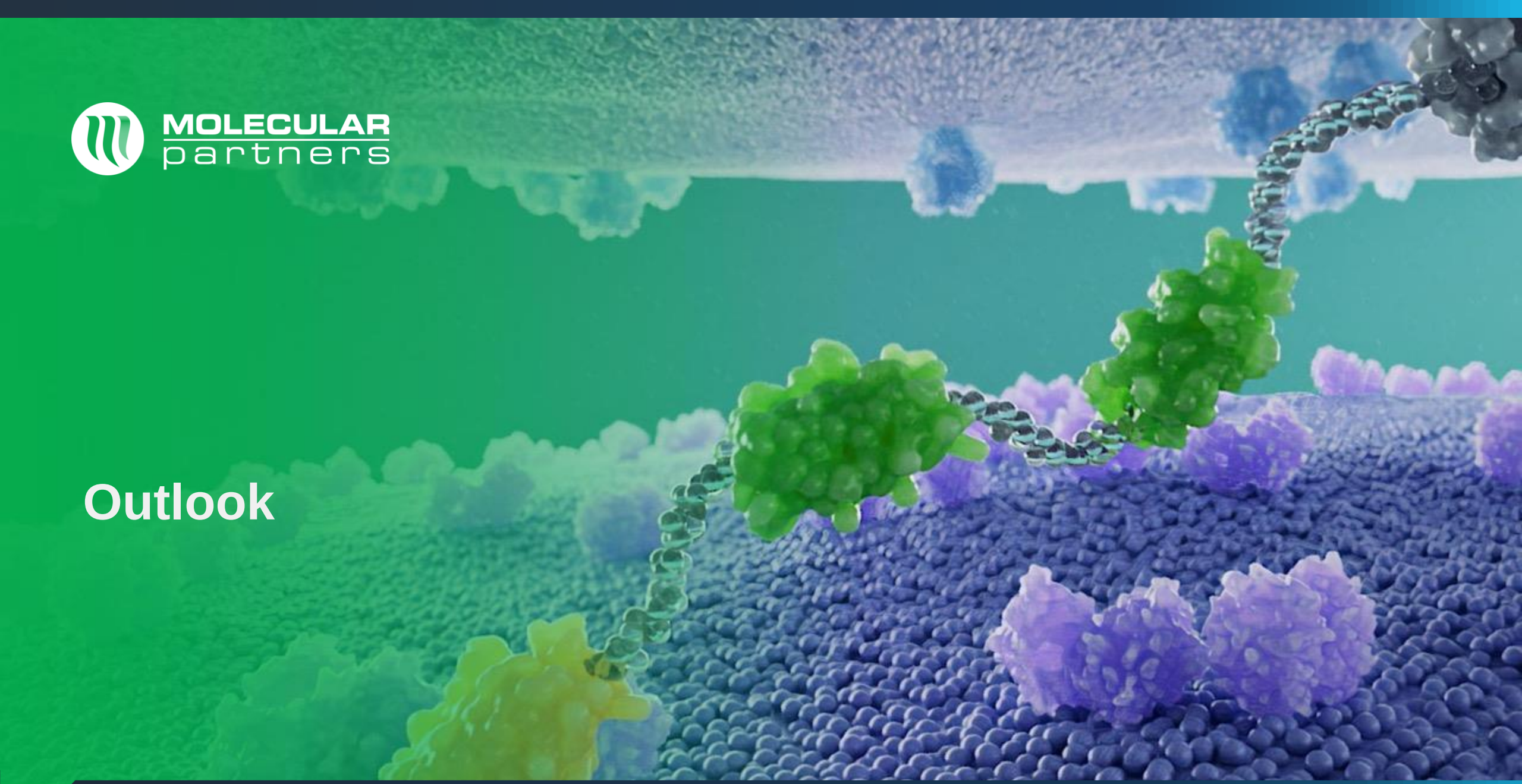
**Partnering model to join forces with leaders in the field**

- Cross-pollination of R&D knowledge
- Access radioisotopes & supply chain




*The co-development agreement with Oranomed includes up to 3 potential oncology targets including DLL3 (Delta-like ligand 3)



# Outlook

# 2024 Outlook and Upcoming Milestones

| | |
|---|---|
| **MP0533** | • Interim update from Phase 1/2a trial to be presented in H1 2024<br>• Expansion of enrolment to higher dose cohorts (protocol amendment ongoing) planned in H2<br>• Plans for future clinical development strategy, incl. preparation of potential US IND application |
| **Switch-DARPin & cKIT** | • Initial preclinical data presentation on cKIT x CD16a x CD47 program in H1 2024<br>• Preclinical proof-of-concept data from NHP study in H2 2024, with strong translational value<br>• Leverage Switch-DARPin platform for next-generation immune cell engagers |
| **Radio-DARPin Therapy** | • DLL3 lead RDT candidate selection in H1 2024 to advance into IND-enabling studies with FIH in 2025<br>• Nominate additional RDT targets and pipeline candidates<br>• Continue to broaden clinical and supply collaborations with radionuclide companies |
| **MP0317** | • Full data from the Phase 1 dose escalation in H1 2024<br>• Partnering for clinical development in combination settings |

**CHF ~187 million** cash* (incl. short-term time deposits) ensures **funding well into 2026**



*As of December 31, 2023.
AML, acute myeloid leukemia; IND, investigational new drug; NHP, non-human primate; R/R, relapsed/refractory; ASH, American Society of Hematology.

