Building Tomorrow's Breakthroughs

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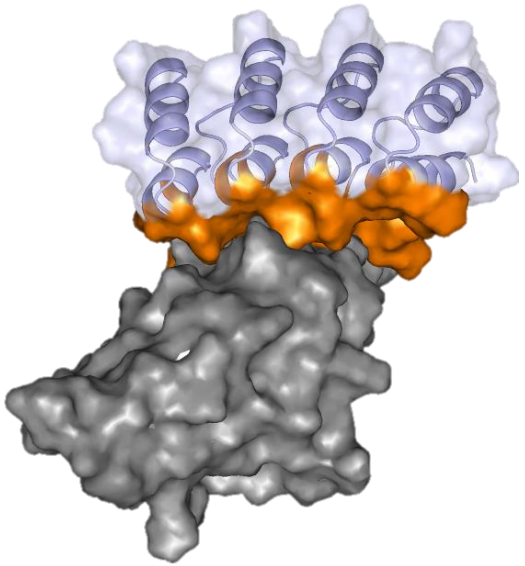
Molecular Partners at a Glance

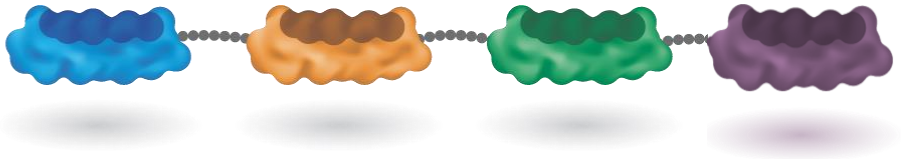
WHAT WE INVENTED	• New class of therapeutics – **Designed Ankyrin Repeat Proteins** or **DARPins** • DARPin as therapeutic modality to **close the gap between small molecules and antibodies** • Validated with **6 clinical-stage compounds**, **>2500 patients treated,** manufacturing established at scale
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 **targeted radioligand therapy** (RLT) • More to come as we are building additional compounds and DARPin platforms
AND	• We are **well capitalized** with cash into **2026**

What are DARPins: DARPin Modality



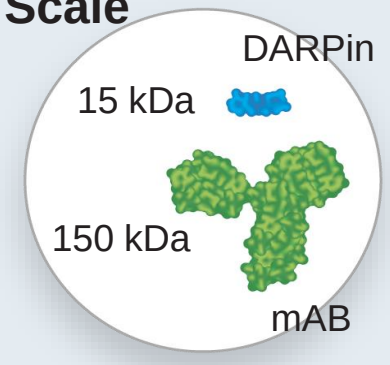
Mono-DARPin

Multi- DARPin



- Derived from natural binding proteins – ankyrin repeat proteins
- High affinity and specificity
- Small size: 15 kDa (1/10 of monoclonal antibody)
- Tunable half-life
- High-yield microbial manufacturing
- Simple architecture: 1 protein chain - basis for multi-DARPins
- Validated with 6 clinical DARPin Candidates

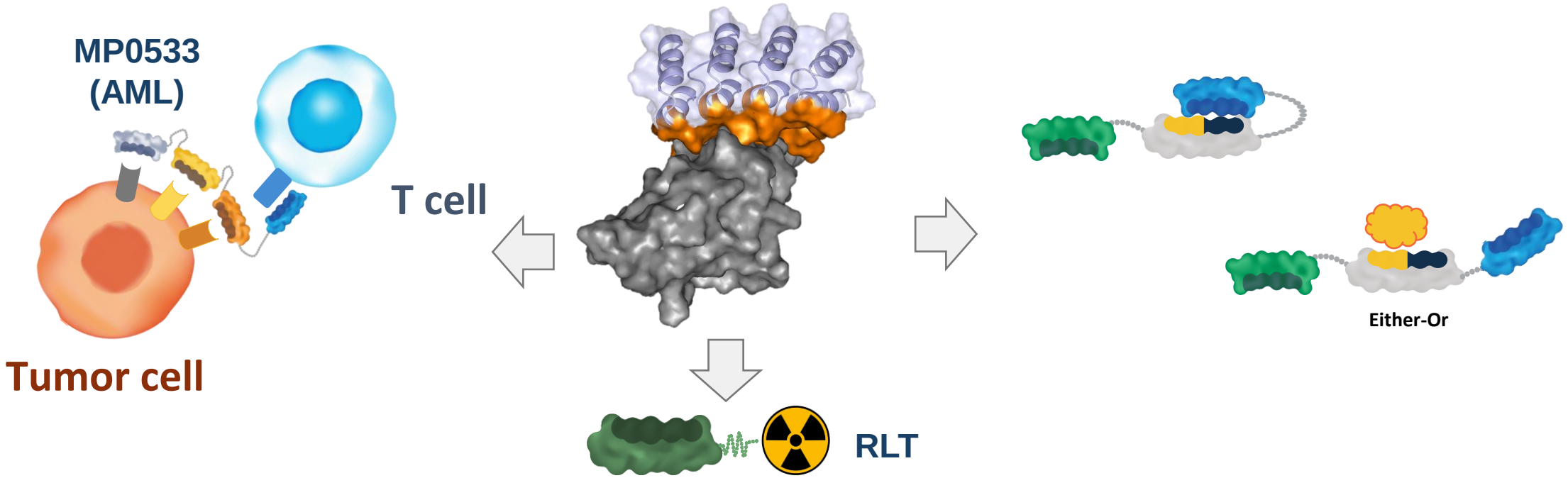
Scale



DARPin ADVANTAGES

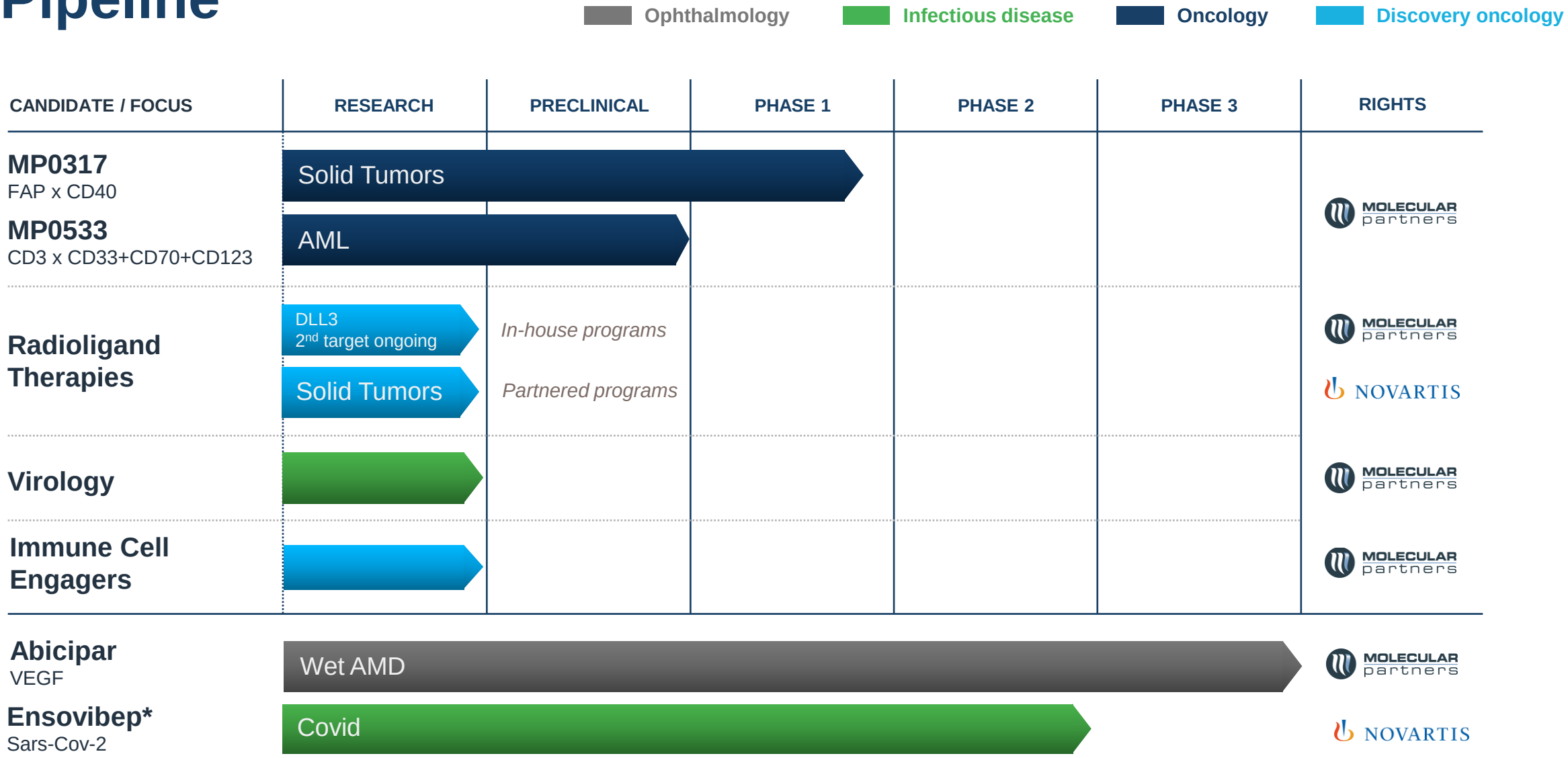
T-cell Engager Platform
Ultra Selective

SWITCH
Localized Activity



RLT Platform: Small size & high affinity
Deep Tumor Penetration

Pipeline



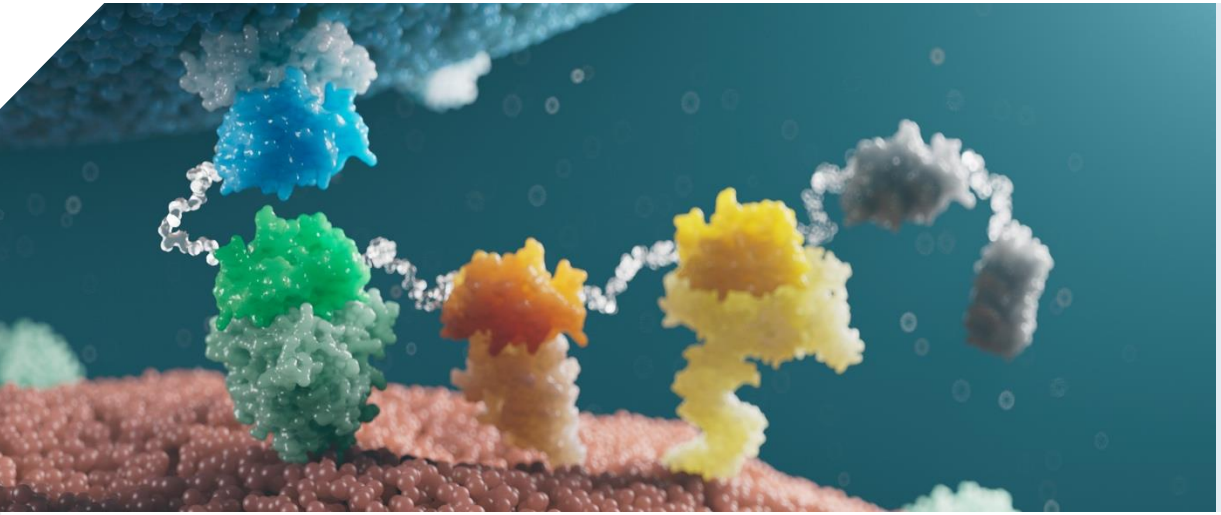
*Molecular Partners was informed by its partner Novartis that it has submitted a request to withdraw the Emergency Use Authorization (EUA) application from the U.S. Food and Drug Administration (FDA) for ensovibep, a DARPin therapeutic candidate to treat COVID-19. As previously disclosed, ensovibep is not presently in clinical development.

