

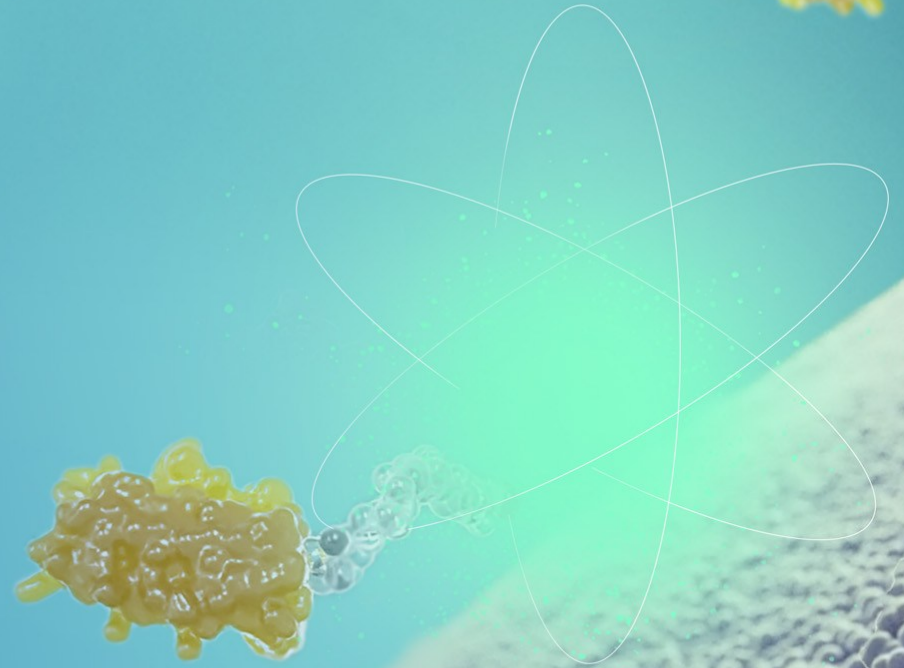


DARPin for Targeted Alpha Therapy

From promising MP0712 first in-human data to opportunities for next Radio-DARPin candidates

RDS Shanghai 2026

Daniel Steiner, PhD



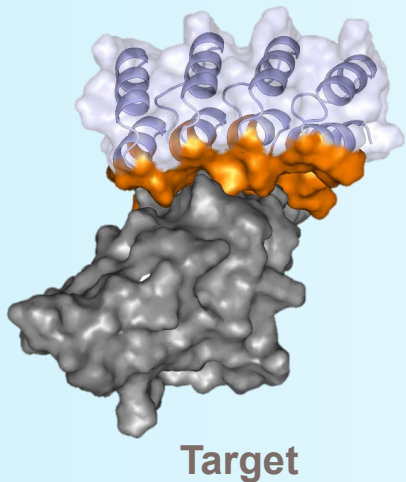
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The DARPin Modality and Our Focus

DARPin
Designed Ankyrin
Repeat Protein



We pioneer DARPins as a new class of therapeutics

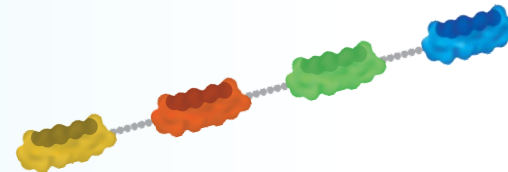
- DARPins close the gap between small molecules and antibodies
- DARPins address complex disease biology (i.e. multi-specifics)
- 8 clinical-stage candidates, > 2500 patients treated

Our company focus

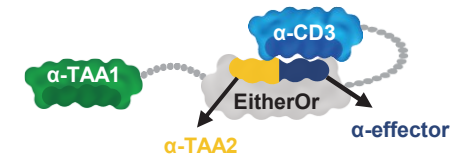
Radio-DARPin
Therapeutics





Multi-specific immune
cell engagers



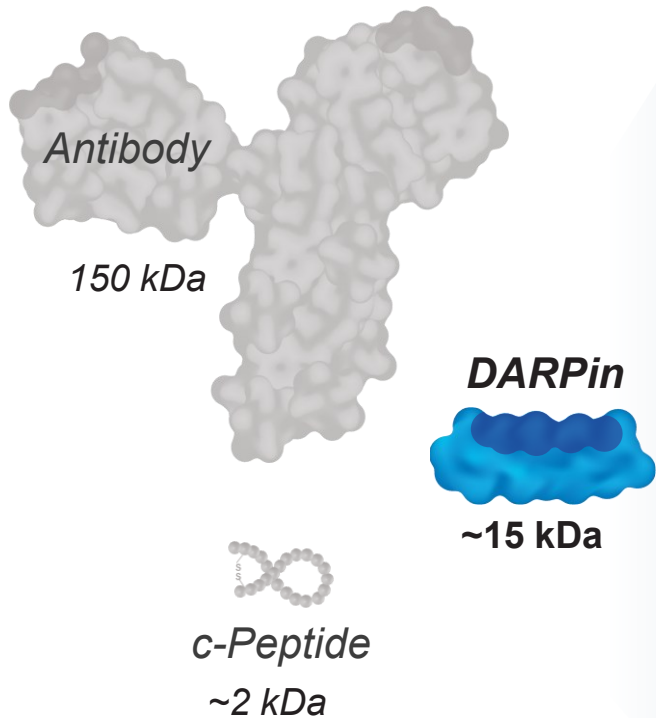
Conditional "Switch"
T cell engagers



Our Pipeline – Differentiated Therapeutics for Patient Value

PLATFORM	CANDIDATE	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	
Radio-DARPin Therapy (RDT)	MP0712	SCLC & NECs <i>²¹²Pb x DLL3</i>		 oranomed Co-development*			
	MP0726	Ovarian Cancer <i>²¹²Pb x MSLN</i>		 oranomed Co-development*			
	Undisclosed Programs (Solid Tumors)	Radio - C					
		Radio - D					
		Radio - E					
		Radio - F					
Next-Gen Immune Cell Engagers	MP0317	Advanced Solid Tumors <i>FAP x CD40</i>					
	MP0533	r/r AML and AML/MDS <i>CD33 x CD123 x CD70 x CD3</i>					
	Switch-DARPin T Cell Engager	<i>CD3 x CD2 x MSLN x EpCAM</i>					

DARPin Features for Tumor Targeting of Radionuclides

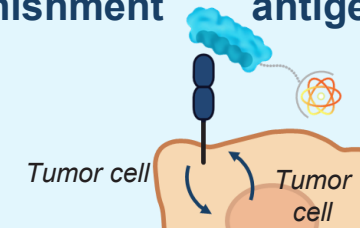


DARPins are small binding proteins derived from natural ankyrin repeat proteins

DARPin key features

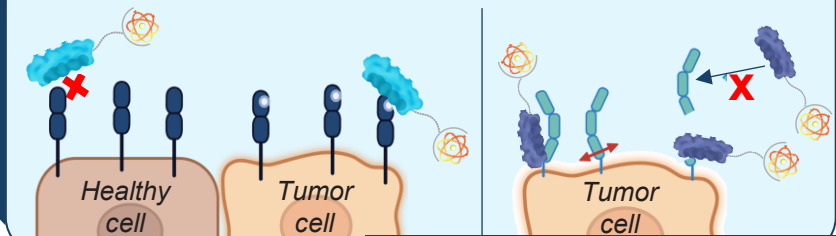
- ✓ **Small size** (~15 kDa)
→ Deep tumor penetration
→ Short systemic half-life
- ✓ **Broad target range** (100's)
→ Opening indications
- ✓ **High affinity** (low pM range)
→ Long tumor retention
- ✓ **High selectivity**
→ Low normal tissue
- ✓ **High stability**
→ Kidney engineering
- ✓ **Clinical Validation**
8 clinical compounds
> 2500 patients treated