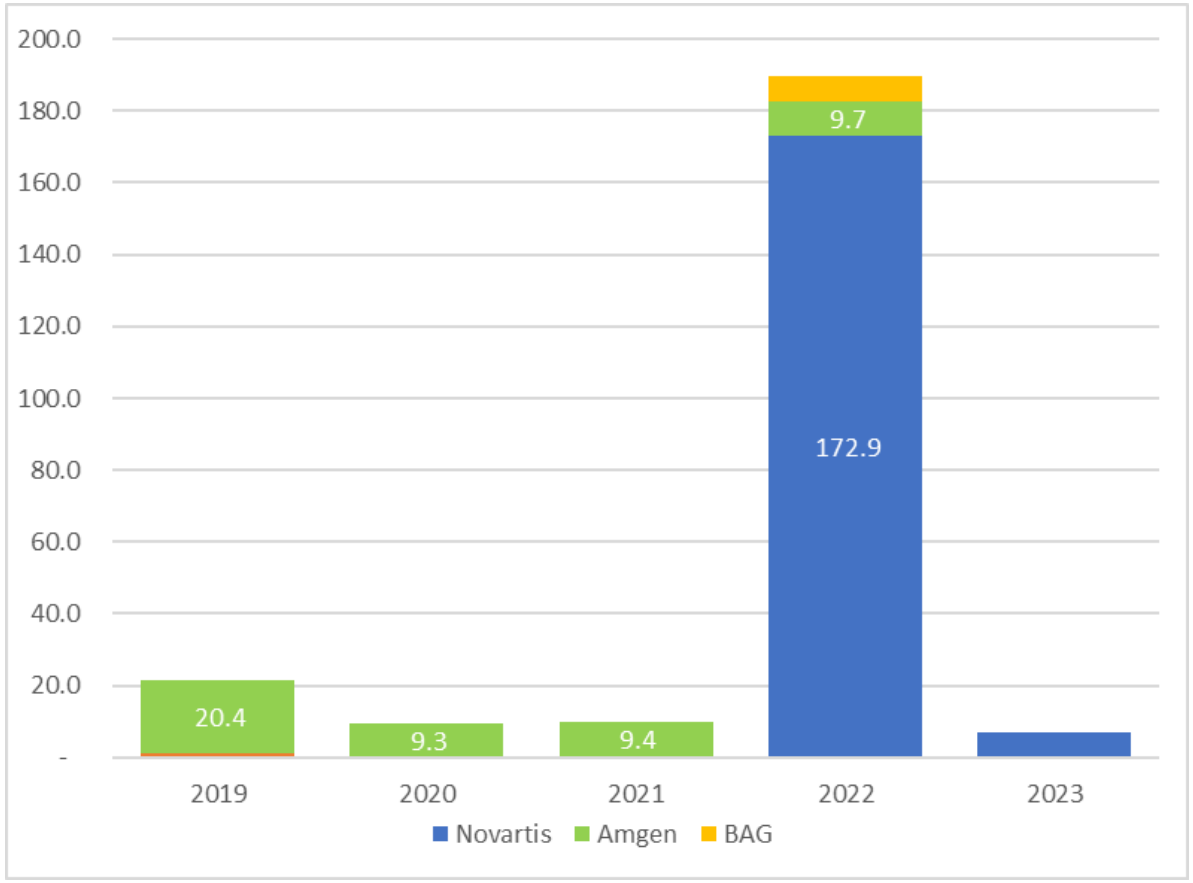

# Thank You

# Back-up

2023 Financials

# Revenues Development

*in CHF million*

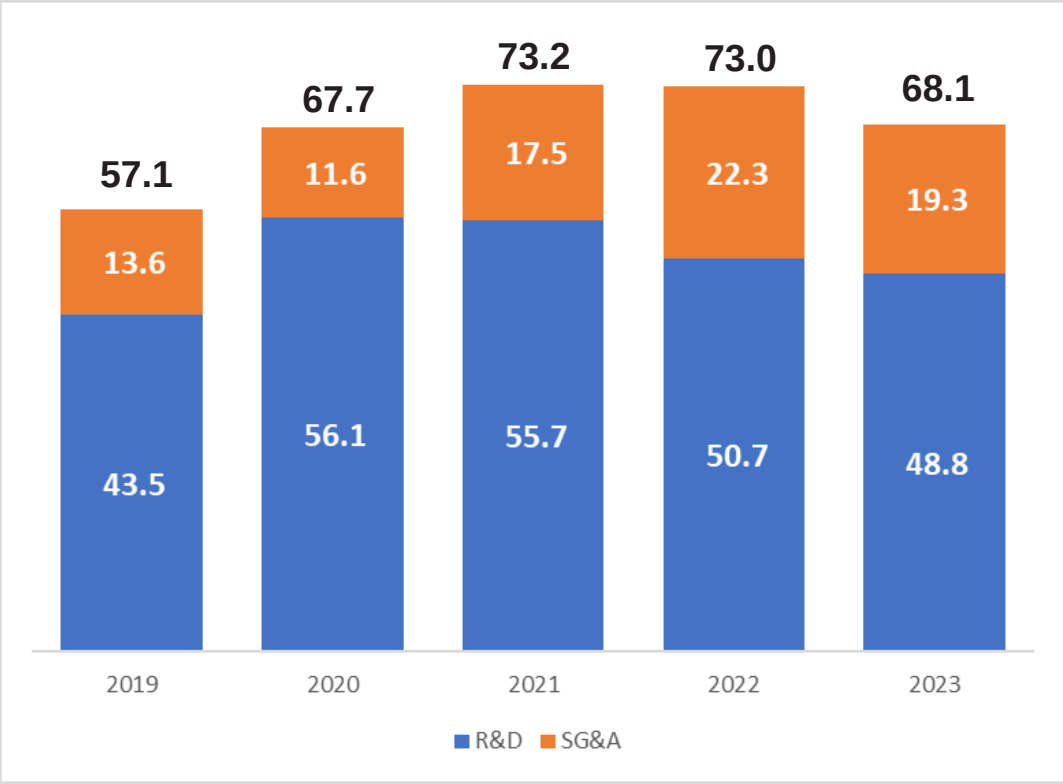



- CHF 7.0 million revenue in 2023, Novartis RLT collaboration
- CHF 190 million revenues in 2022, largely driven by Novartis collaboration
- Revenues in prior years mostly related to Amgen collaboration