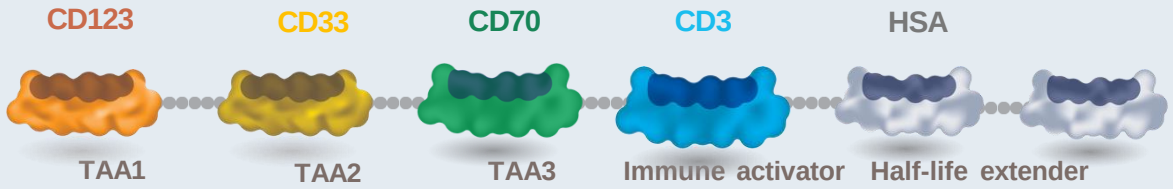
MP0533: Multi-specific DARPin for AML

Targeting three tumor-associated antigens

Clinical study underway

MP0533: Phase 1 Unique Trispecific for AML Patients





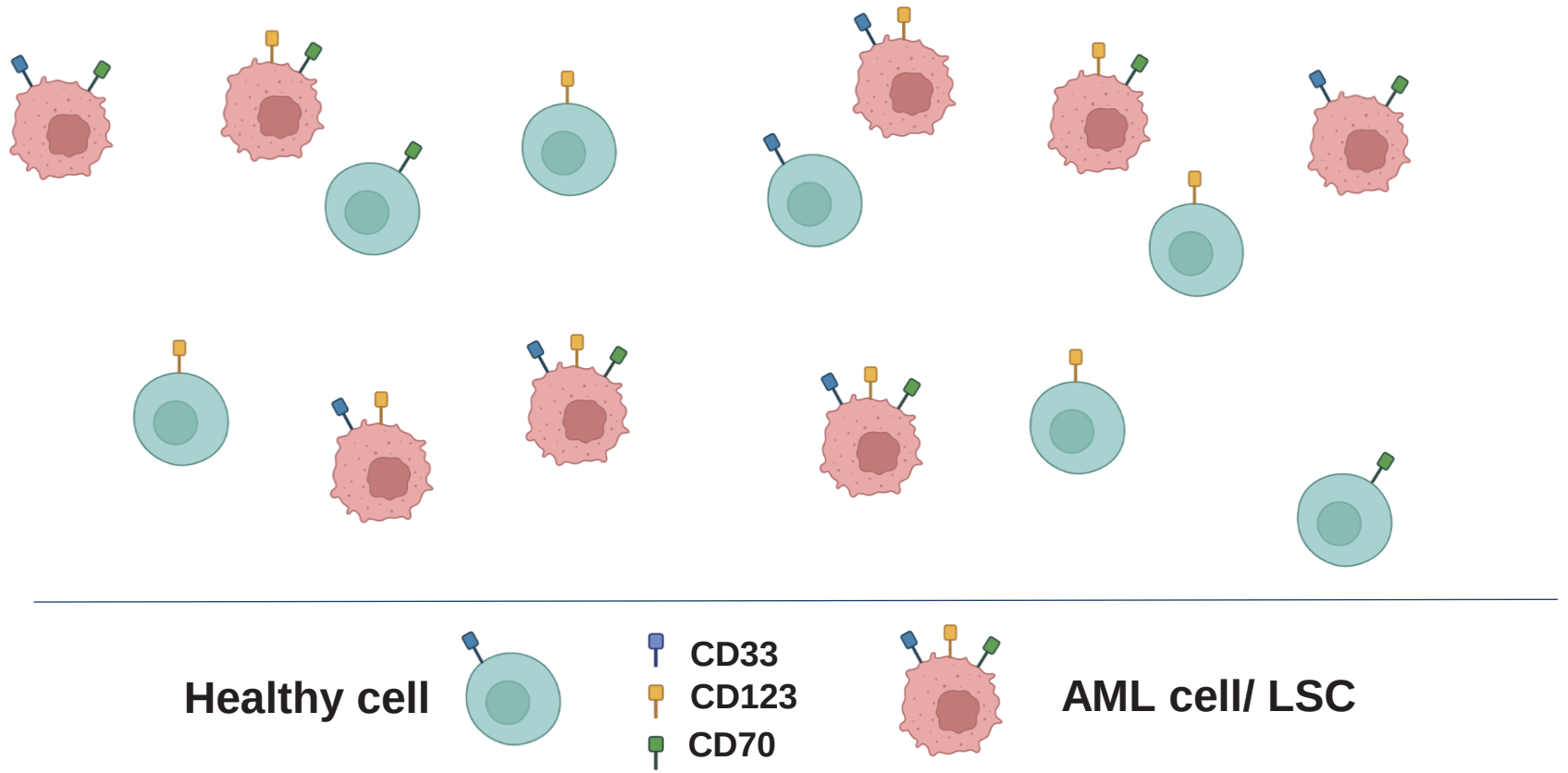
CD33, CD70, CD123: Tumor-associated antigens far more likely found in combination on leukemic stem cells than healthy cells

CD3: Cytoxic T-cell stimulator

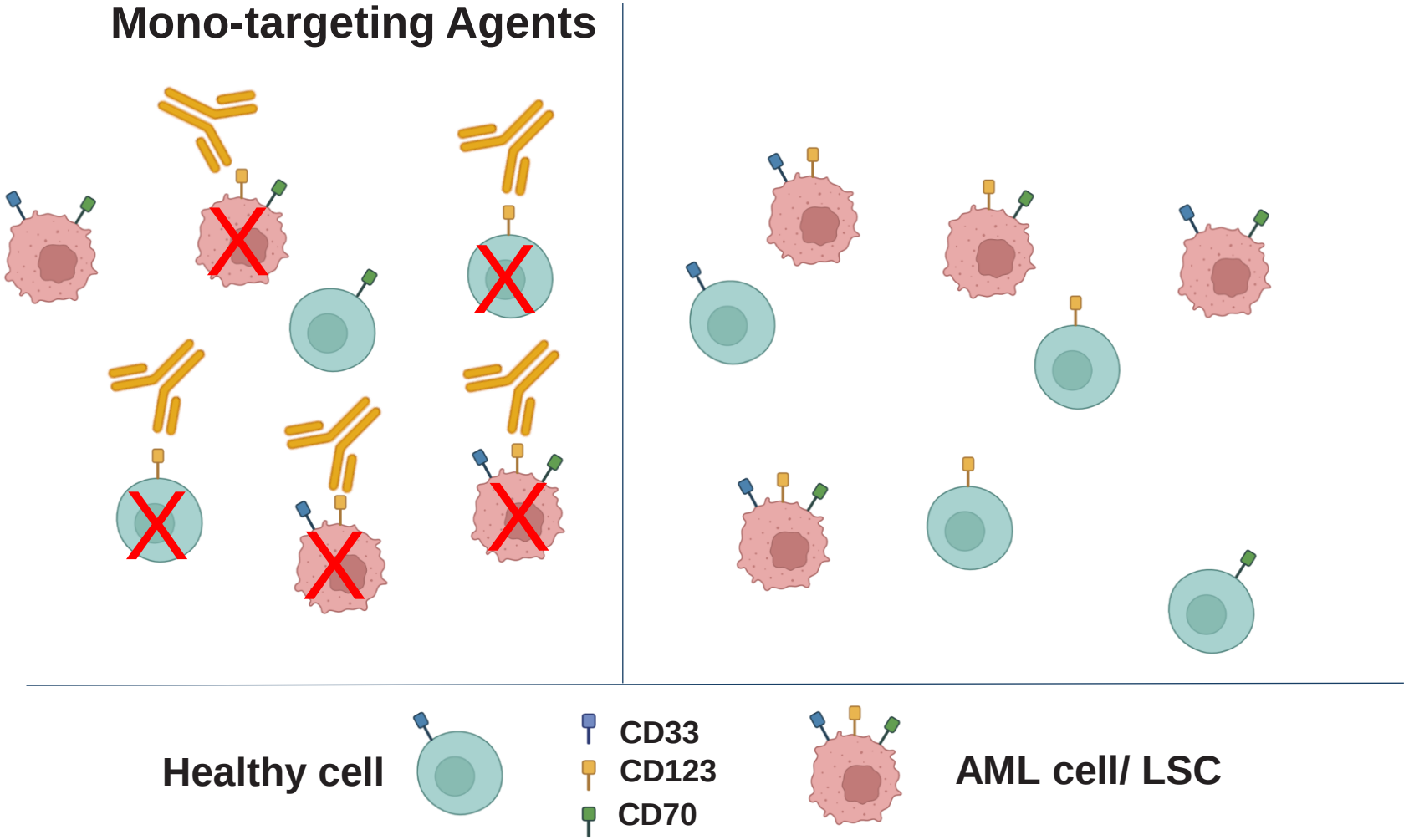
- **Candidate design goal**: Trispecific affinity for leukemic stem cells to dramatically increase efficacy of T-cell engager CD3 without systemic toxicity
- **Outcomes**: Critical data delivered on MoA, safety & efficacy, biomarker plan, competition analysis, CMC feasibility. Phase 1 clinical trial initiated.
- **Next milestones**:
  - Phase 1 clinical trial initiated
  - **2H 23:** First readout

Avidity-guided selectivity for cancer cells in AML

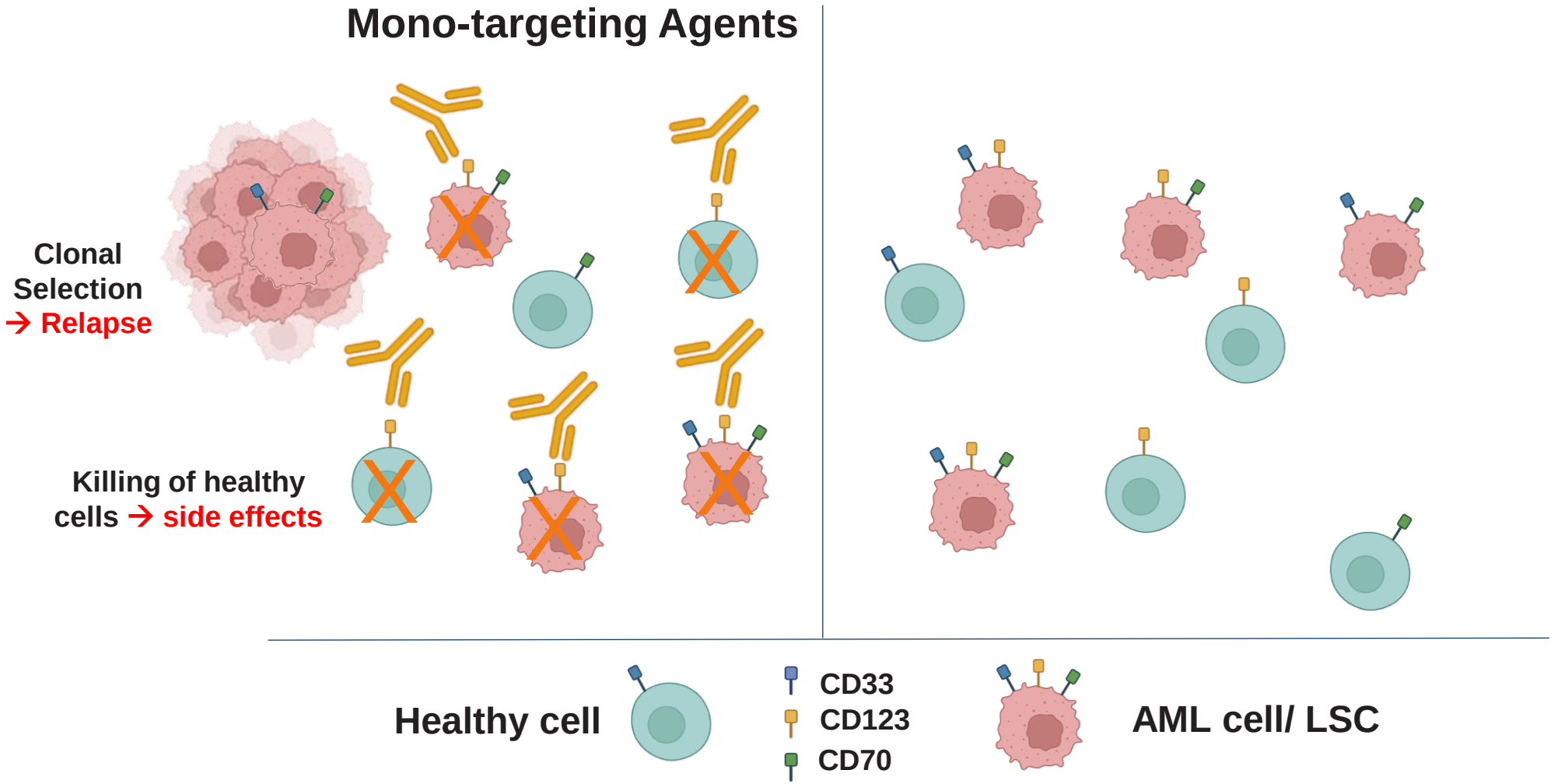
AML targets are heterogeneous and expressed healthy cells with co-expression of on AML cells/LSCs



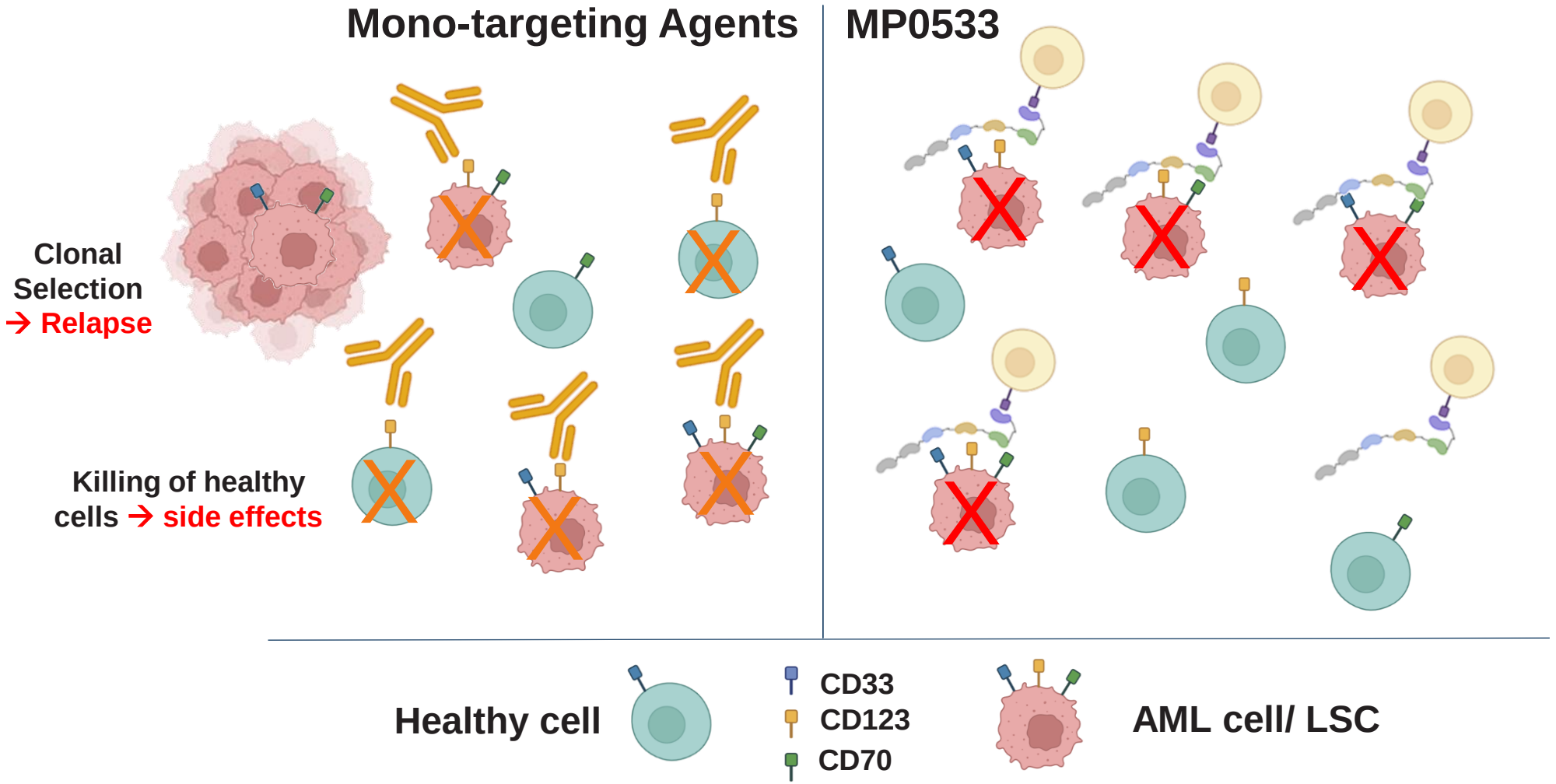
Avidity-guided selectivity for cancer cells in AML