Low density – rapid internalization & replenishment antigens



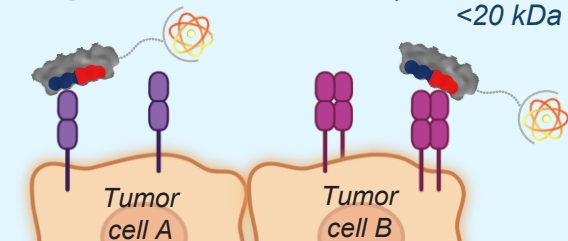
MP0712 (^{212}Pb x DLL3)

High selectivity to tumor antigens



MP0726 (^{212}Pb x MSLN)

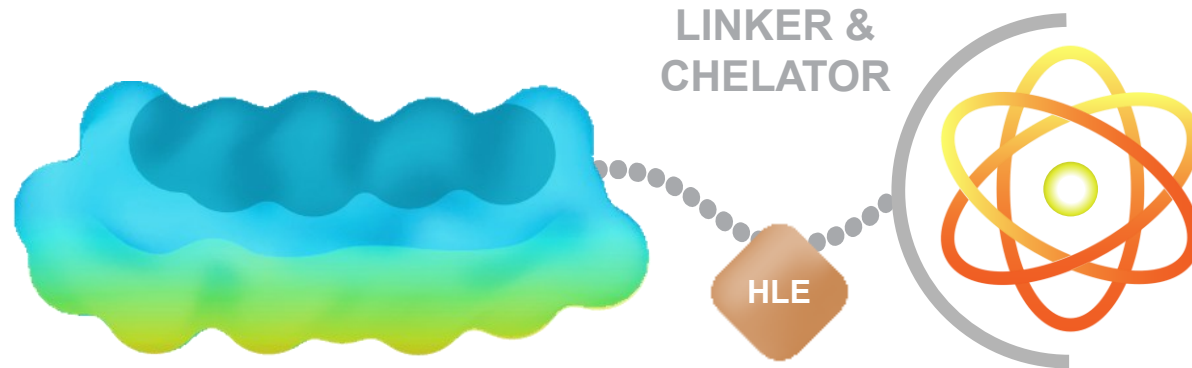
Small bi-specific DARPins (*2in1* DARPin)
<20 kDa



Radio DARPin Platform for Therapeutic Candidates

DARPin: IDEAL VECTOR FOR RADIOPHARMACEUTICALS

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



SURFACE ENGINEERING

- Enabled by high stability
- Reduce kidney accumulation

HALF-LIFE EXTENDER

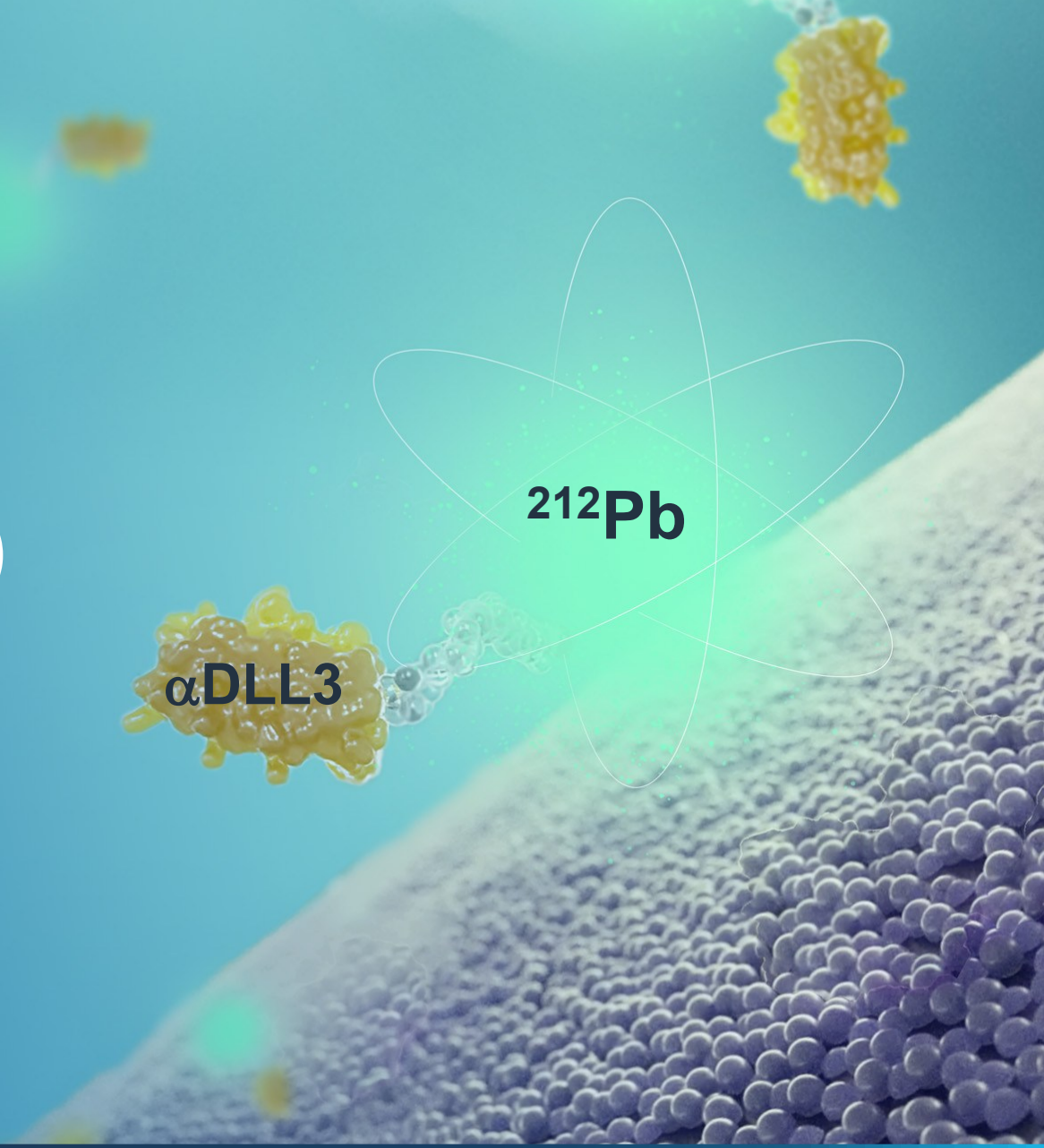
- Tailored systemic exposure
- Promote tumor uptake

ALPHA-EMITTING THERAPEUTIC ISOTOPES

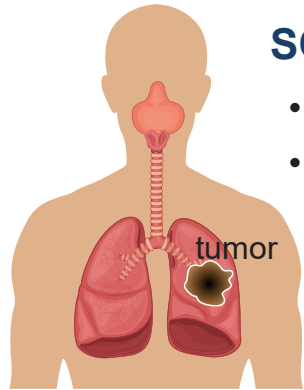
- Proven clinical efficacy
- High energy deposition
- Lead-212 (^{212}Pb)
- Actinium-225 (^{225}Ac)



**Progressing the first Radio-DARPin
Therapeutic MP0712 (^{212}Pb x DLL3)
for SCLC into the clinic**



MP0712: Why DLL3-Targeting Radiotherapy for SCLC?