Note: Rounding differences may occur

# Operating Expenses

*in CHF million*



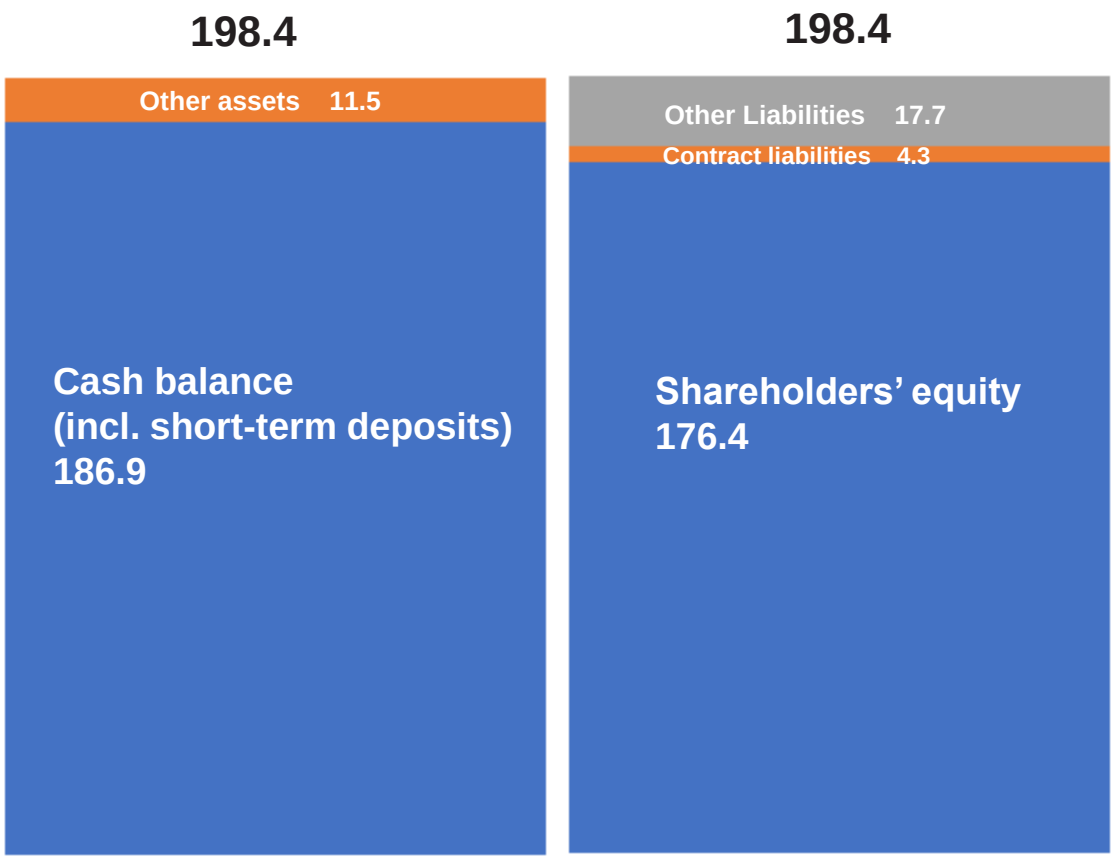

*Highlights 2023*

- Expense development in line with expectations
- Expenses include CHF 8.1 million non-cash effective costs
- Main drivers of changes to prior year
  - Year on year reduction in costs related to US listing of CHF 2.7 million
  - Personnel cost, reflecting effective FTE numbers
  - Lower R&D cost reflect reduction of expenses associated with legacy programs, but also increase in core research and RDT

Note: Rounding differences may occur

# Balance Sheet (as of December 31, 2023)

*CHF million*




*Highlights*

- CHF 186.9 million cash balance (incl. short-term deposits)
- Contract liability of CHF 4.3 million to be recognized as revenue in 2024
- Strong equity base with CHF 176.4 million
- Debt free

# Balance Sheet (as of December 31, 2023)

| *(CHF million)* | FY 2023 | FY 2022 | FY 2021 | FY 2020 | FY 2019 |
|---|---|---|---|---|---|
| **Non-current assets** | **5.9** | **7.5** | 8.5 | 9.7 | 5.0 |
| **Other current assets**[1] | **5.6** | **5.6** | 31.4 | 4.1 | 4.8 |
| **Cash balance** | **186.9**[1] | **249.1** | 132.8 | 173.7 | 95.1 |
| **Shareholders' equity** | **176.4** | **235.2** | 107.3 | 107.2 | 54.1 |
| **Non-current liabilities** | **7.5** | **9.8** | 18.5 | 22.7 | 22.2 |
| **Current liabilities** | **14.4** | **17.3** | 46.9 | 57.7 | 28.6 |

[1] Includes CHF 119.6 million of short-term time deposits
Note: Rounding differences may occur

# Income Statement

| *(CHF million)* | FY 2023 | FY 2022 | FY 2021 | FY 2020 | FY 2019 |
|---|---|---|---|---|---|
| **Revenues / other income** | **7.0** | **189.6** | 9.8 | 9.3 | 20.4 |
| **R&D expenses** | **(48.8)** | **(50.7)** | (55.7) | (56.1) | (43.5) |
| **SG&A expenses** | **(19.4)** | **(22.3)** | (17.5) | (11.6) | (13.6) |
| **Operating result** | **(61.1)** | **116.6** | (63.4) | (58.3) | (36.7) |
| **Net financial result** | **(0.9)** | **1.2** | (0.4) | (4.4) | 0.4 |
| **Net result** | **(62.0)** | **117.8** | (63.8) | (62.8) | (36.3) |

Note: Rounding differences may occur

# Cash Flow Statement

| *(CHF million)* | FY 2023 | FY 2022 | FY 2021 | FY 2020 | FY 2019 |
|---|---|---|---|---|---|
| **Net cash from / (used in) operations** | **(59.0)** | **118.6** | (91.0)[1] | (29.0) | (1.2) |
| **Net cash from / (used in) investing[2]** | **44.6** | **(101.1)** | (22.2) | (21.7) | (19.8) |
| **Net cash from / (used in) financing** | **(1.2)** | **(1.6)** | 50.6[3] | 113.2[3] | (0.2) |
| **Exchange gain / (loss) on cash** | **(5.1)** | **0.3** | 0.7 | (4.5) | (2.0) |
| **Net cash increase / (decrease)** | **(20.6)** | **16.1** | (61.9) | 58.0 | (23.2) |
| **Cash balance at year end** | **186.9** | **249.1** | 132.8 | 173.7 | 95.1 |