Avidity-guided selectivity for cancer cells in AML



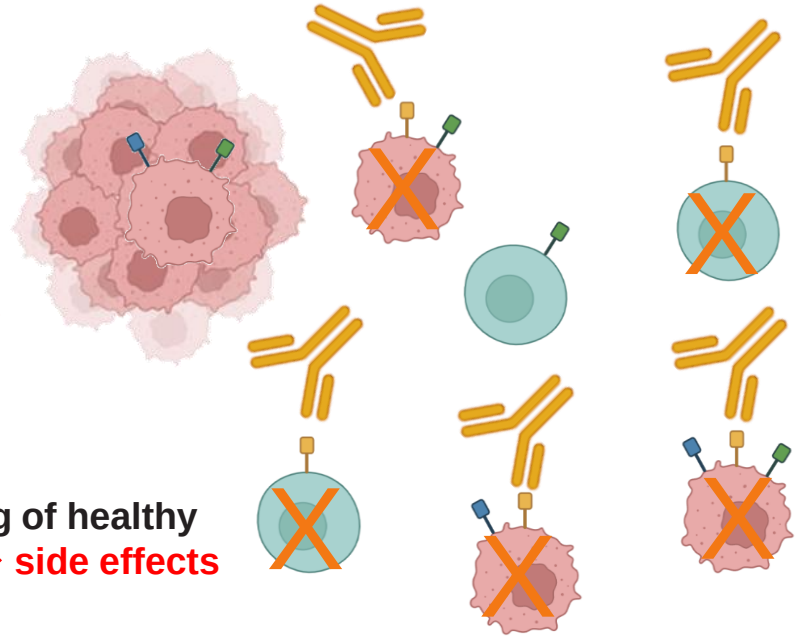
Avidity-guided selectivity for cancer cells in AML



Avidity-guided selectivity for cancer cells in AML

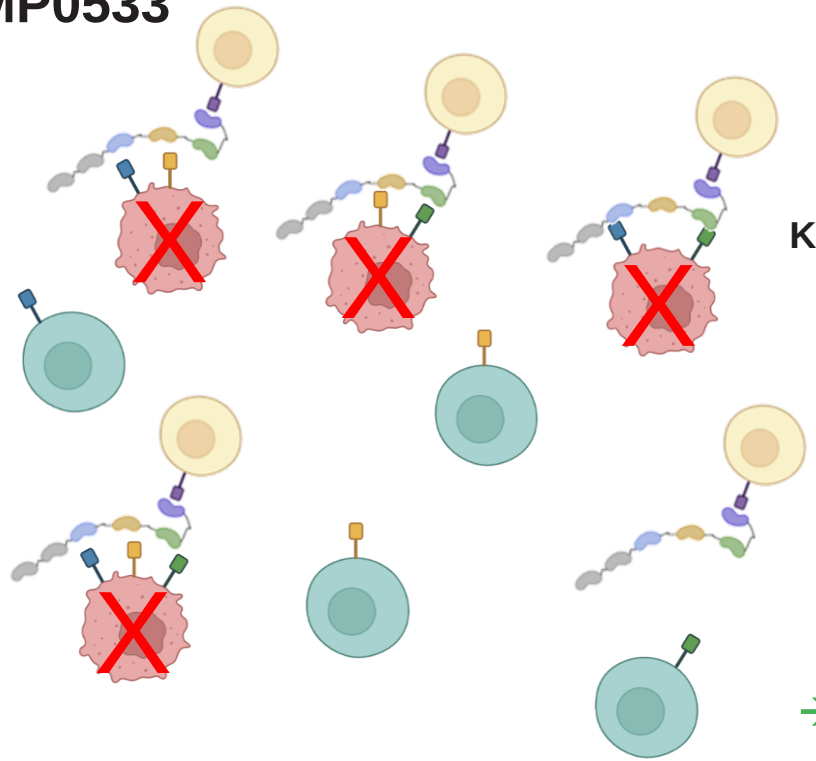
Mono-targeting Agents

Clonal Selection → Relapse



Killing of healthy cells → side effects

MP0533



Killing of AML cells & LSC despite heterogeneity → long-term disease control

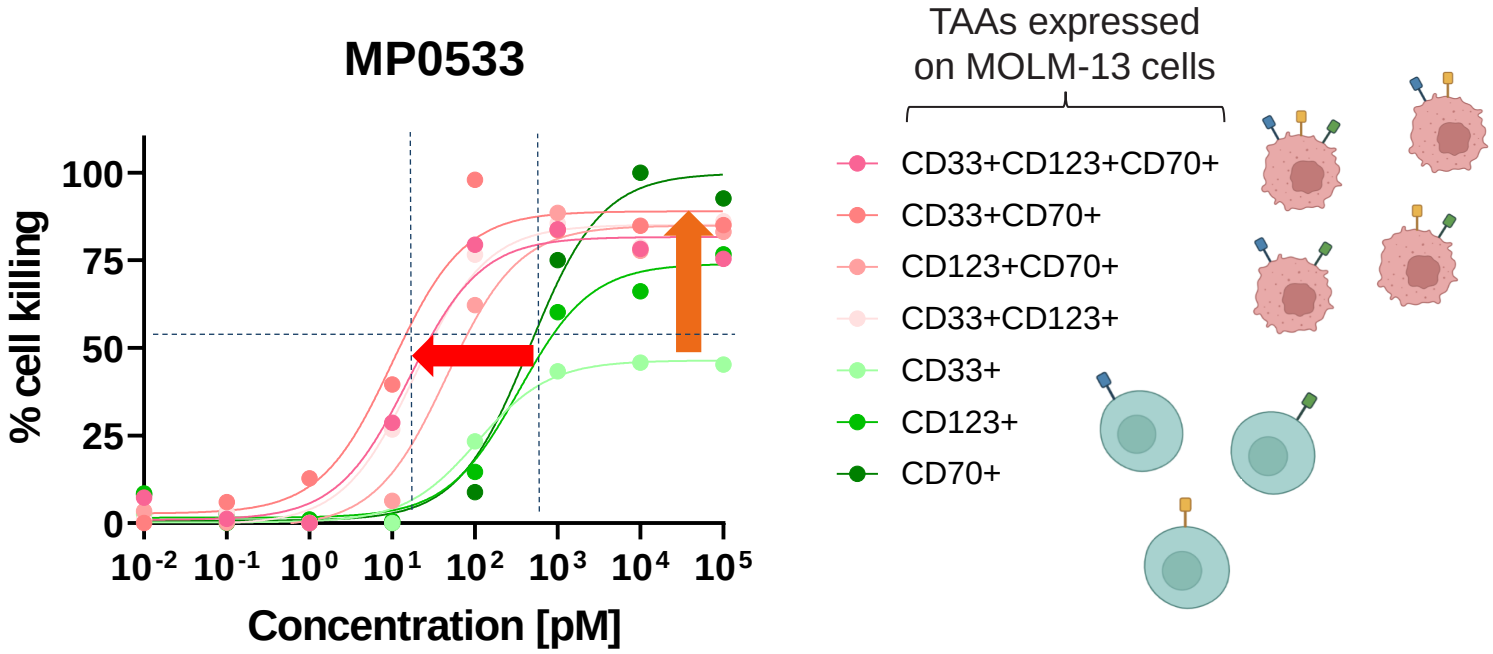
Preservation of healthy cells → therapeutic window

Healthy cell

CD33
CD123
CD70

AML cell/ LSC

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



MOLM-13 cells WT
or KO for CD70, CD33 and/or CD123
+ Healthy donor T cells (E:T = 5:1)

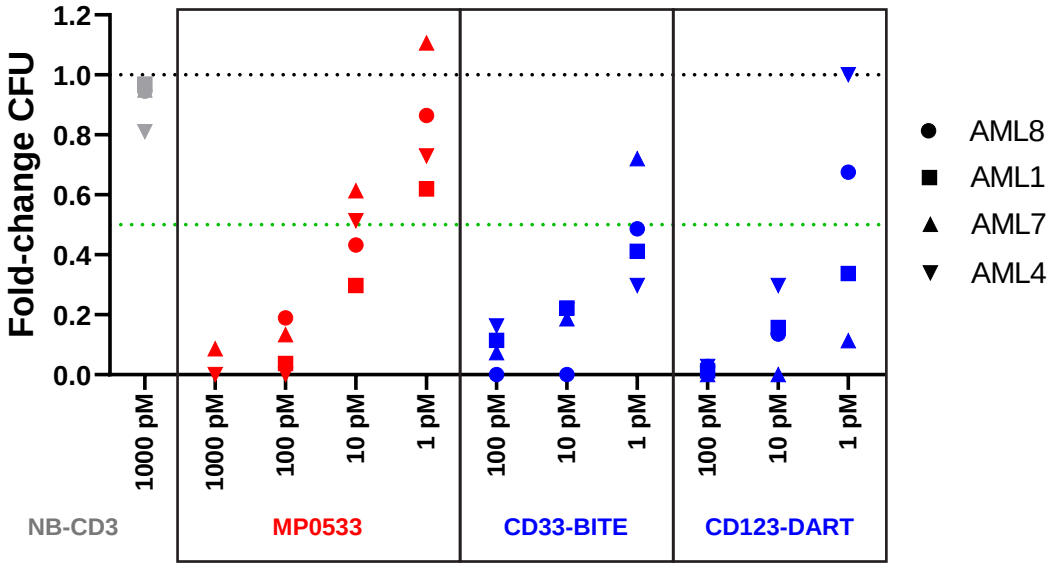
MP0533 or controls

48 hours

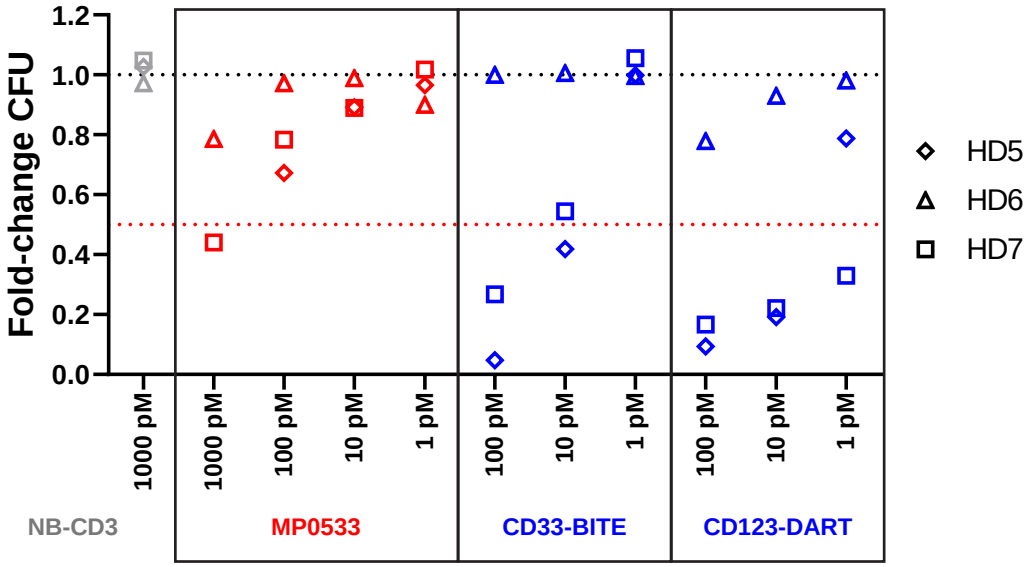
Tumor cell killing
T cell activation

Preclinical data strongly supportive of target profile

Allogeneic killing of **AML CD34+ LSC**



Allogeneic killing of **healthy donor CD34+ HSC**



Efficacy

Safety

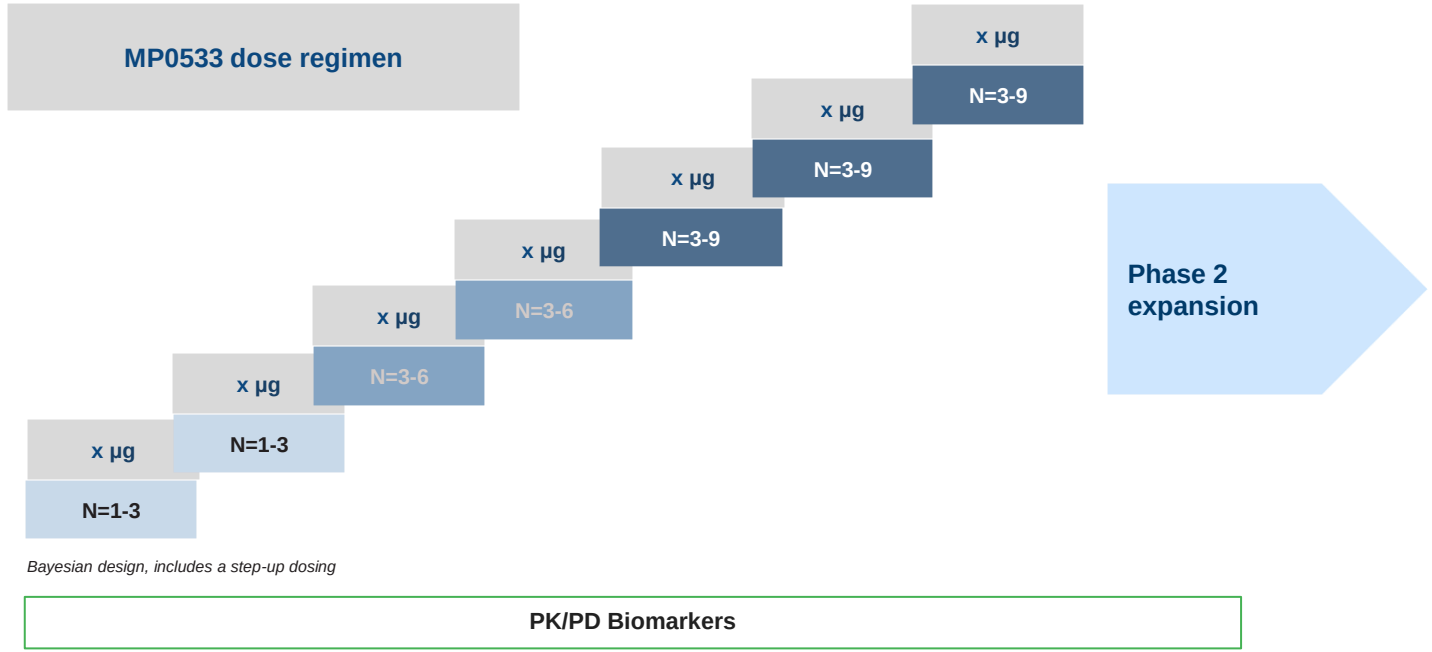
As presented at ASH 2022

Phase I Dose Escalation Trial in R/R AML patients

Patient population: **AML or MDS/AML relapsed/refractory** to HMA, induction CT or allogenic HSCT
N= 20-45 patients