SCLC: critical unmet need (2L)

- mPFS: ~3 months^{1,2}
- 5-year OS: ~3%^{1,2}

DLL3: validated target

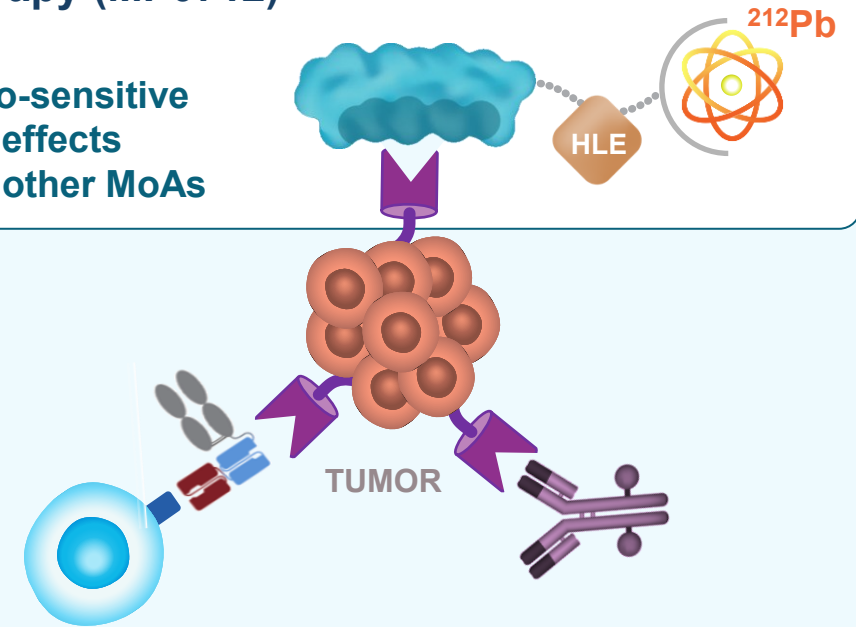


DLL3

- Expressed in >85% of patients with SCLC³
- Expression in multiple neuroendocrine cancers (e.g., LC, Bladder, GEP)
- No expression in healthy tissues
- Tumor-targeting shown with DLL3 radio-diagnostic mAb (⁸⁹Zr-Sc16.56)^{4,5}
- Clinical validation by T cell engagers (e.g., tarlatamab)⁶ and ADCs (e.g., ZL-1310)⁷

Targeted radiotherapy (MP0712)

- Phase 0/1
- **SCLC highly radio-sensitive**
- **Manageable side effects**
- **Combinable with other MoAs**



T cell engagers

- Tarlatamab approved
- **40% RR**
- 9.7 months DoR
- **Substantial side effects**

Antibody-drug conjugates

- Phase 1/2
- 70% RR
- **DoR: 5–6 months**
- Manageable side effects

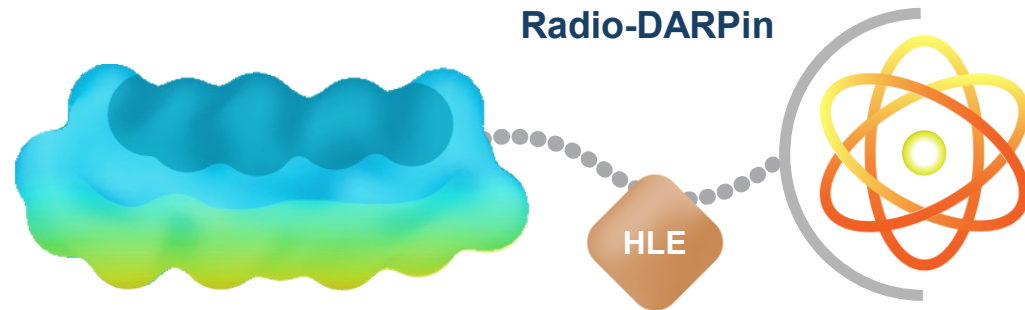
Making Alpha Therapies a Reality with DARPins and ^{212}Pb



MOLECULAR PARTNERS
PIONEERS of DARPIN THERAPEUTICS

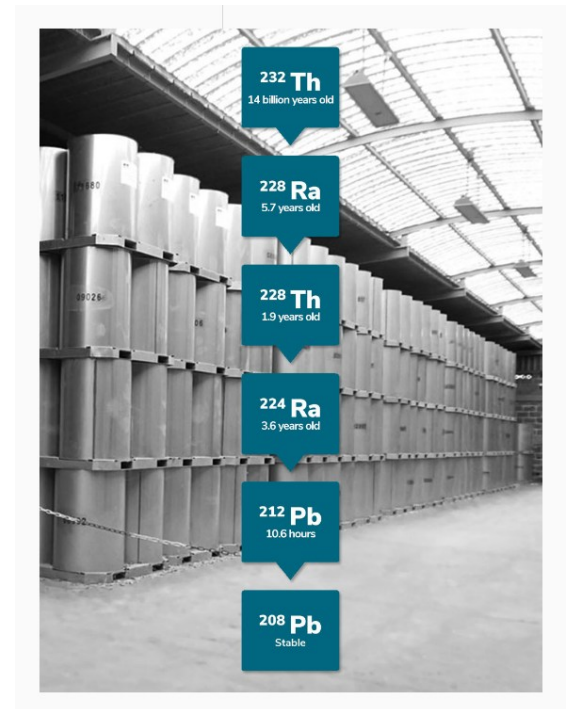
ORANO MED

PIONEERS of TARGETED ALPHA THERAPY



FULL VALUE CHAIN PARTNERSHIP:

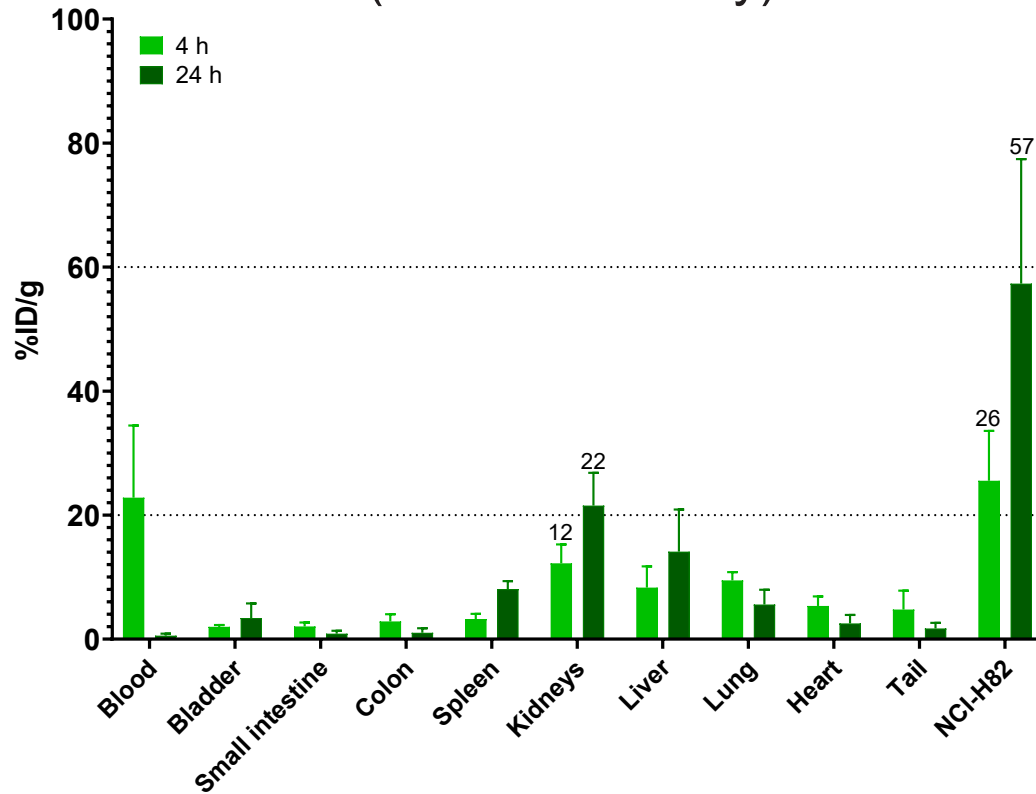
- ✓ World class technologies & capabilities combined
- ✓ DARPins as well-suited vectors for radiopharmaceuticals
- ✓ ^{212}Pb as potent therapeutic payload, proven clinical efficacy