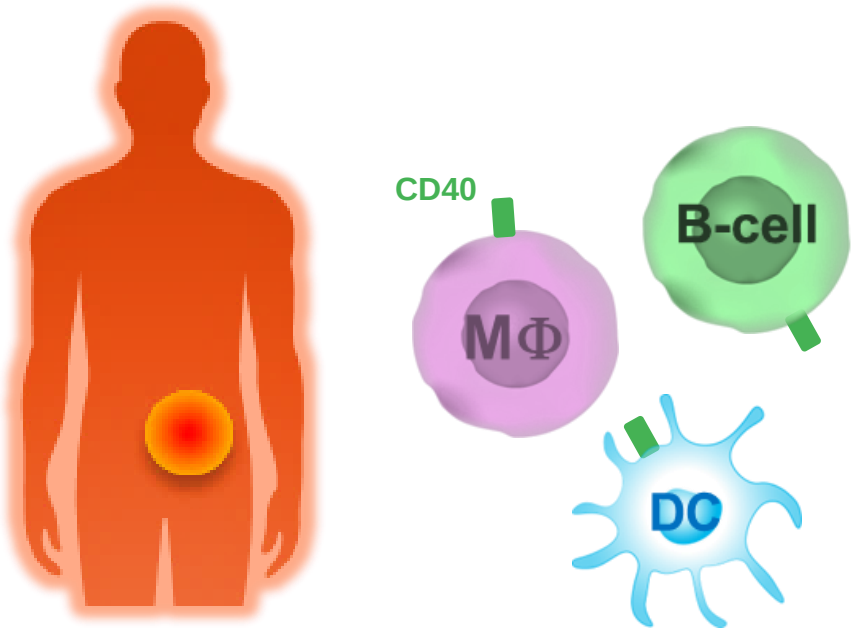
[1] Includes CHF 20 million paid to Novartis
[2] Includes movements in short-term time deposits
[3] For 2021 this includes the funds received from the listing in the US; for 2020 this includes two capital raises
Note: Rounding differences may occur

# MP0317

Tumor-localized Immunotherapy

# MP0317: Unlocking CD40 Activity Through Local Activation

**PROBLEM:** Toxicity of CD40 Agonists has so far limited their potential




**CD40 agonists** can activate **B cells, DCs and MΦ** to enhance the efficacy of anticancer treatment, especially in “cold tumors”

**Systemic activation of CD40** via mAbs has been hampered by **significant toxicities**

- Limiting potential CD40 agonists to reach therapeutically active doses

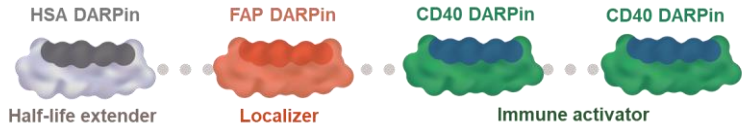


DC, dendritic cell; MΦ, macrophage; mAb, monoclonal antibody.

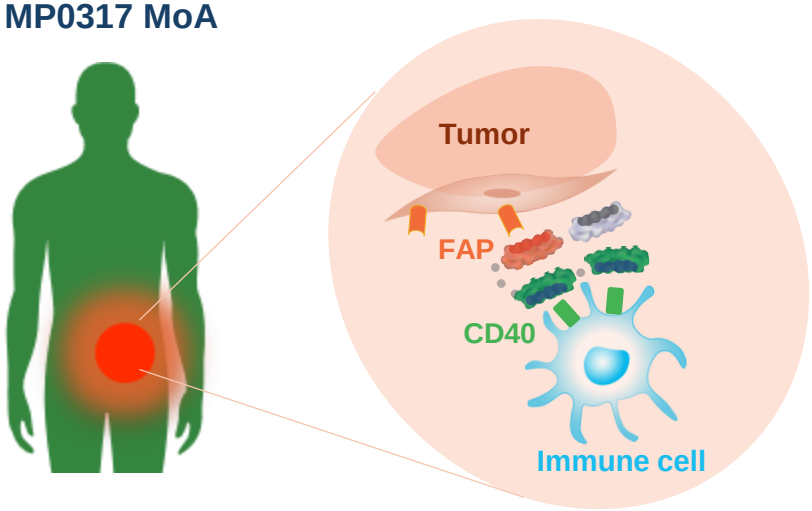
# MP0317: Unlocking CD40 Activity Through Local Activation

**SOLUTION:** MP0317 – FAP-dependent tumor-localized CD40 activation

**MP0317 design**




**MP0317 MoA**




**FAP** is a **validated tumor target**

- Overexpressed in ≥ 28 different cancer types
- Expression not downregulated during disease progression