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

Centers: 5 sites at initiation (Switzerland/ The Netherlands)



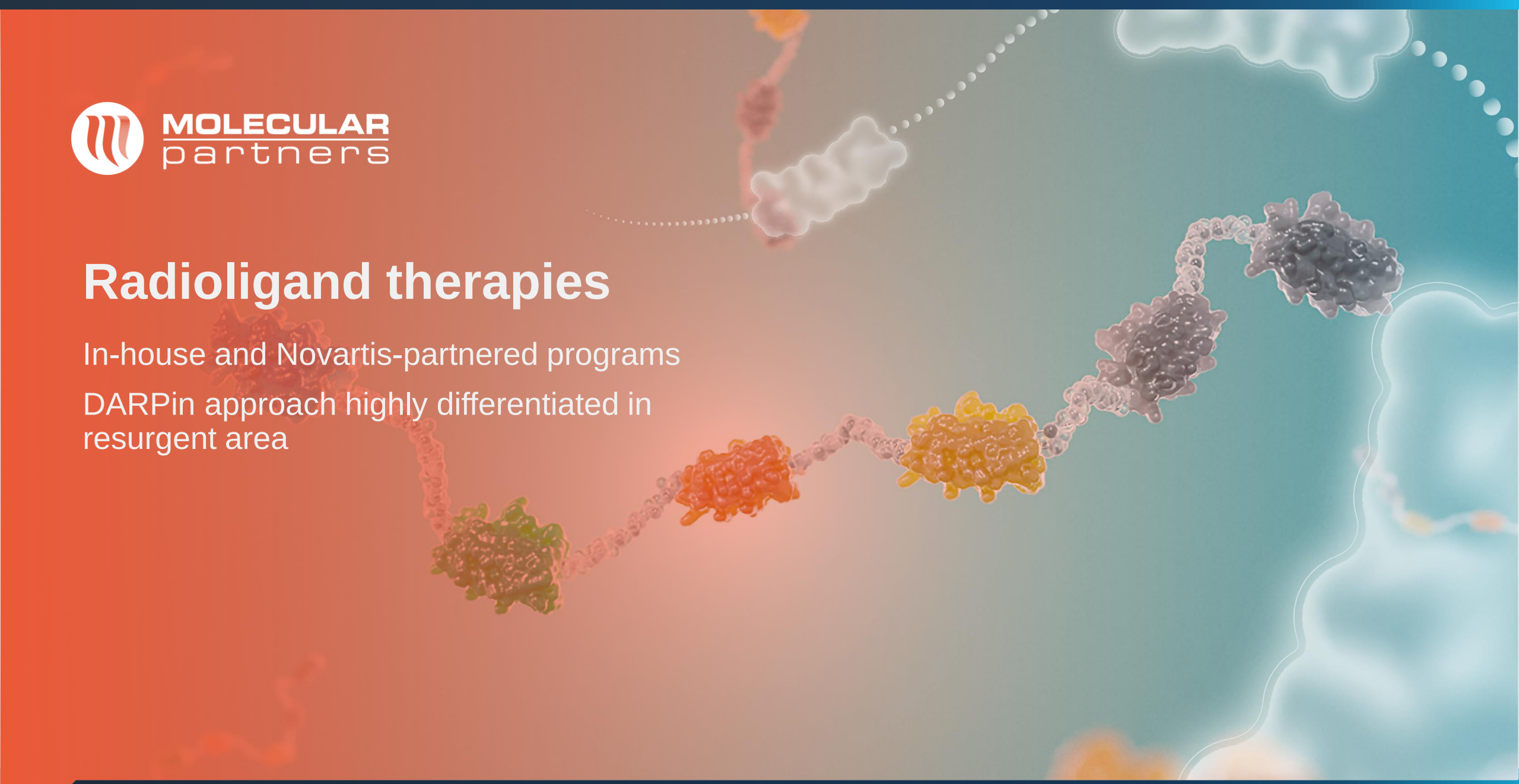
Study Open and Recruiting

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

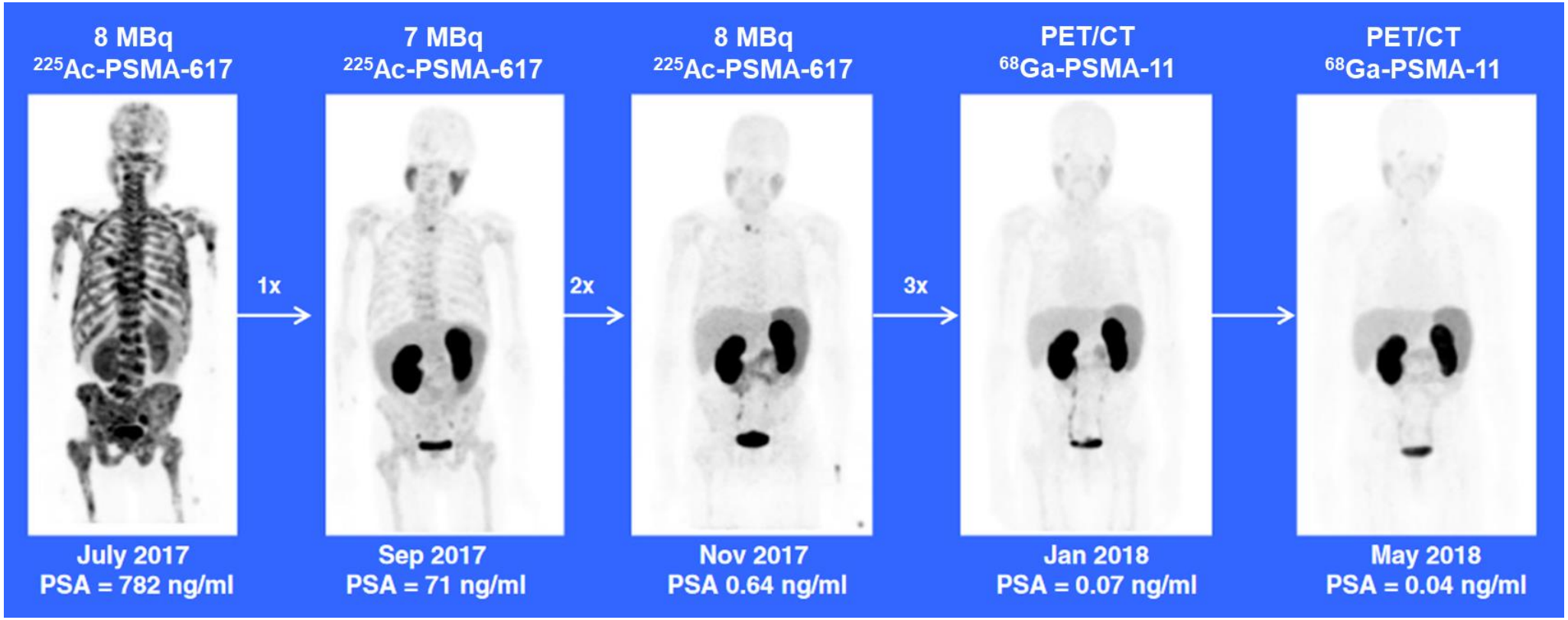
Radioligand therapies

In-house and Novartis-partnered programs

DARPin approach highly differentiated in resurgent area



The Anti-Cancer Potential of Radioligand Therapy (RLT)

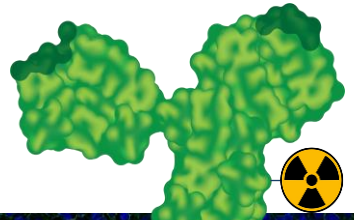


Example: Treatment of a naïve prostate cancer patient with extensive bone metastasis at primary diagnosis with ^{225}Ac-PSMA-617
→ Complete remission after 3 cycles of treatment (symptom free at 11-month follow up)

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

Small Size Leading to Deep & Even Tumor Penetration

Even tumor penetration: In-vivo mouse model, IHC analysis 4 hours after equimolar injection



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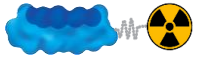
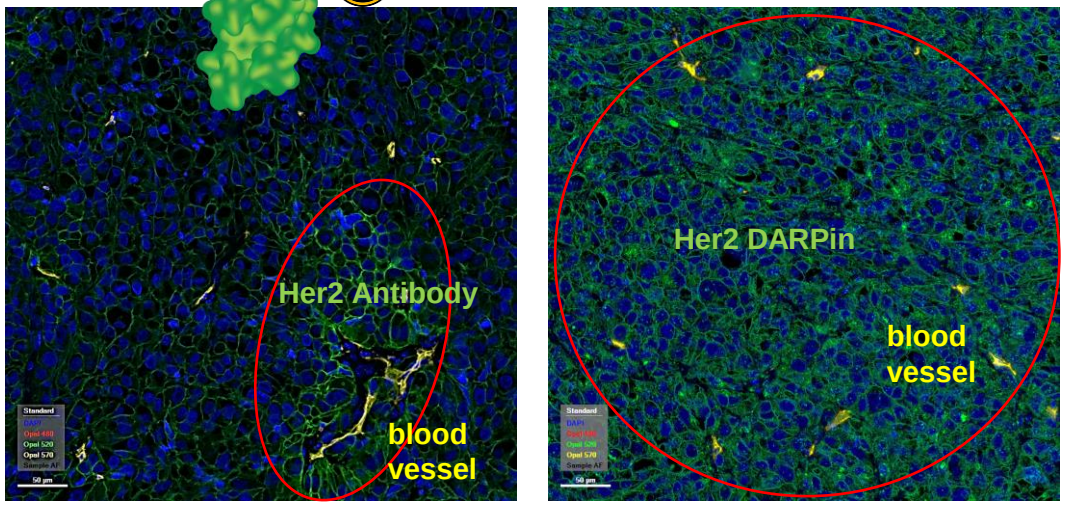
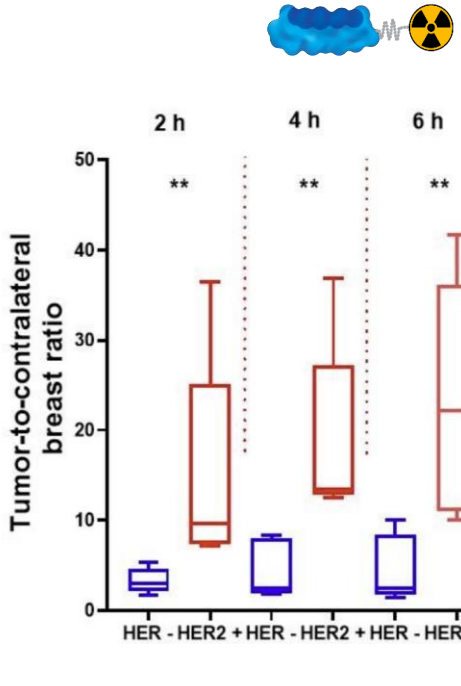
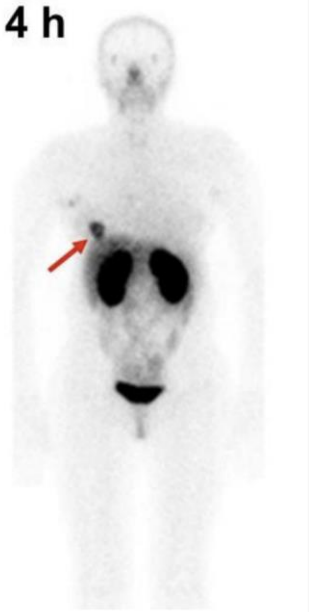




DAPI (Nucleus) / Trastuzumab or DARPin / CD31 (Vasculature)

Tumor exposure in humans: Phase I trial of ^{99m}Tc-Her2-DARPin for imaging of HER2 expression in breast cancer