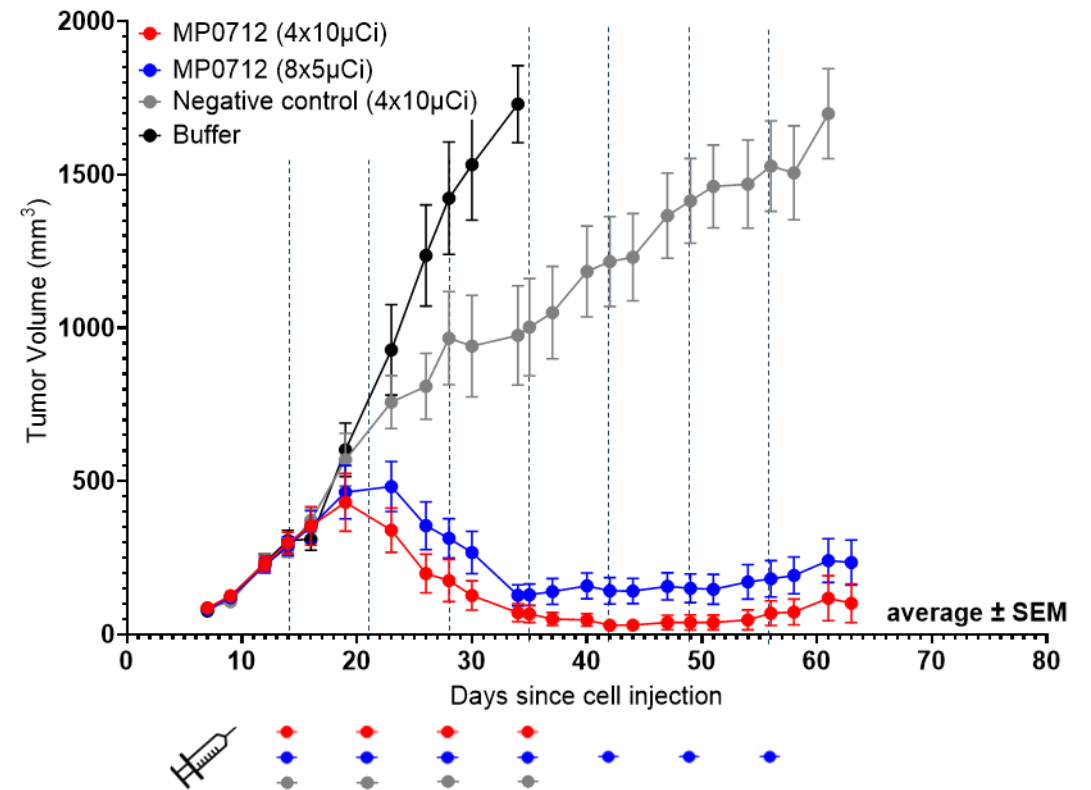
MP0712: Favorable Biodistribution and Potent Efficacy

In mouse models matching the low DLL3 expression levels of patients

High Tumor Accumulation (Tumor > Kidney)



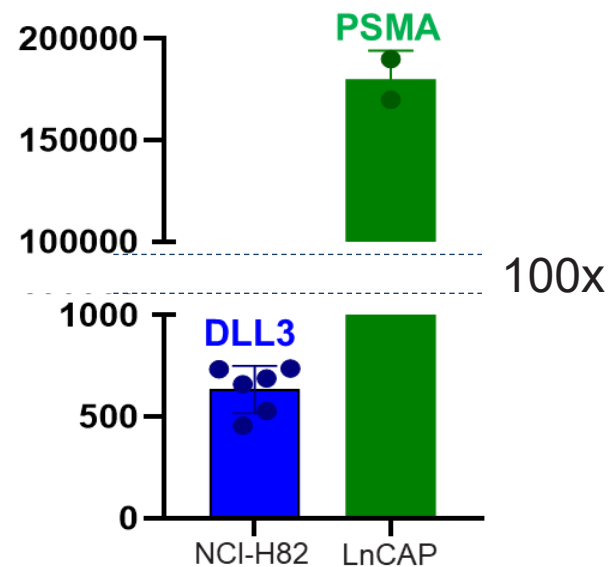
Reduction of Established Tumors



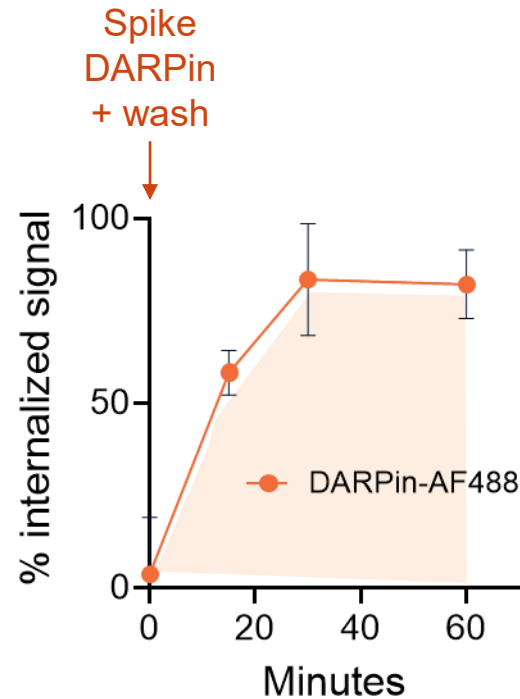
MP0712: Rapid Internalization and Accumulation in Cells

Very low DLL3 copy number

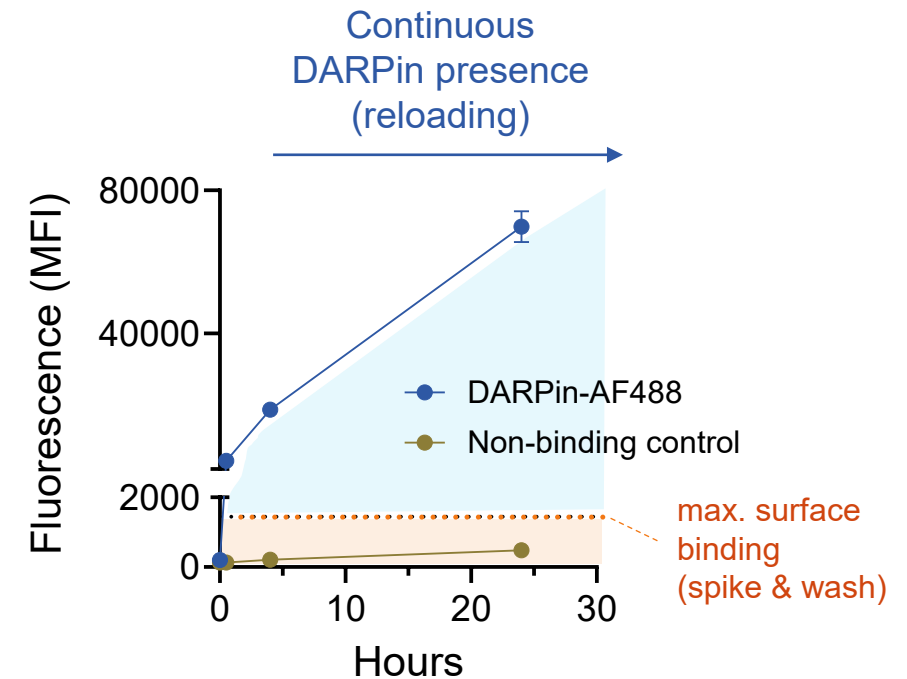
DLL3: <1000 receptors/cell
PSMA: >100'000 receptors/cell