**MP0317** designed to

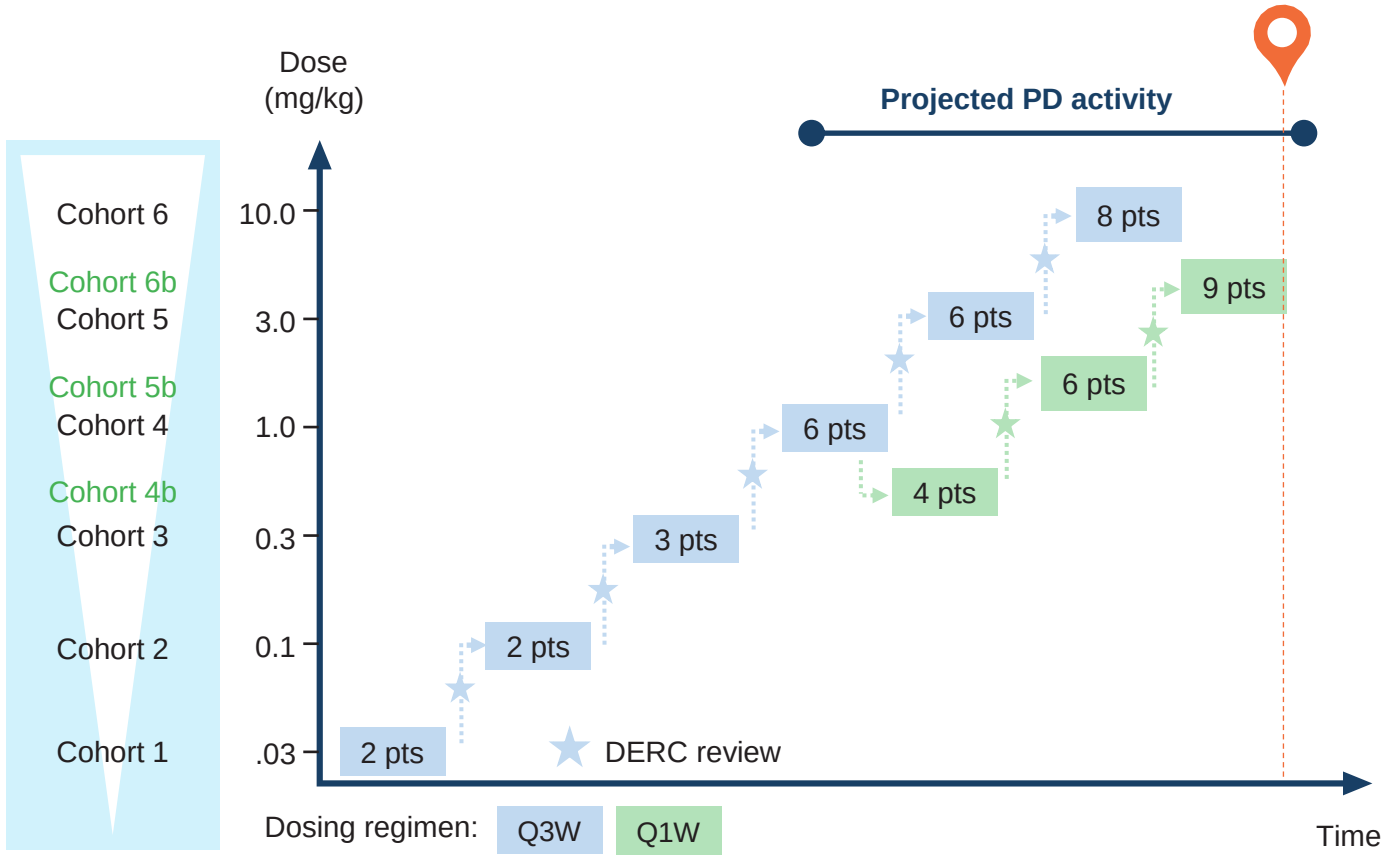
- **Bind tumor-localized FAP** and induce **CD40-mediated activation** of immune cells **in the tumor**
- Overcome systemic toxicity, allowing a wider therapeutic dosing range



FAP, fibroblast activation protein; HSA, human serum albumin.

# MP0317 Phase 1 Study Design and Status

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




## Primary Study Objectives

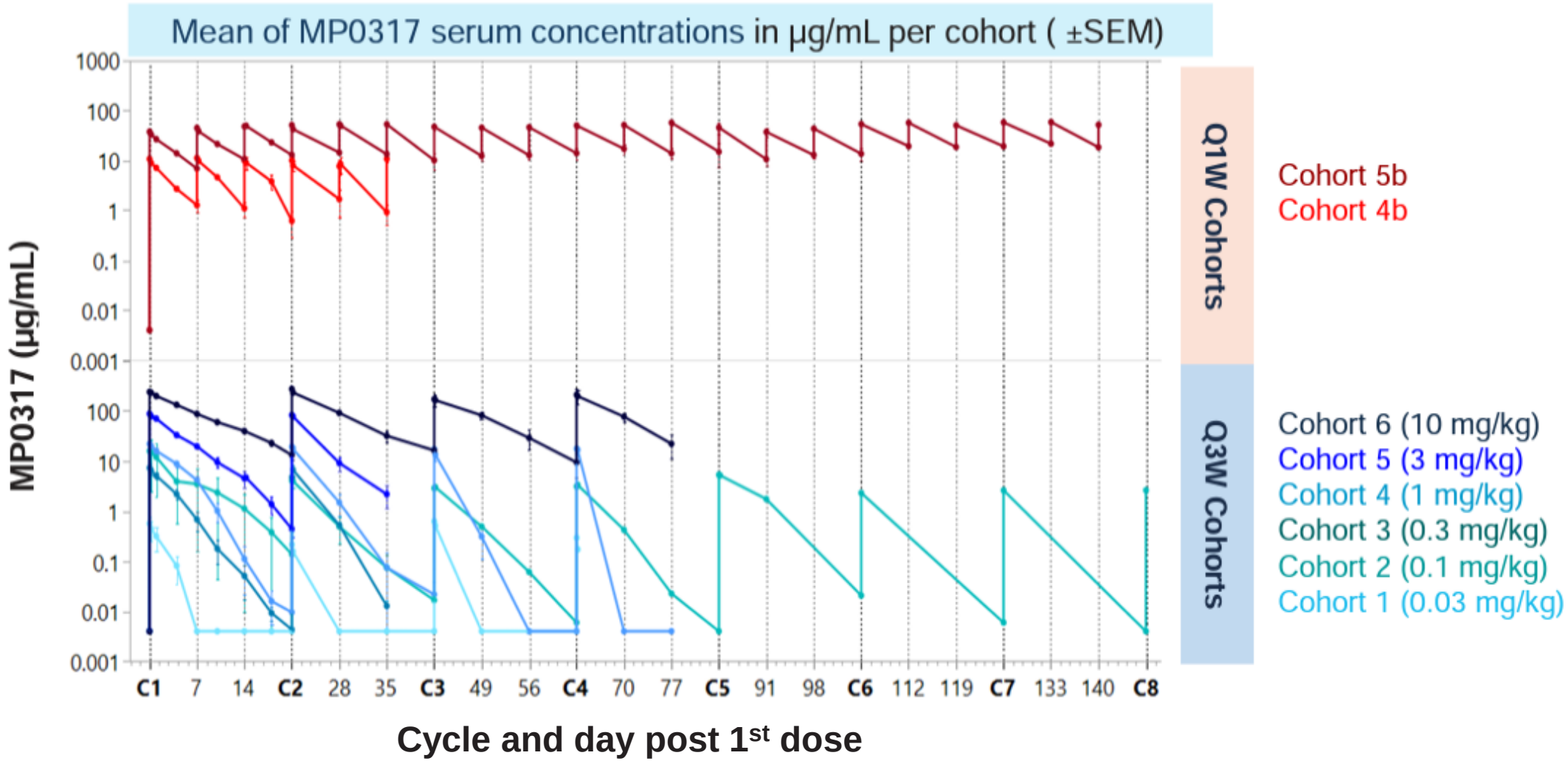
- MP0317 safety and tolerability
- Recommended dose for expansion and combination