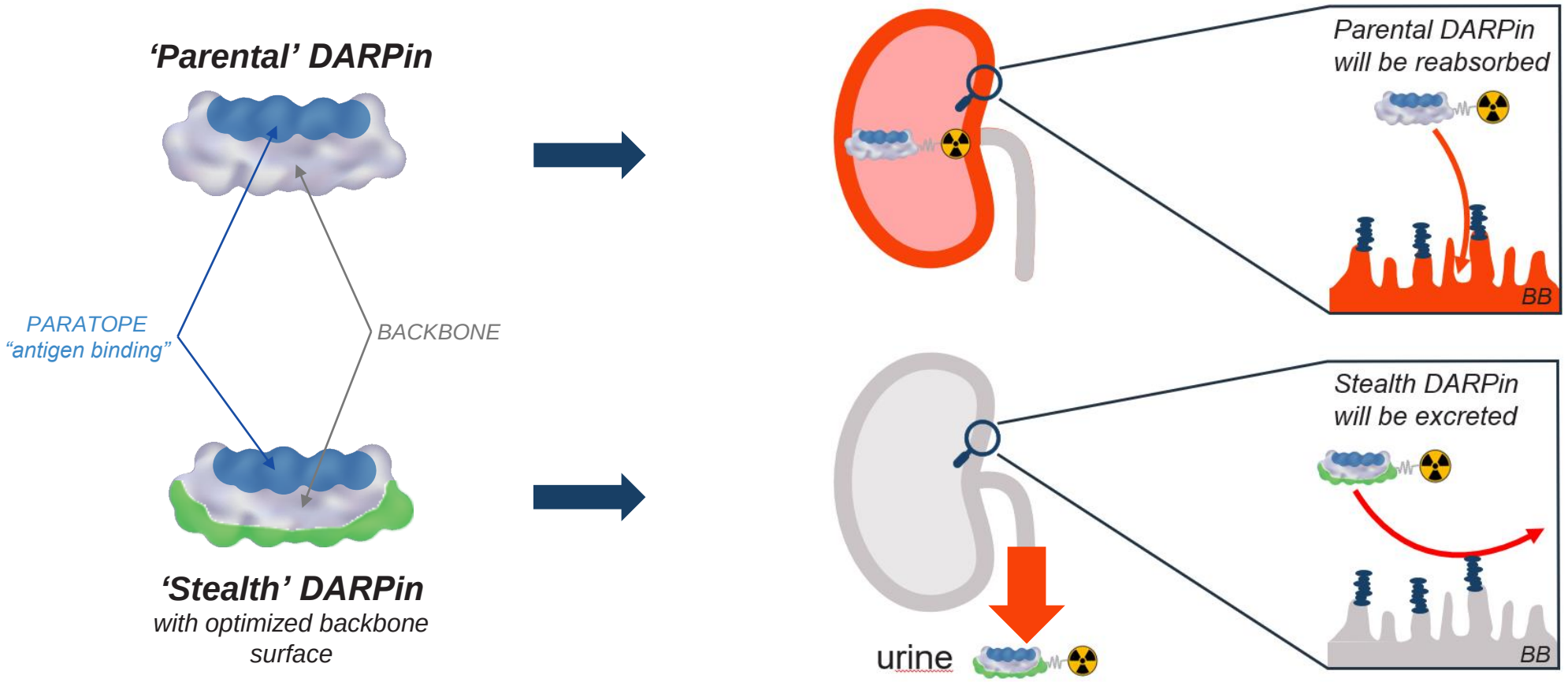




Bragina et al, Journal of Nuclear Medicine, 2021

Solution to Avoid Kidney Accumulation of Radio-DARPin-Therapeutics

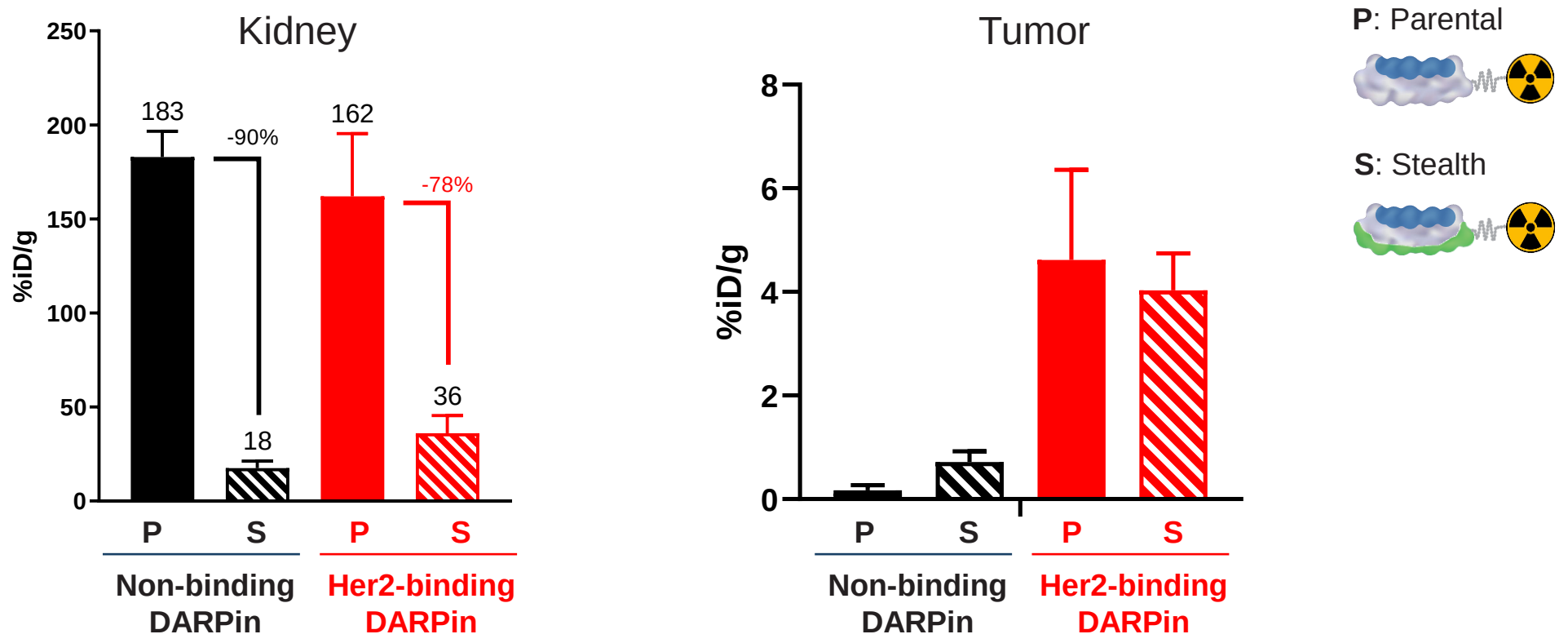
Optimizing the backbone surface greatly increases DARPin excretion over reabsorption in the kidney



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

Stealth DARPin Shows Strongly Reduced Kidney Accumulation and Maintained Tumor Uptake of Radioactivity

Up to 90% reduction in kidney accumulation and maintained ~4% tumor uptake:
In-vivo mouse model, ^{111}In, 4 hours after injection



Stealth DARPin Has no Accumulation of Radioactivity in Other Organs

No significant accumulation in any other organs:
In-vivo mouse model, ^{111}In, 4 hours after injection

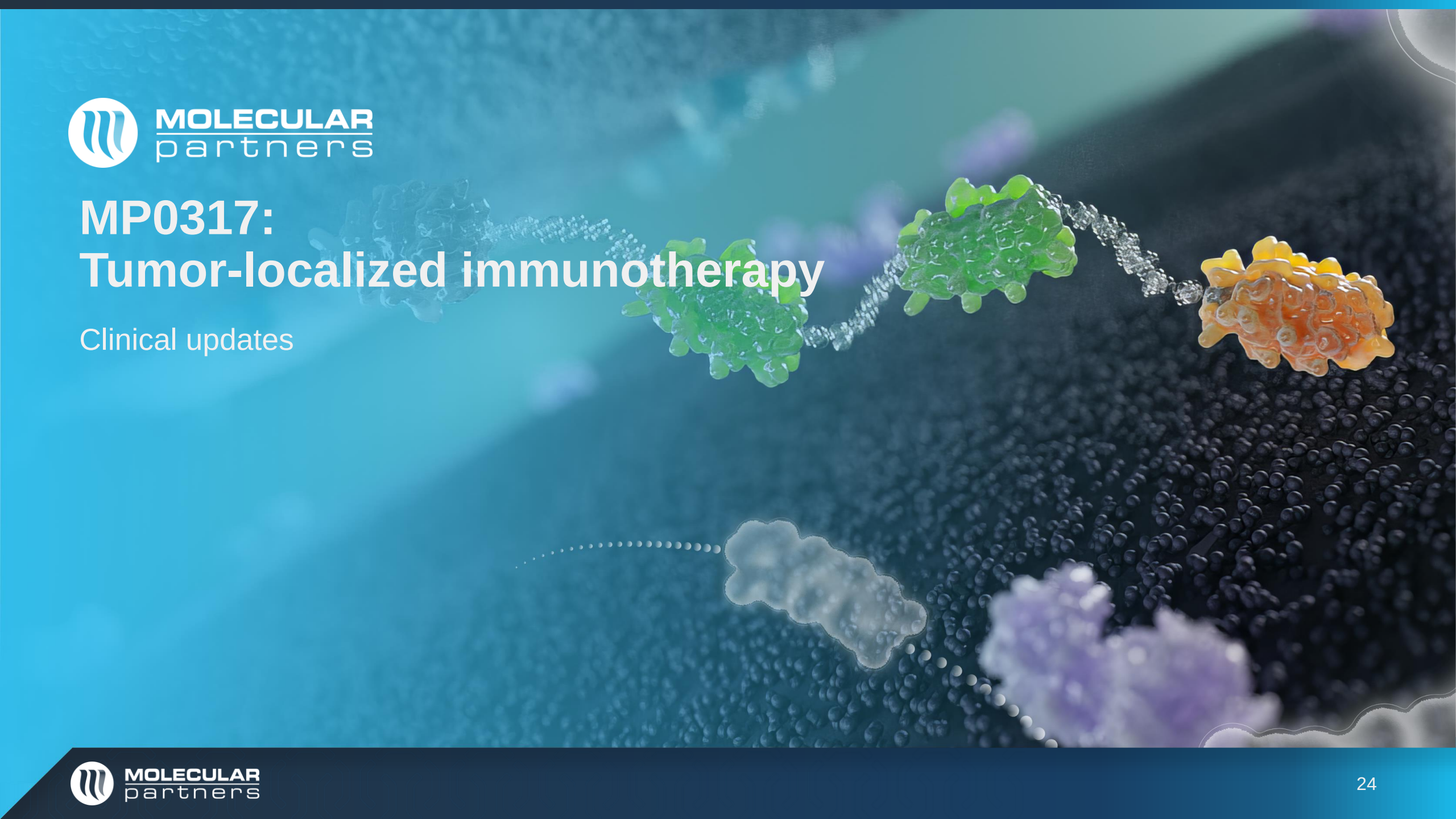
Radio-DARPin-Therapeutics (RDT) Pipeline

Novartis Collaboration on RDTs

- Collaboration with a leader in the RLT field
- Exclusive for two tumor antigens

Molecular Partners portfolio

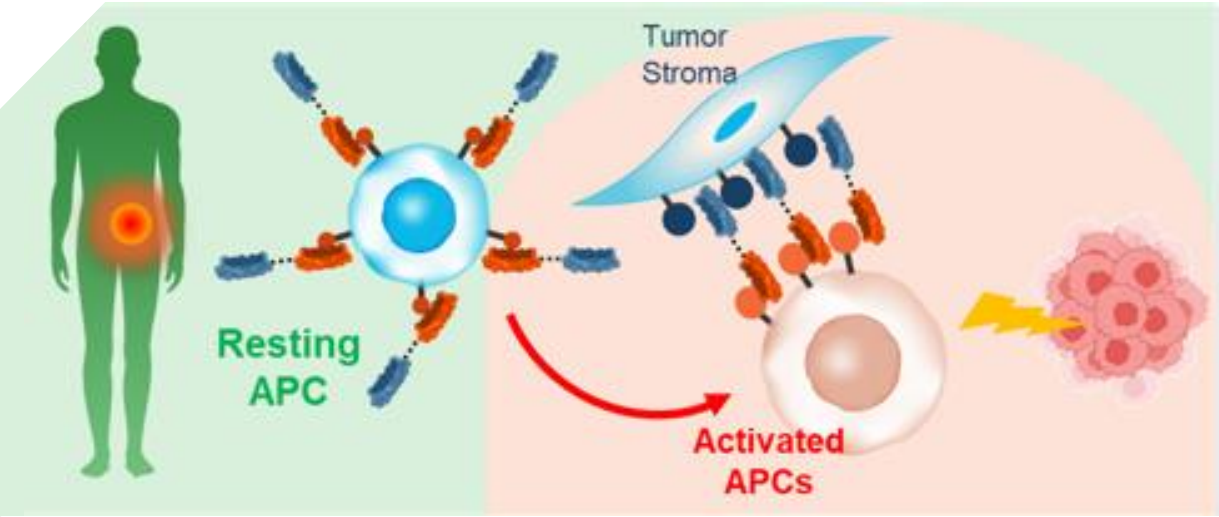
- DLL3 selected as 1st in-house target for RDT
- 2nd target ongoing and further targets in evaluation
- Ongoing discussions with radionuclide providers