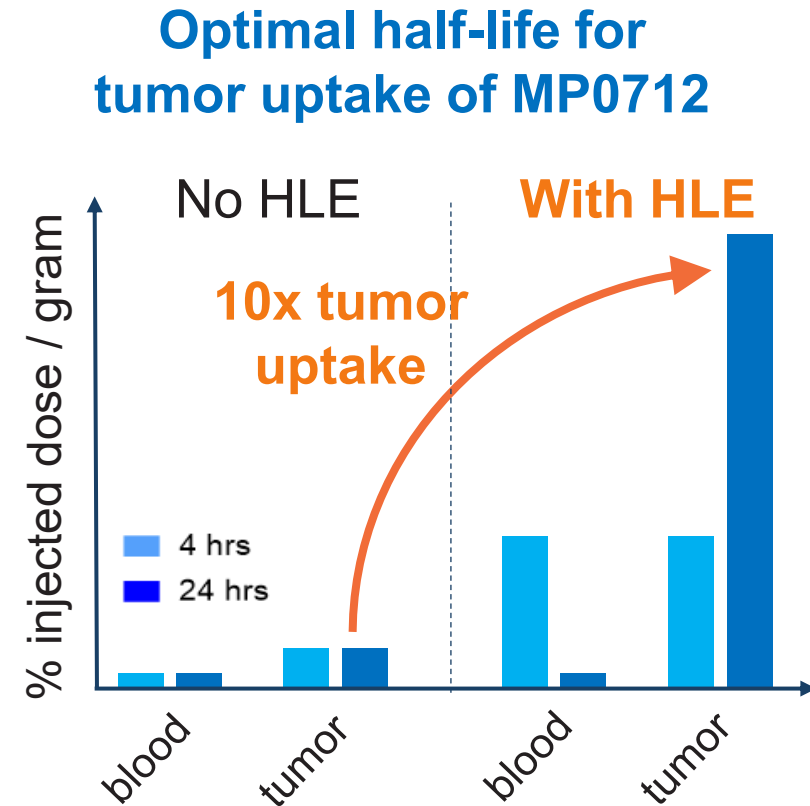
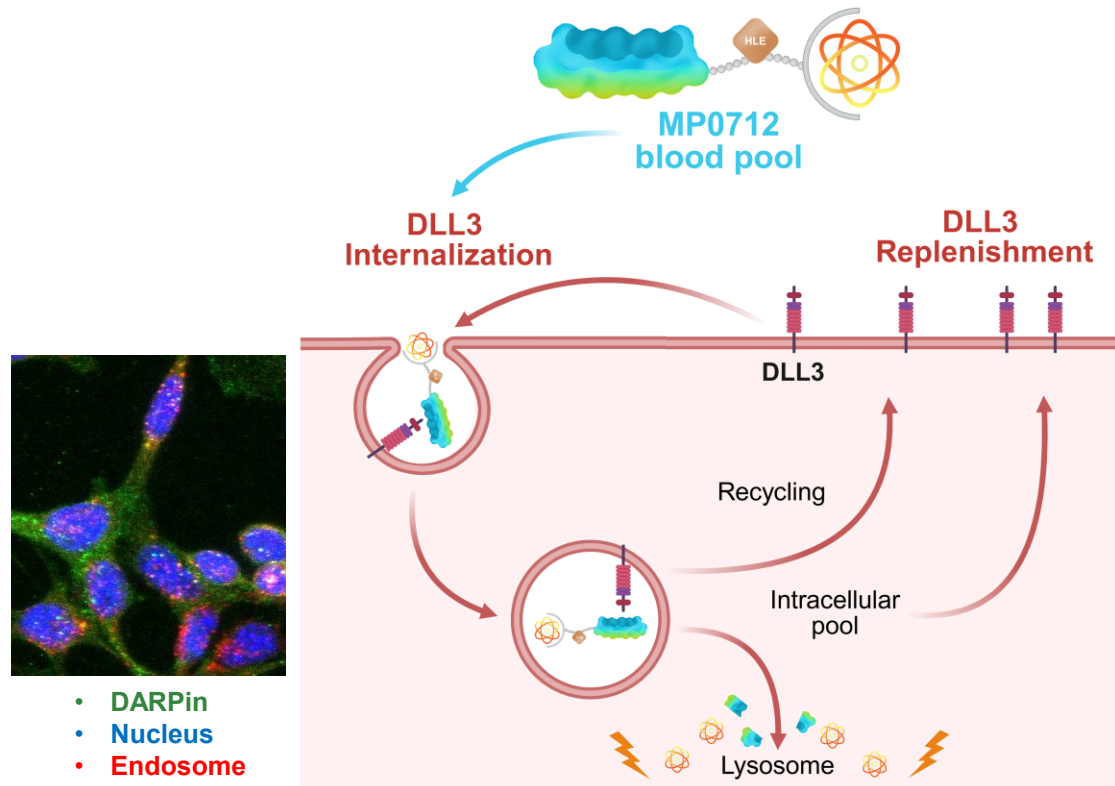
DLL3 DARPin is rapidly internalized* ...



... and accumulates over time in cells**



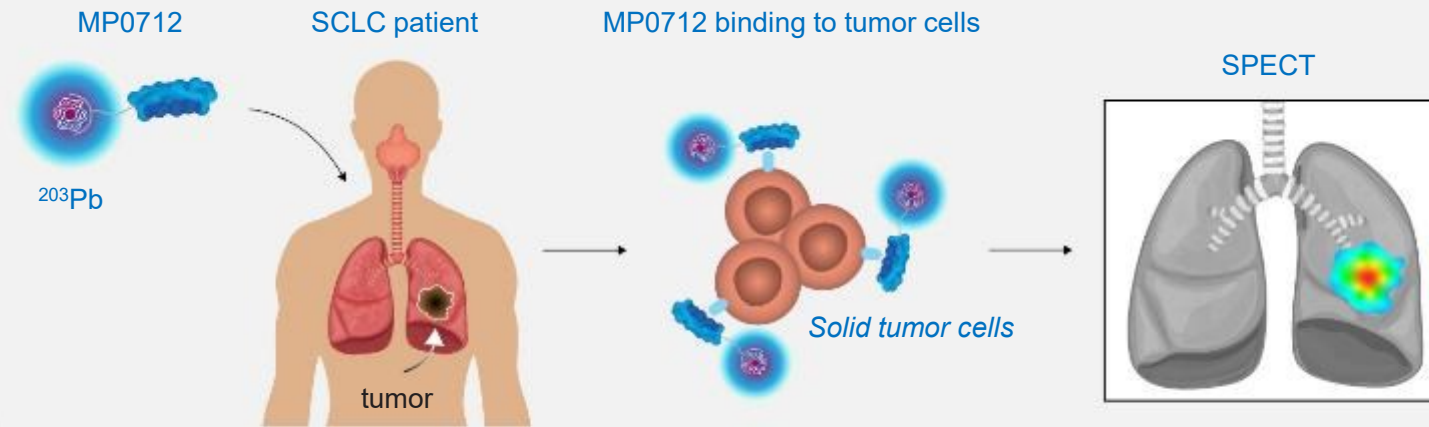
MP0712: High Tumor Uptake via DLL3 Internalization - Replenishment and Half-Life Engineering



DARPin half-life optimization allows to leverage rapid internalization & replenishment of DLL3 for high MP0712 accumulation in tumors