## Updated Data Presented at SITC 2023[1]

- **Enrollment completed** in dose-escalation part; 46 patients treated
- **Favorable safety profile** up to highest planned dose (10 mg/kg); one DLT
- **Favorable exposure profile** across dosing schemes (Q1W, Q3W)
- **Clinical evidence** of tumor-localized CD40 pathway and immune cell activation, leading to **TME remodeling**

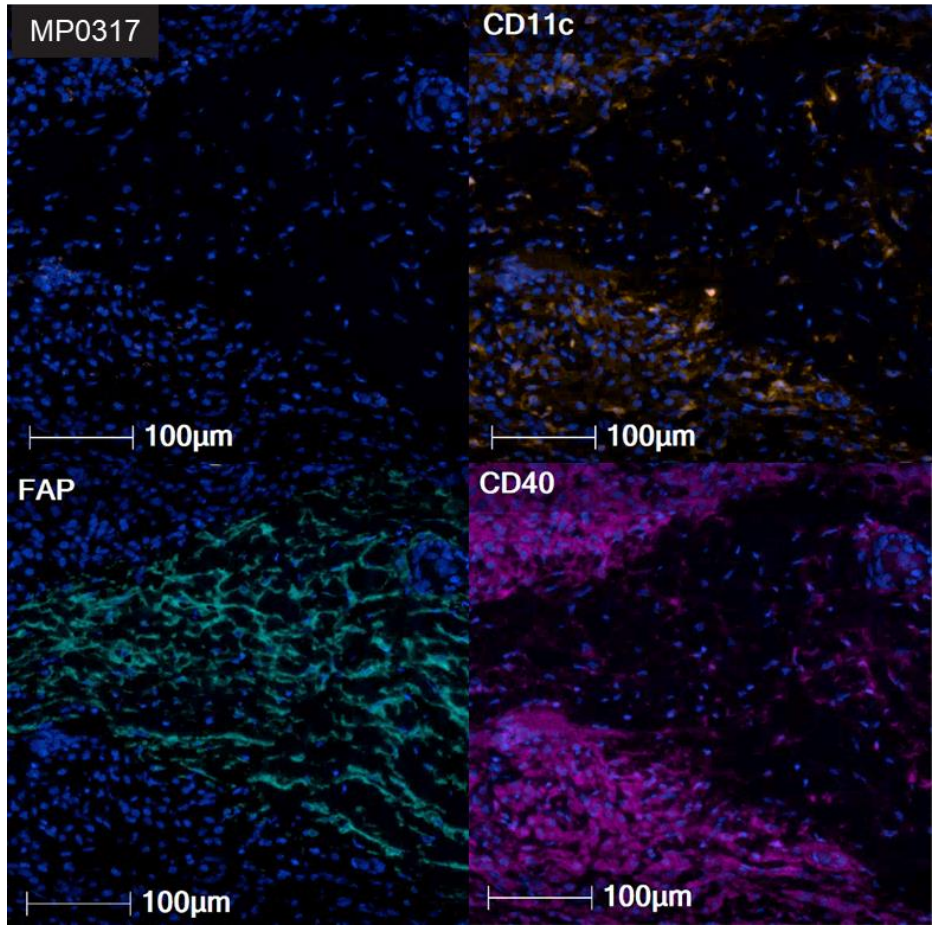
[1]Gomez-Rocca et al. SITC 2023 poster presentation. The study is registered at ClinicalTrials.gov (NCT05098405).
PD, pharmacodynamic; Q1W, weekly dosing; Q3W, every-3-weeks dosing;
DERC, dose escalation review committee; DLT, dose-limiting toxicity; TME, tumor microenvironment.