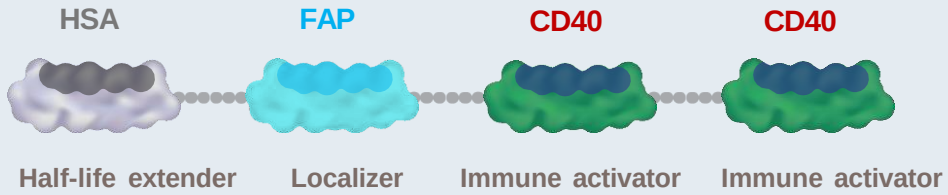


MP0317: Tumor-localized immunotherapy

Clinical updates

MP0317: A Phase 1 Localized CD40 Agonist



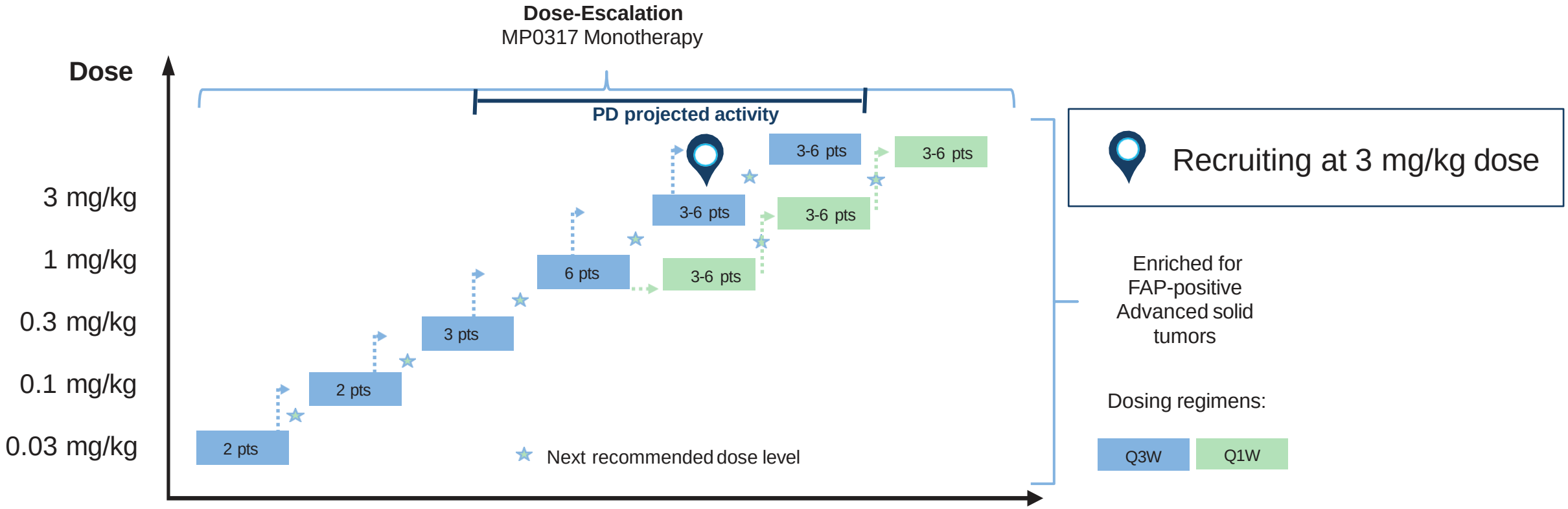


FAP: Expressed on fibroblasts in tumor stroma, local cluster

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**:
  - **Q1 23**: PD markers from paired biopsies to demonstrate tumor local immune cell activation
  - **H1 23**: Partnering for combination trials

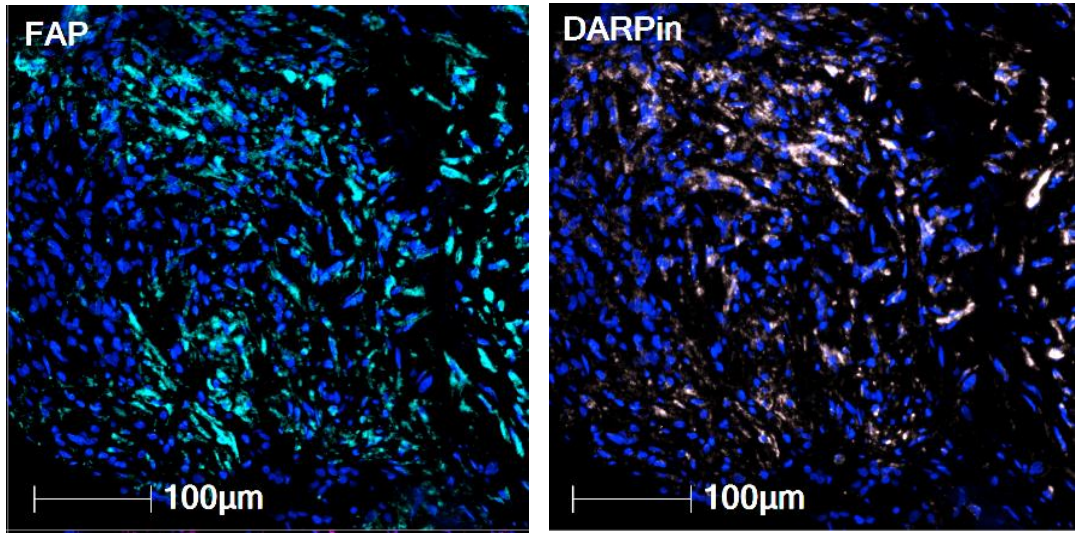
MP0317-CP101 Clinical Trial Update



- Dose escalation ongoing at 3 mg/kg – 2nd to highest dose
- No dose-limiting toxicities to date
- Expected PD activity from 0.3 to 1 mg/kg
- Dosing regimen flexibility

MP0317 Co-localizes and Occupies FAP in Tumor

MP0317 and FAP co-localize in tumor

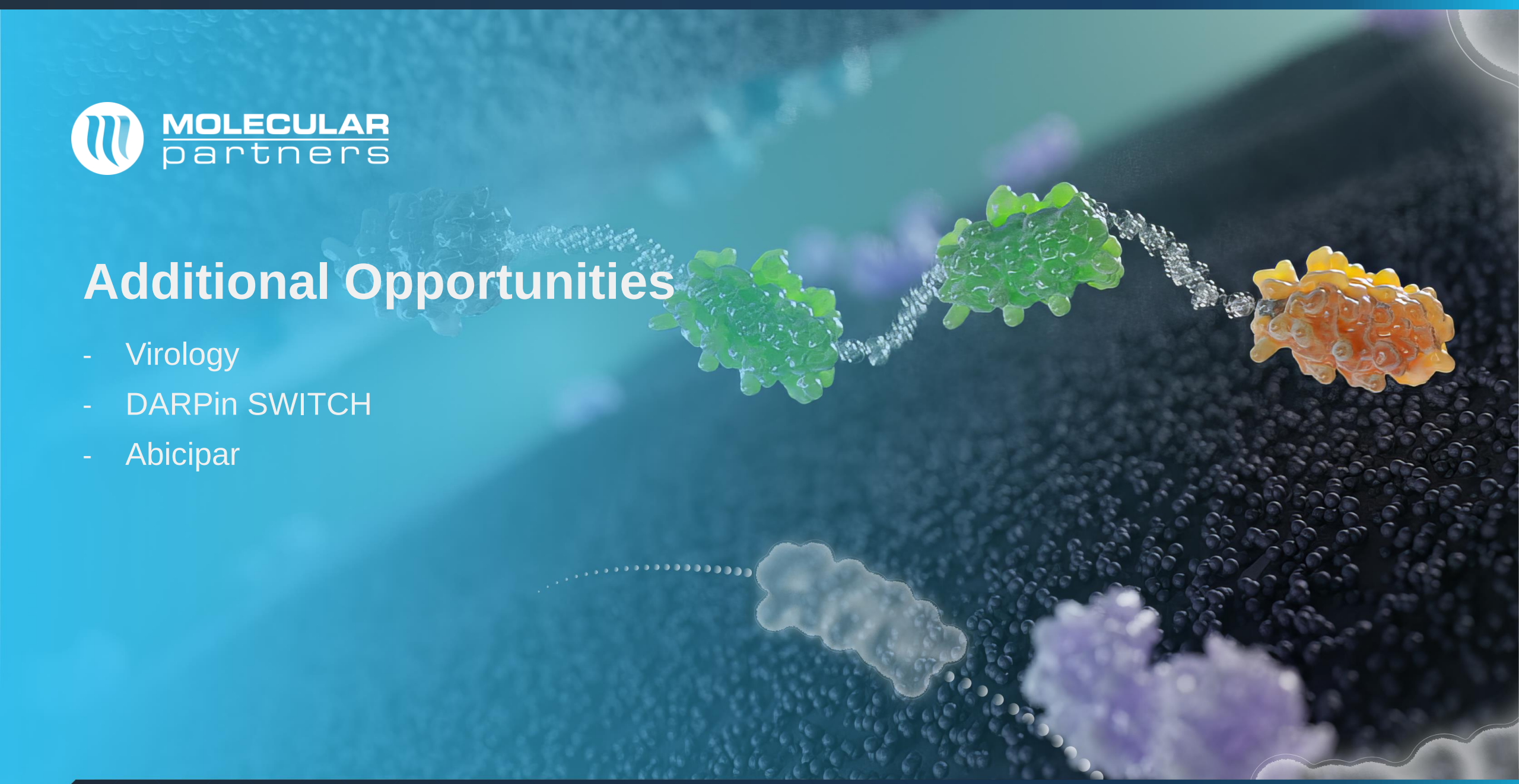


DAPI MP0317 FAP

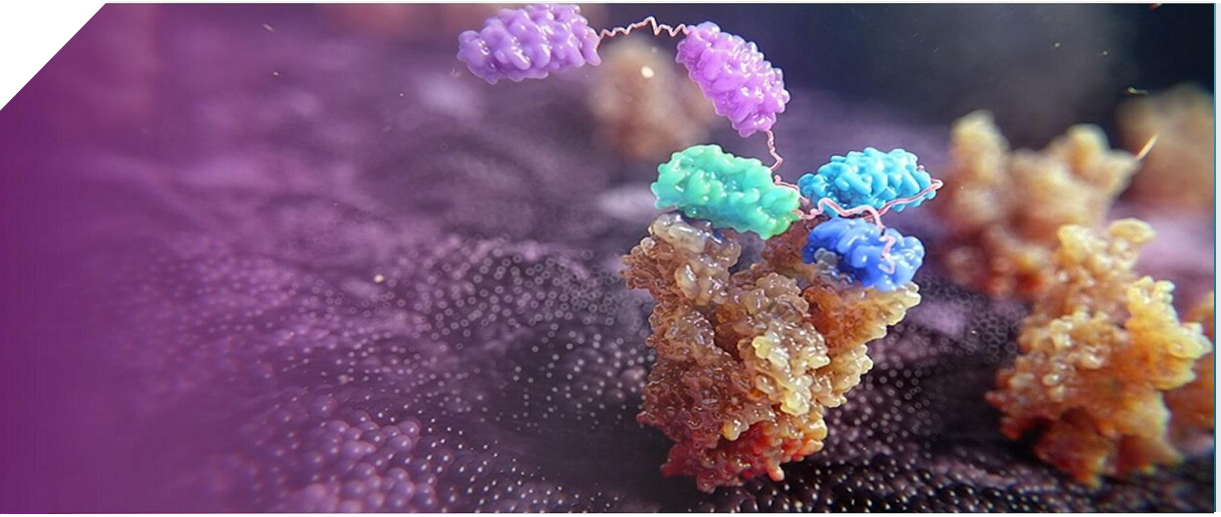
- Representative multiplex-immunofluorescence for subject 03-003, a cervical cancer patient dosed at 0.3 mg/kg
- 26 % of FAP is occupied by MP0317
- Tumor biopsy specimen