MP0712 Development Pathway

1. Imaging

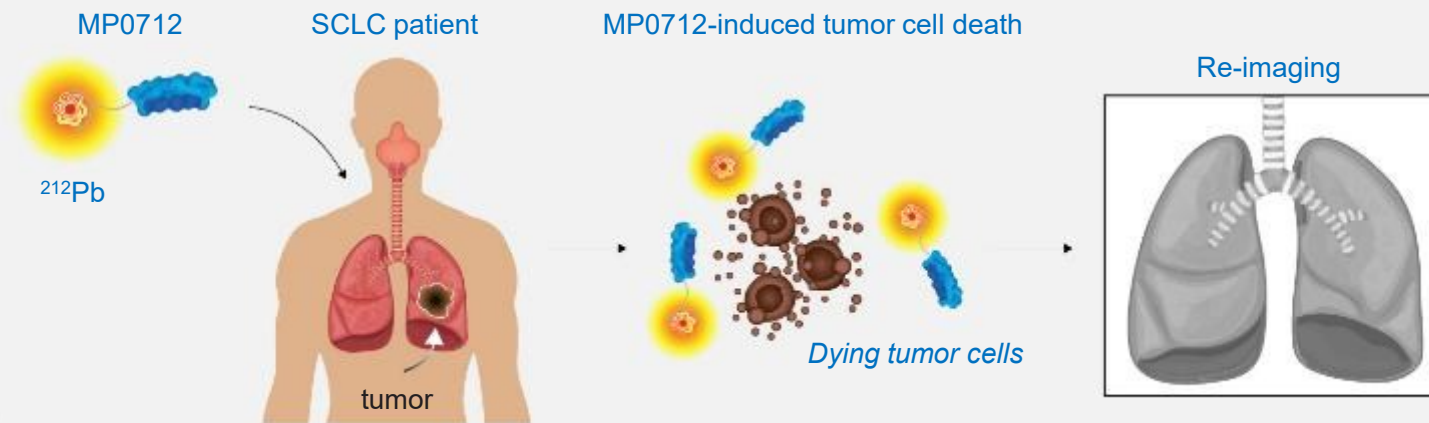


Named Patient Access Program:

- Imaging and dosimetry with ^{203}Pb
- Option for treatment with ^{212}Pb

*Request from NuMeRI, Pretoria, South Africa**

2. Treatment



Phase 1/2a Study:

- Safety of ^{212}Pb
- Efficacy signals
- Includes an imaging and dosimetry step with ^{203}Pb

SPECT/CT Imaging with ^{203}Pb -MP0712 in a Patient with Metastatic Small Cell Lung Cancer (mSCLC)

Patient characteristics

- 69-year-old male (smoker)
- Small cell neuroendocrine carcinoma of the lung
- Stage III at referral (mediastinal lesion)