# Exposure to MP0317 is maintained in patients across dosing schemes and cohorts



# MP0317 Co-localizes with FAP and CD40 in Tumors – Concomitant Increase in Intra-tumoral DCs Observed

**PRIOR TO TREATMENT**

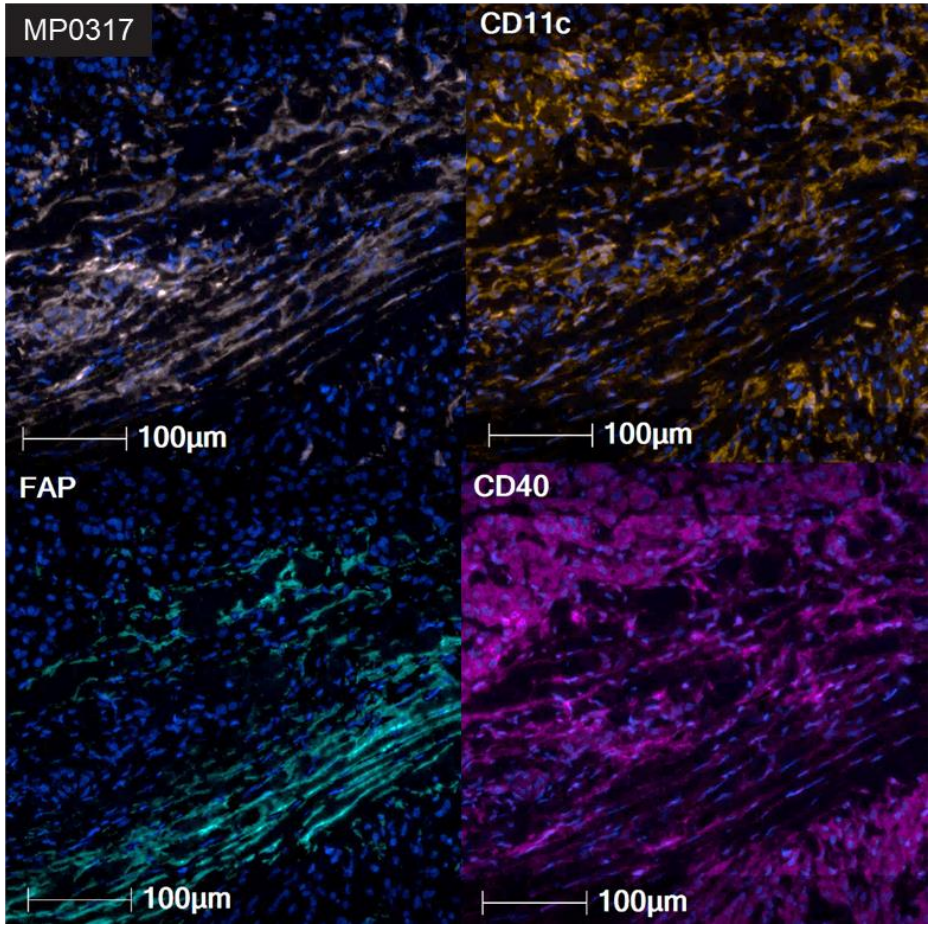



Minimal DC presence in FAP-positive tumor area

**DC infiltration**

**MP0317**

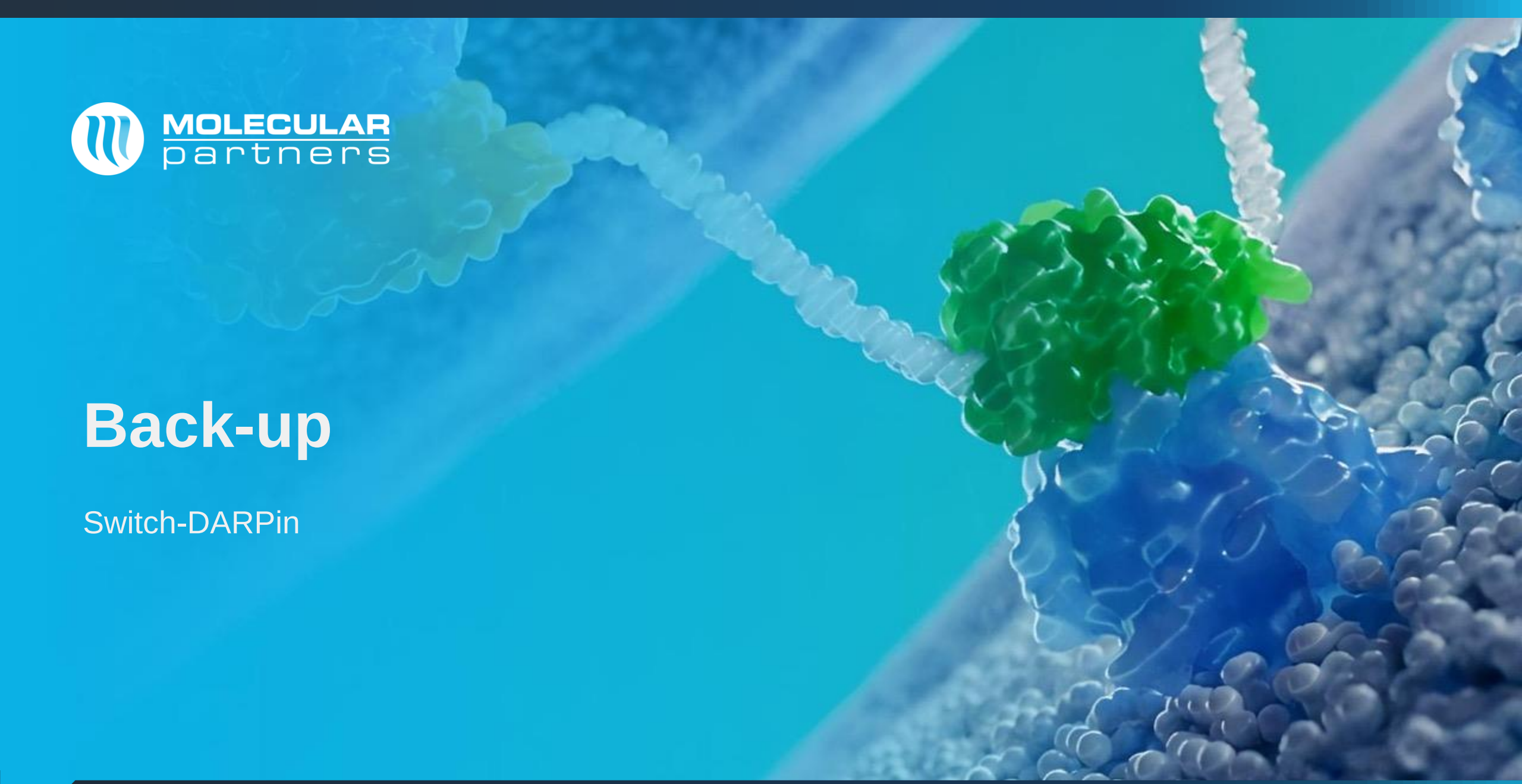
**CYCLE 2 DAY 8**




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.