Additional Opportunities

- Virology
- DARPin SWITCH
- Abicipar



Ensovibep: Our First Antiviral Delivered Clinical Success

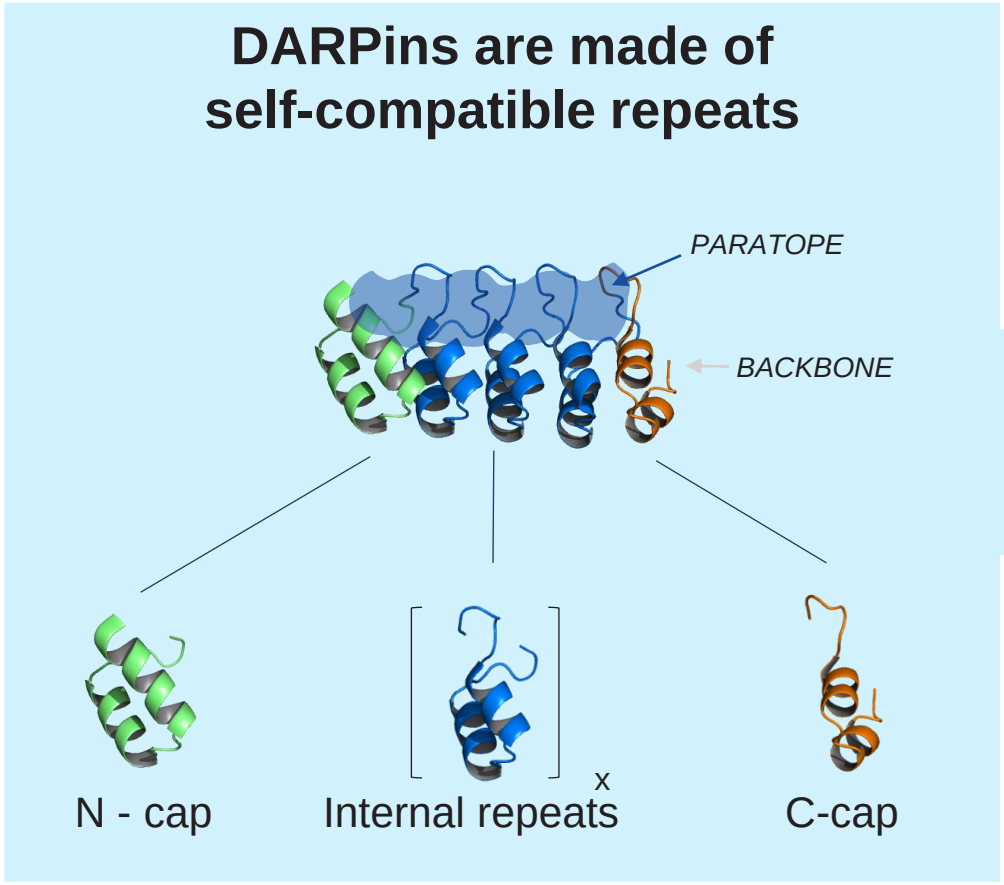


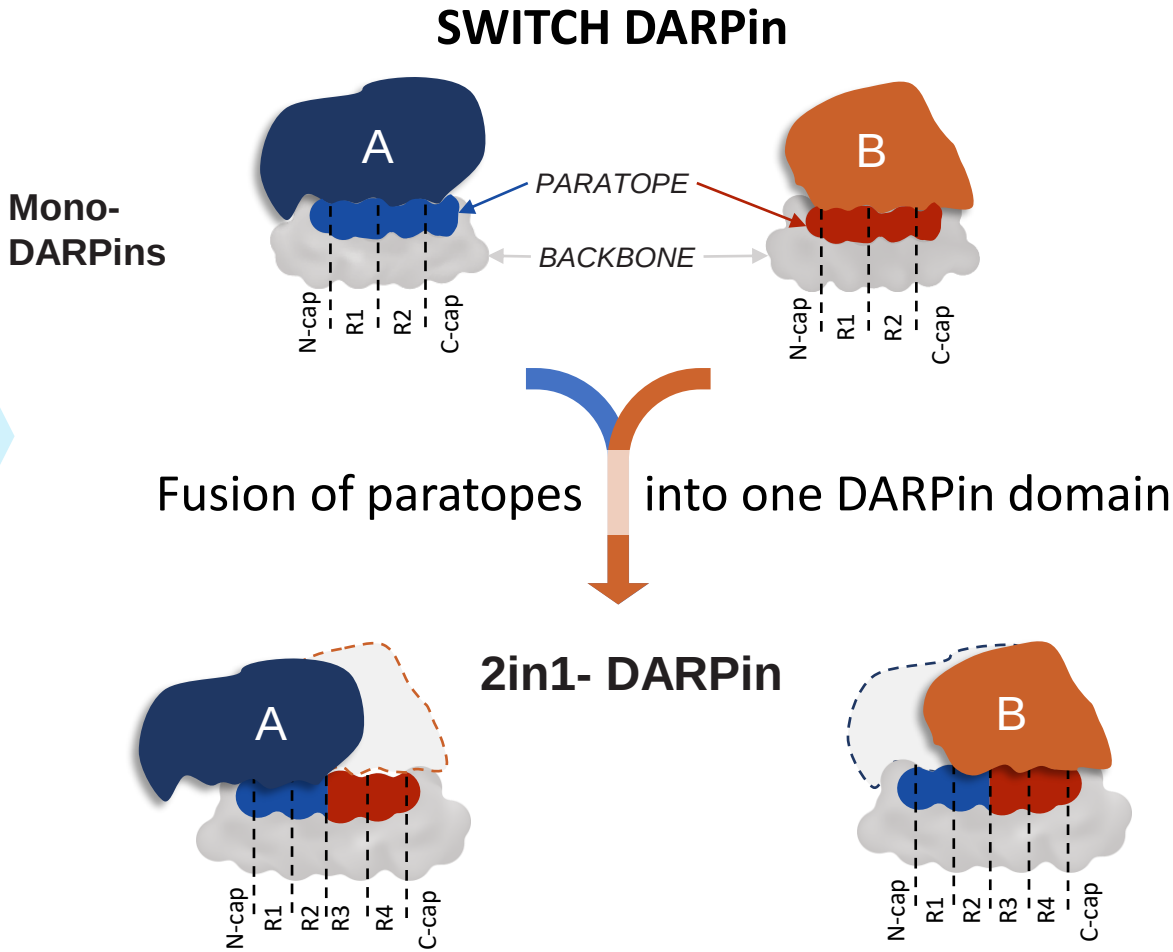
COVID-19 spike protein binders: Binding three separate sites on the viral spike protein simultaneously for enhanced activity relative to mono-binders (e.g. antibodies)

- **Candidate design goal**: Trispecific COVID-19 DARPin to provide deep neutralizing, resistant to viral evolution
- **Outcome**: Successful global clinical study EMPATHY which enrolled 407 patients: Efficacy (~80 % reduction of hospitalization)
- **Status**: Licensed to Novartis. Presently not in clinical development
- **Outlook**: Potential collaboration with Novartis under discussion to fight viruses with global need for new treatments

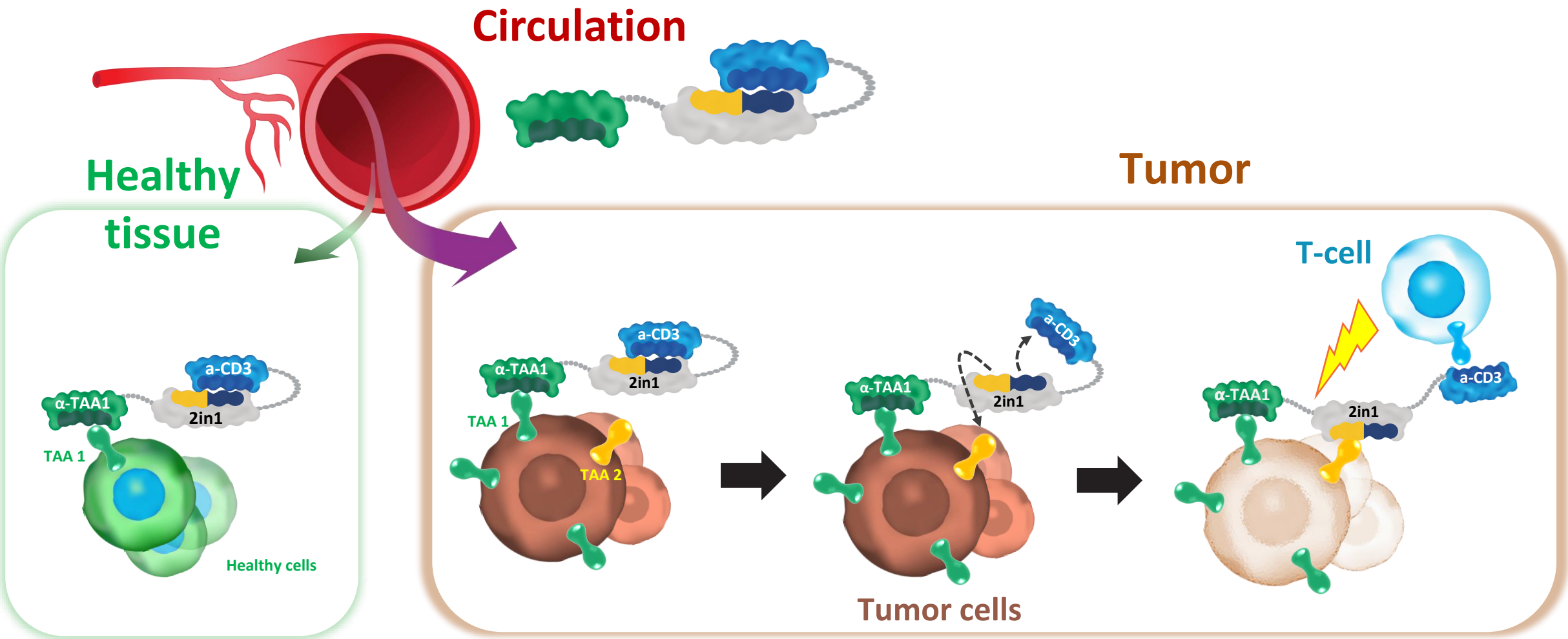
SWITCH DARPin

Binding Two different Targets with One DARPin in an Exclusive Way





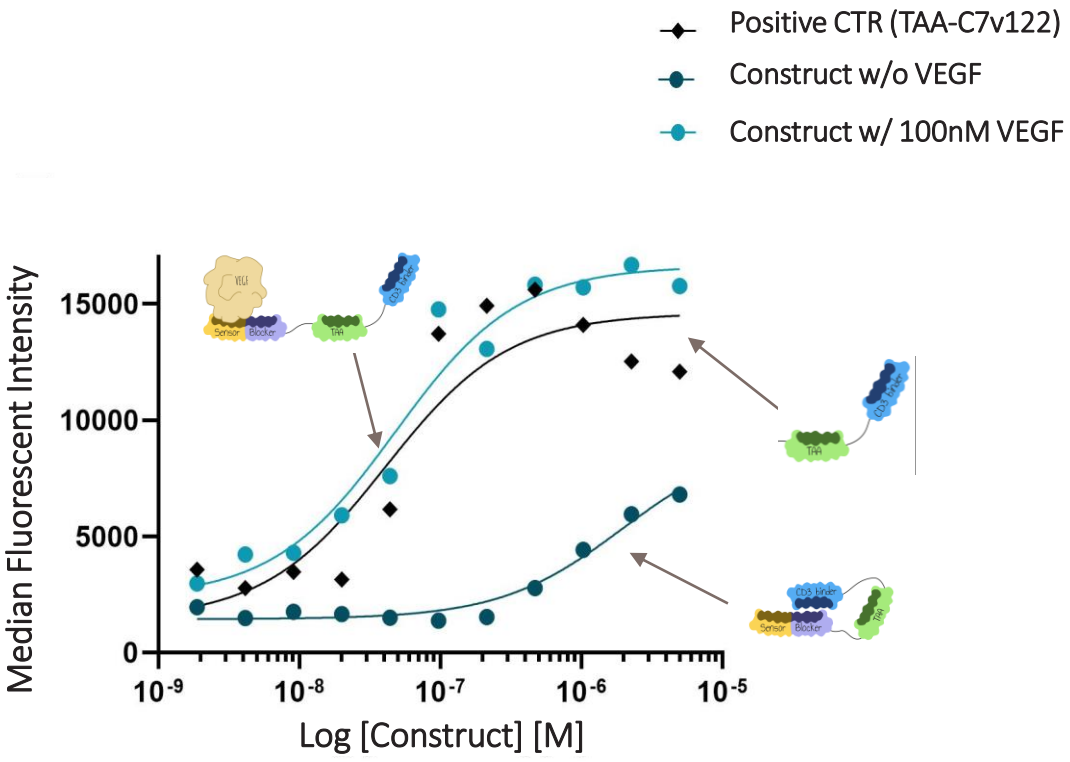
SWITCH DARPins: “Smart Biologics” of Potent Effectors



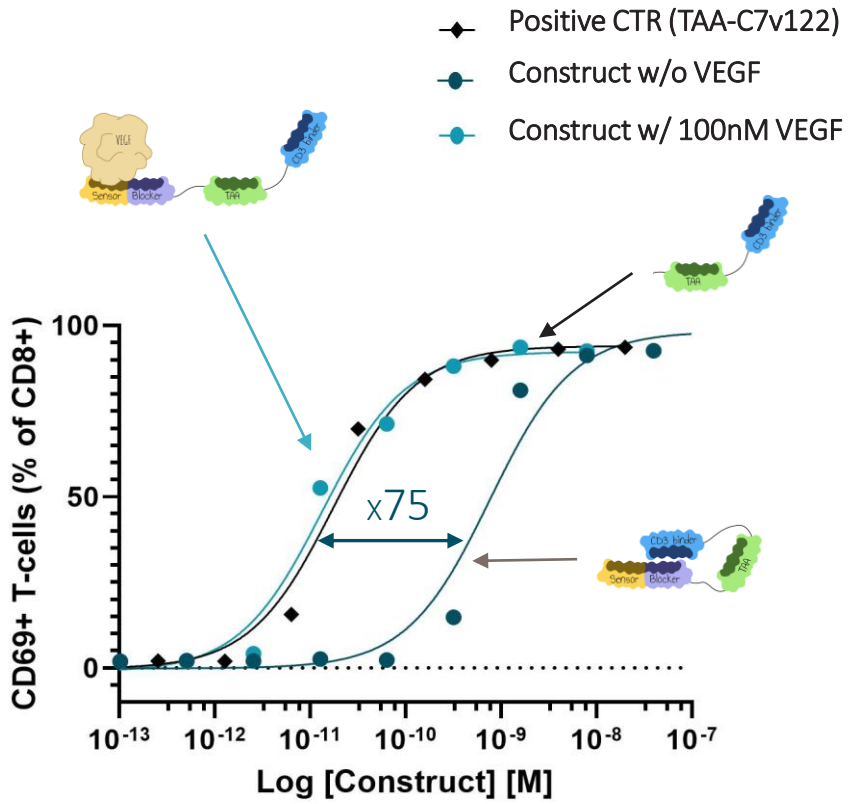
***TME**: tumor microenvironment; **TAA**: tumor-associated antigen*

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

T-cell binding



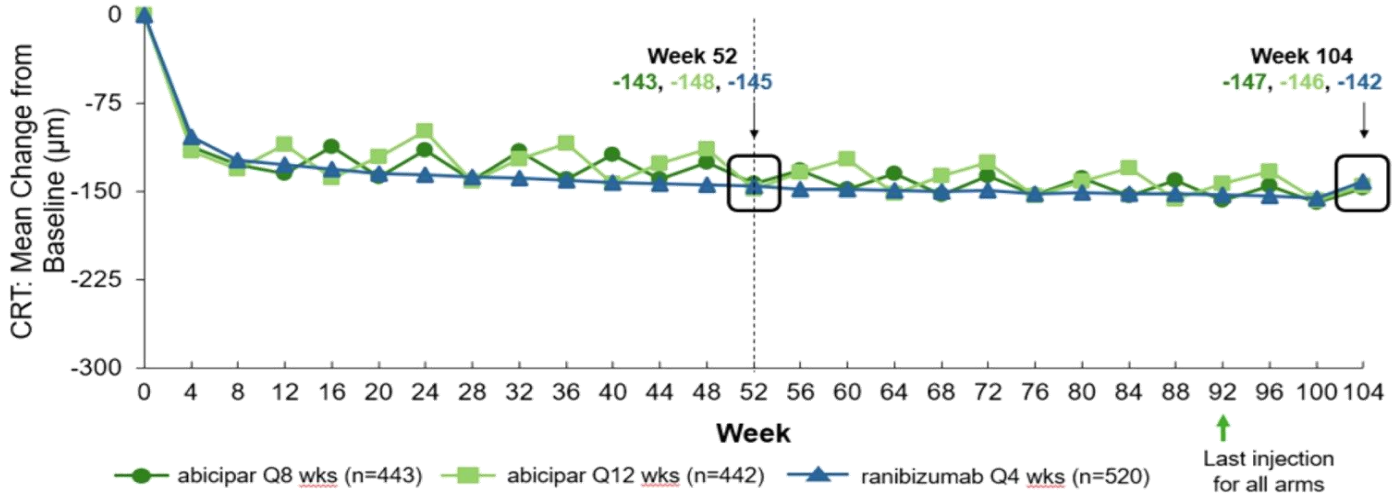
T-cell activation



Abicipar: Efficacy met in 2 P3 trial – CRL on inflammation

Secondary Endpoint: Mean Change in CRT From Baseline at Weeks 52 and 104

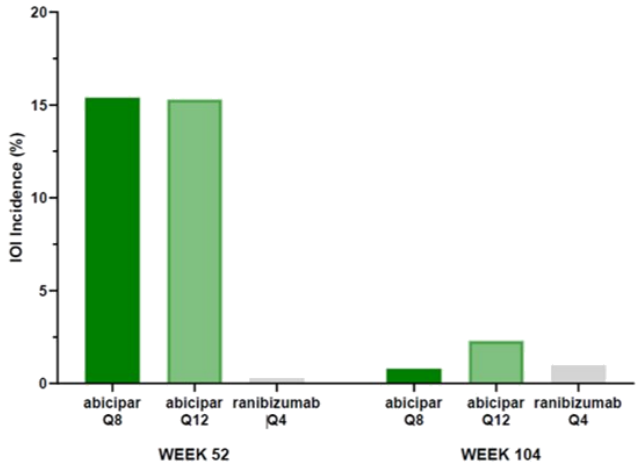
Phase III CEDAR & SEQUOIA



CRT improvement after initial doses were maintained to Week 104 with quarterly abicipar injections (10) vs. monthly ranibizumab injections (25)