Treatment history

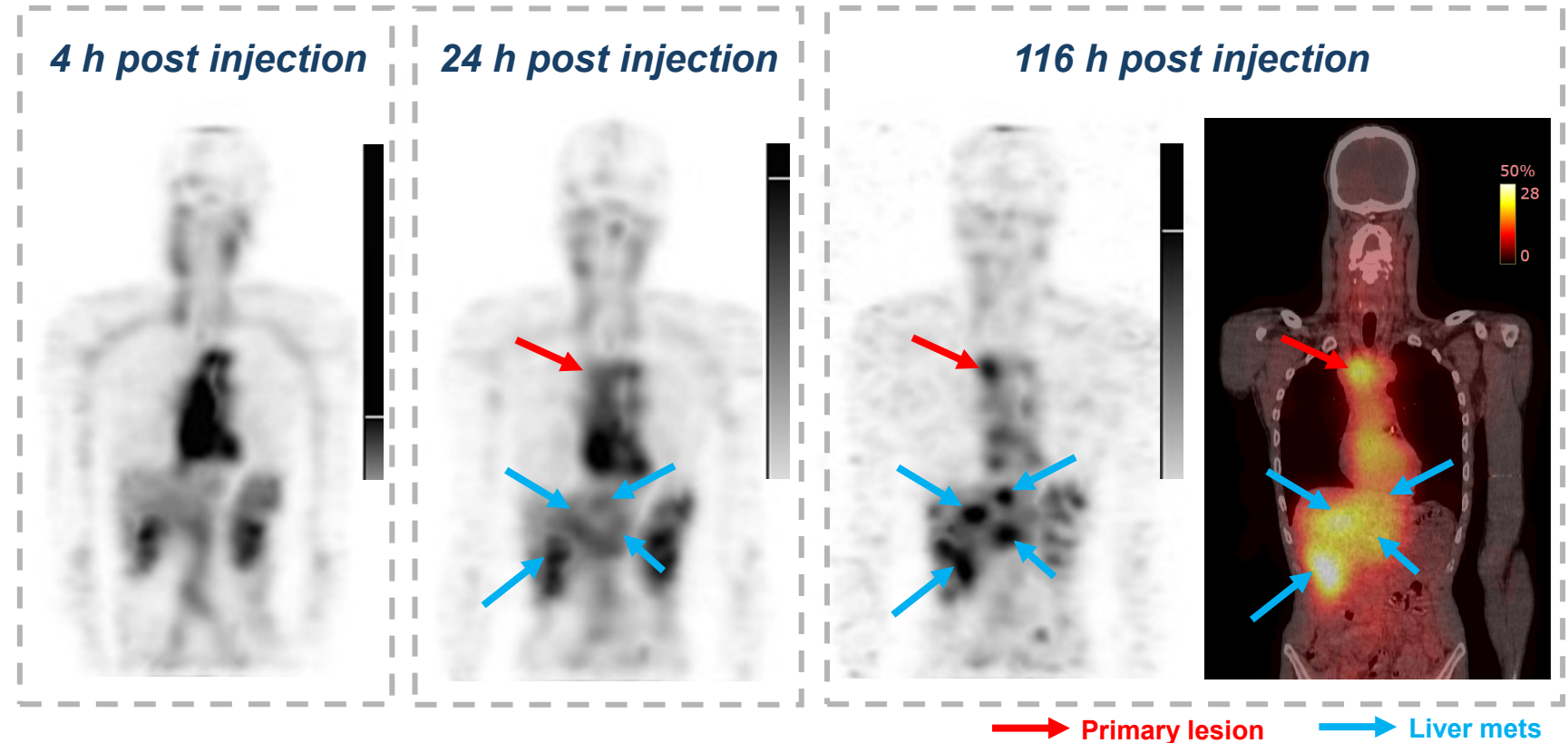
- Radio- & chemotherapy

Dosing

- 185 MBq of ^{203}Pb -MP0712

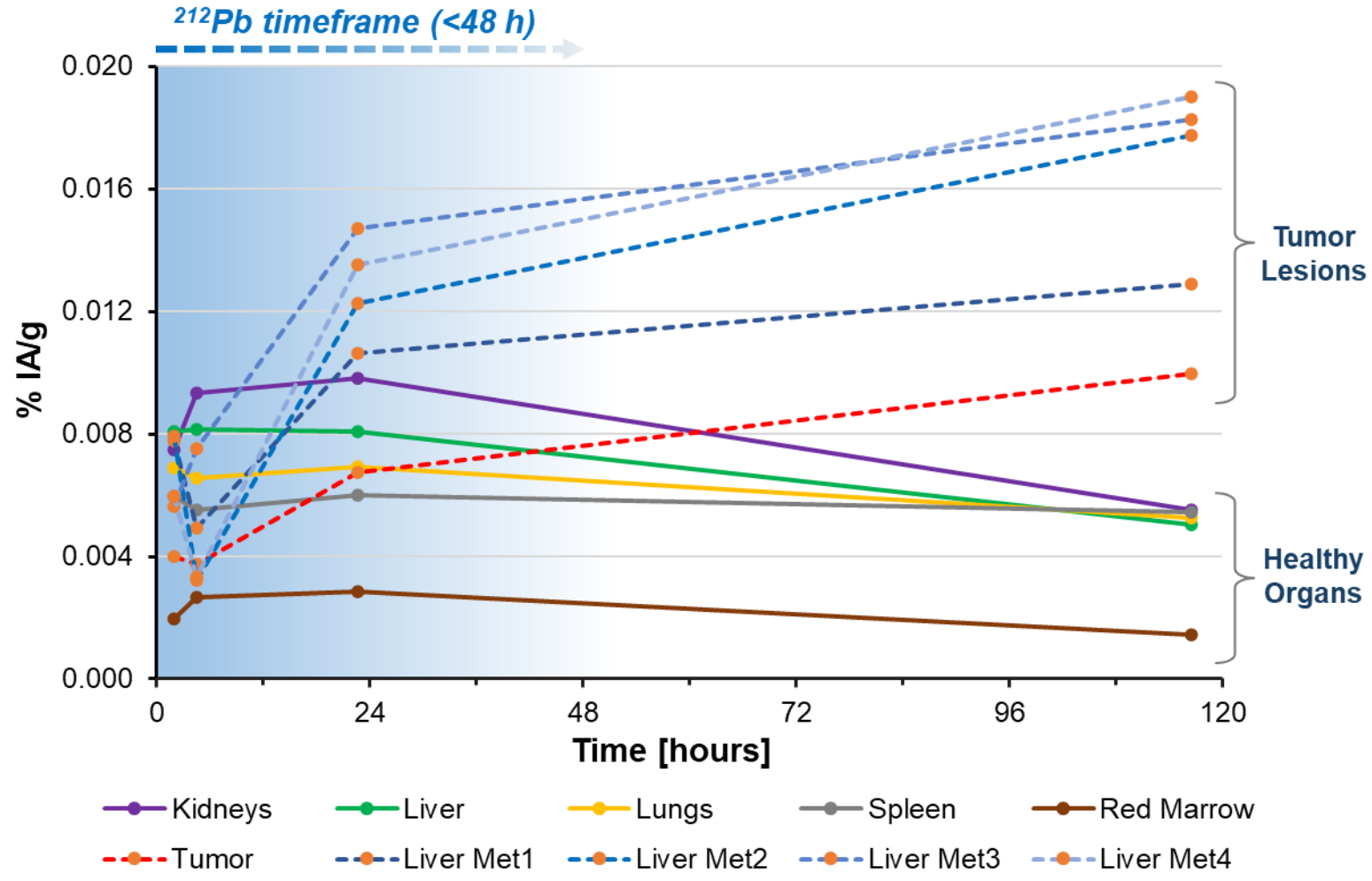
Result

- Stage IV by MP0712 - SPECT with 4 liver mets



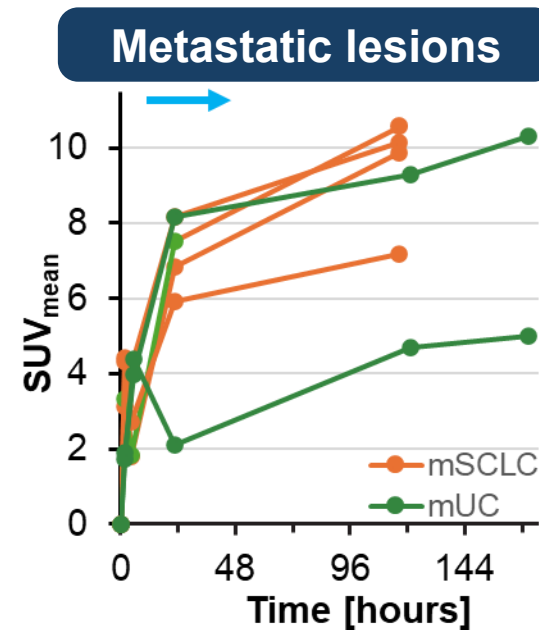
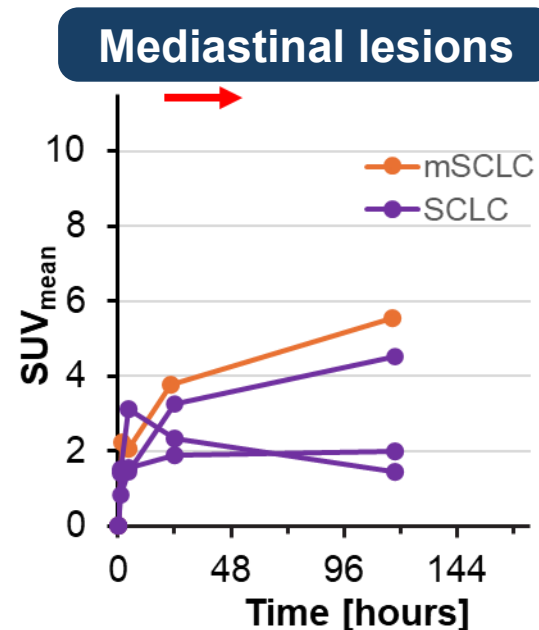
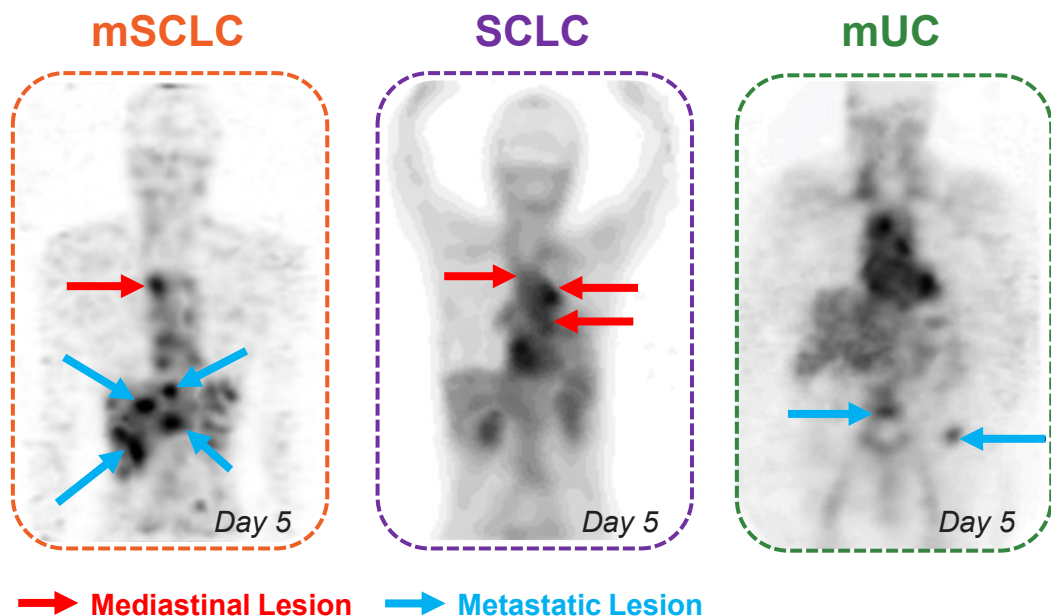
Initial high blood pool, followed by specific uptake in primary & metastatic lesions over time in line with MP0712 MoA

Biodistribution Profile of ^{203}Pb -MP0712 in mSCLC Patient



- **Continued tumor uptake** during imaging period (up to 116 h)
- **Higher uptake in liver metastases** as compared to primary lesion
- **Washout from healthy organs** visible from 24 h onwards
- Healthy organ profile consistent with profile observed in other patients