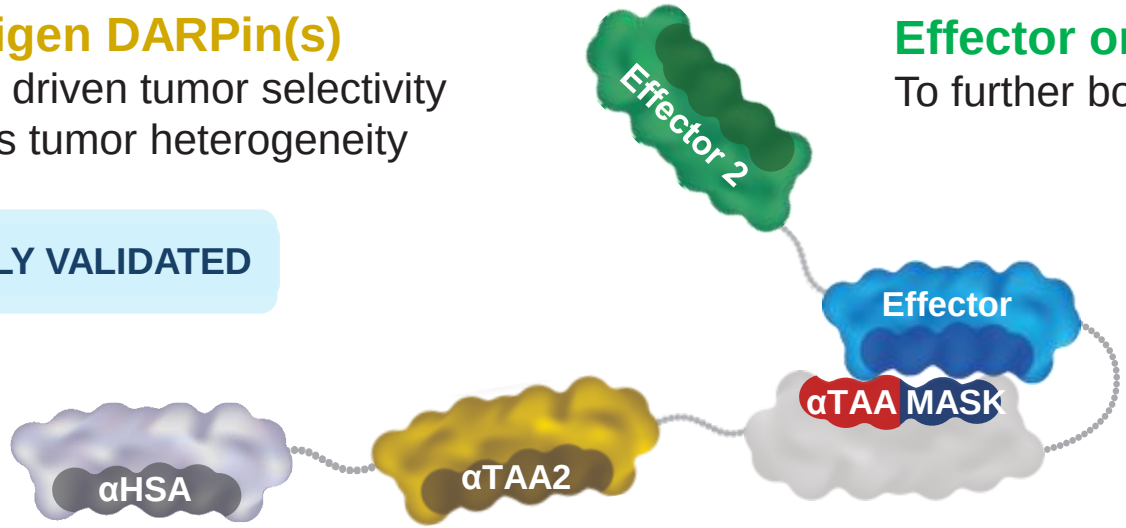
# Back-up

Switch-DARPin

# Logic-gated Switch-DARPins
# Swiss knives for enhanced immune engagers

**Tumor Antigen DARPin(s)**
+1 for avidity driven tumor selectivity
+2 to address tumor heterogeneity

✓CLINICALLY VALIDATED




**Effector or Co-stimulating DARPin**
To further boost immune response

**Effector DARPin**
CD3 engager, CD47 Blocker, ...

✓CD3 ENG CLINICALLY VALIDATED

**HSA DARPin(s)**
For Half life extension

✓CLINICALLY VALIDATED

**Switch-DARPin**
to prevent systemic immune-cell activation
- Allows safe use of potent immune-cell effectors
- Better biodistribution (no immune target-mediated sink)

*hypothetical sketch*



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

# Back-up

Radio-DARPin

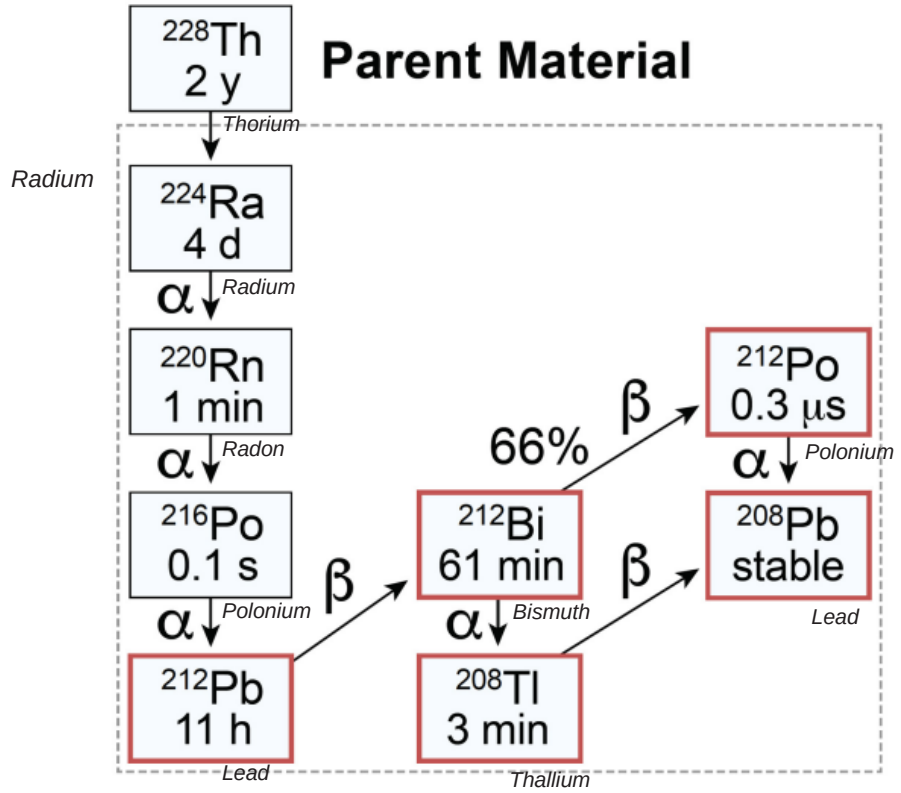
# Rationale for Developing $^{212}$Pb-based RDTs

## Collaboration with Orano Med

- **$^{212}$Pb has key advantages as radioisotope [1]:**
  1) **Efficacy** – short decay half-life is leading to high energy deposition on tumor in short time frame and might be beneficial for early combination with immunotherapy
  2) **Safety** – clean decay chain – $^{212}$Pb is an alpha precursor with low risk for long-lived free daughter radionuclides
  3) Less problematic **waste management** due to short half-life

- **RadioLigand Therapy commands excellent logistics with all isotopes**

- **OranoMed as strong collaboration partner**
  - Leading the field of $^{212}$Pb for Targeted Radiotherapy
  - "Endless" radioactive starting material as basis for supply
  - Collaboration between MP / OM established over >12 months
    - Strong platform & product progress
    - Trust, Complementary and deep expertise




*Adapted from Li et al., Current Medicinal Chemistry, 2020*



*[1] Zimmermann, Journal of Nuclear Medicine, 2023*