CRT = central retinal thickness

Intra Ocular Inflammation in CEDAR/SEQUOIA (Phase 3)

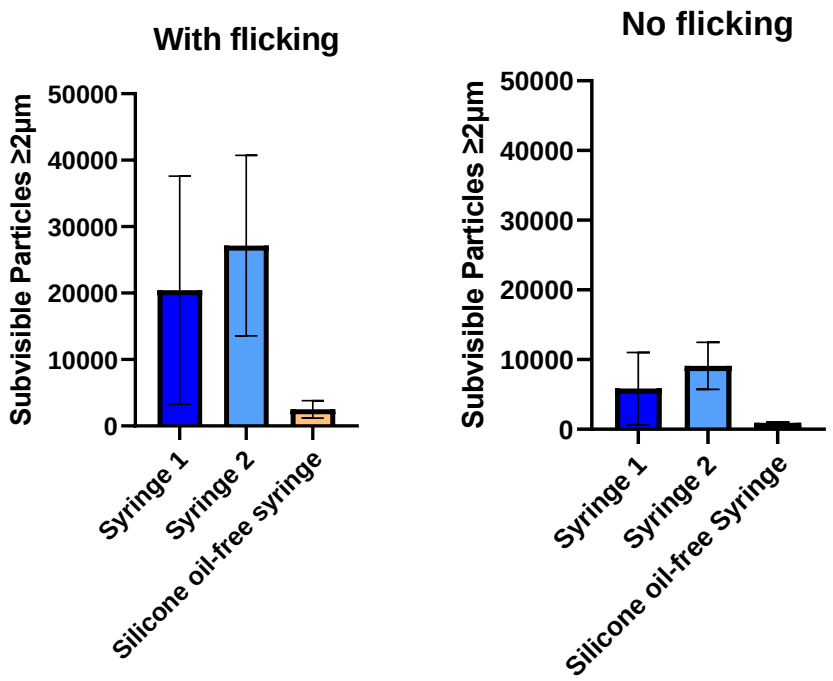


Abicipar is under investigation and the safety and efficacy of this product have not been established.

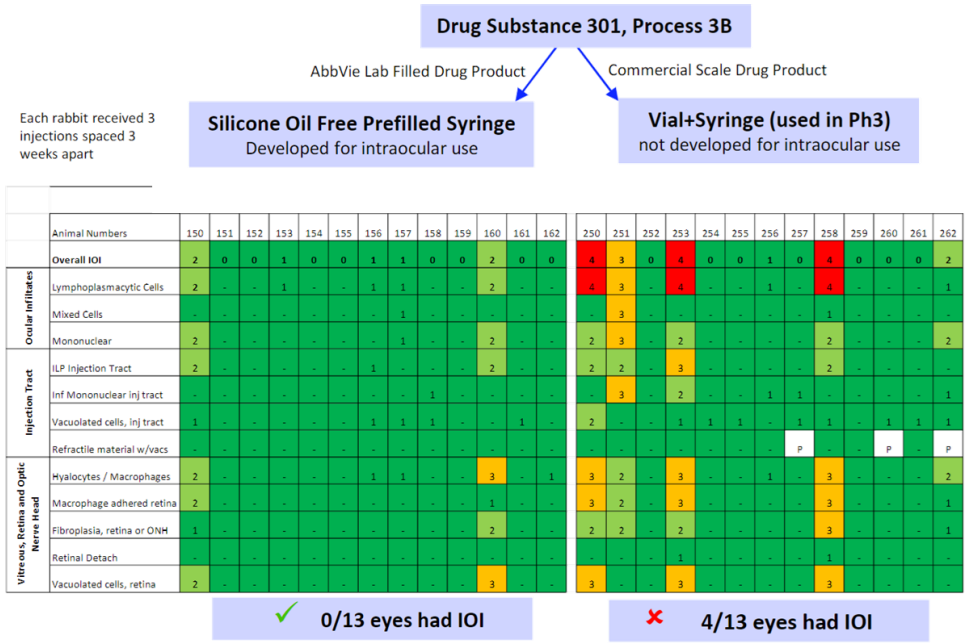
1. Khurana RN, et al. Presented at AAO 2019 Annual Meeting in San Francisco, CA, USA; Oct 12-15, 2019.

Subvisible particles (SVPs) depend on syringe type & handling

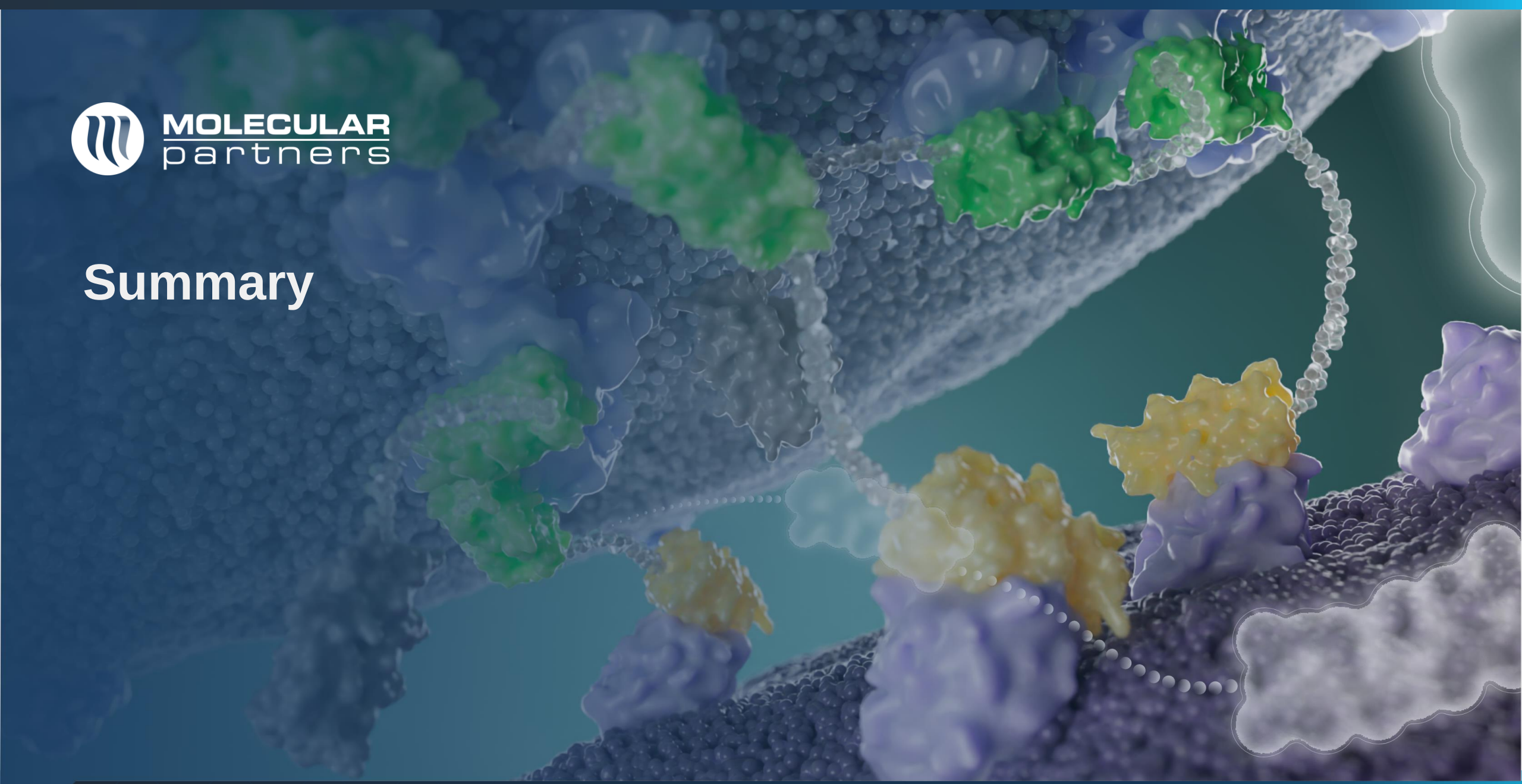
Silicone oil effect on sub-visible particles



Silicone oil effect on IOI in rabbit study

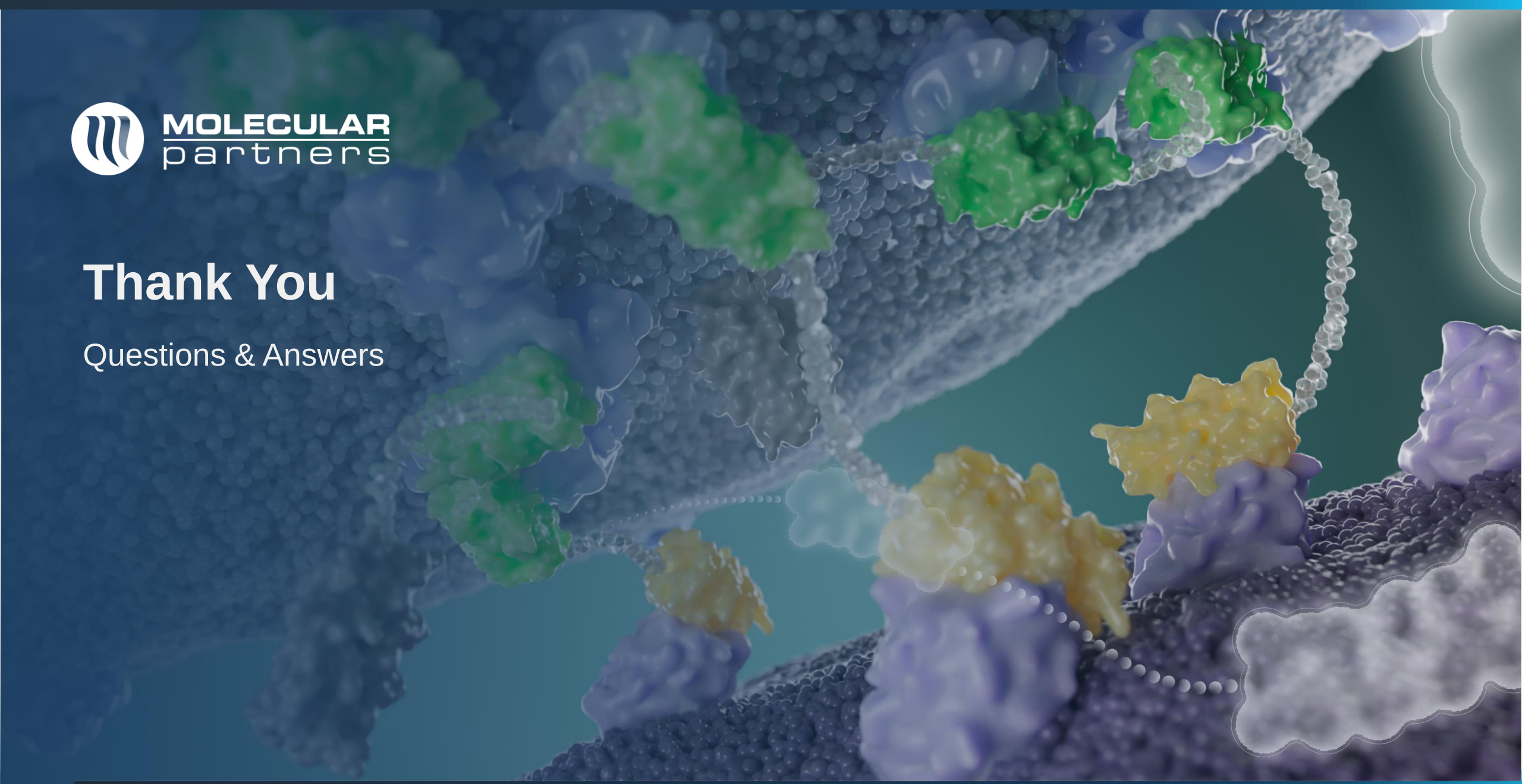


Summary



Summary

DARPin ADVANTAGES	• Our engine is a **rapid, versatile and validated source** of unique solutions for patients • DARPins allow **complex & differentiated multispecific drug candidates (AML DARPin)** • **Small size, high affinity and "stealth engineering"** makes DARPins ideal for **RLT**
PIPELINE OUTLOOK	• First clinical data from **MP0533** in **AML** expected in 2023 • Preclinical data from **RLT programs** – Candidate Selection on DLL3 expected in 2023 • **I/O partnering opportunity** for MP0317 – FAPxCD40 • Creation of additional (SWITCH) **DARPin platforms**
CORPORATE	• **Well-capitalized** with cash into 2026 • Multiple opportunities for success via **in-house and partnered efforts** across broad portfolio



Thank You

Questions & Answers