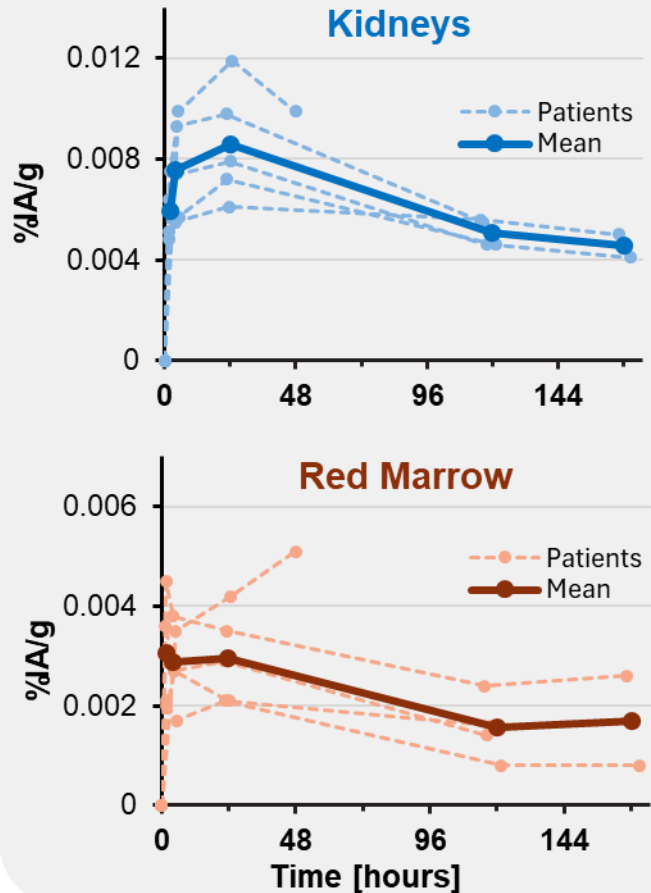
^{203}Pb -MP0712 Uptake in Tumor Lesions



- **Progressive uptake** of MP0712 across different tumor types
 - ~80% of uptake reached at 24 h
 - **Strong tumor retention** with continued uptake during imaging period (up to 7 days)
- **Preferential uptake in metastatic lesions**
 - **Phase 1 study** in US expected to enroll **metastatic SCLC patients**

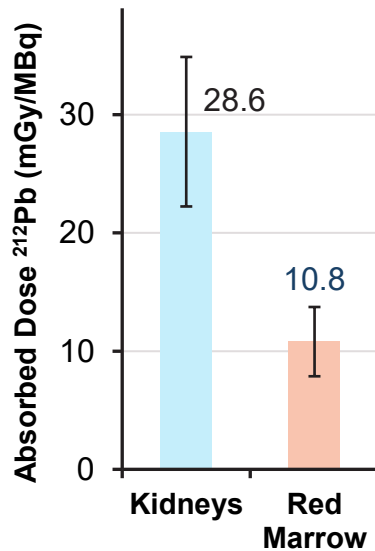
MP0712 Organ Dosimetry and Projection to Phase 1

²⁰³Pb Time-activity curves

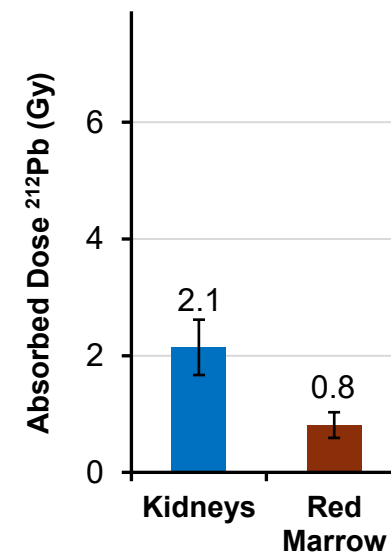


Dosimetry extrapolations suggest kidneys & red marrow as potential dose-limiting organs for ²¹²Pb-MP0712

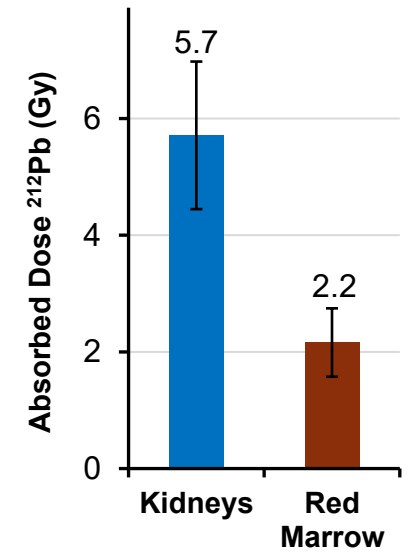
²¹²Pb Dose Coefficient



1x 75 MBq ²¹²Pb

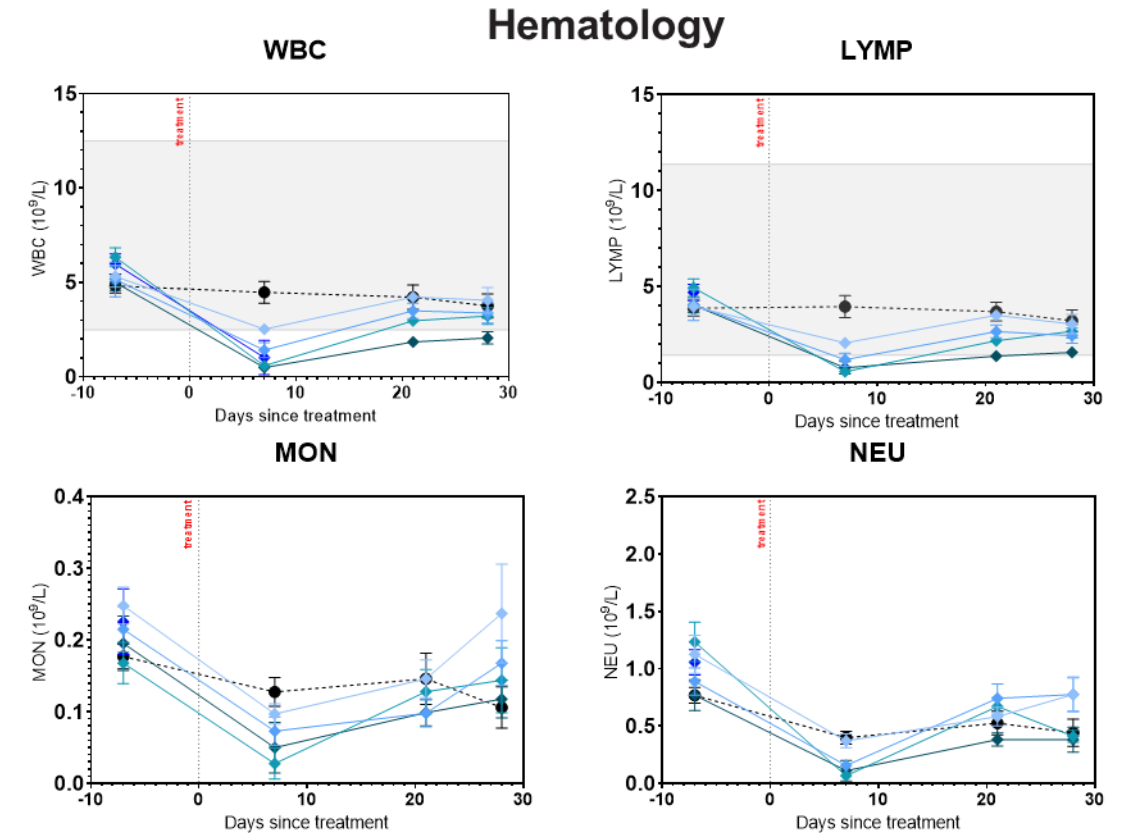
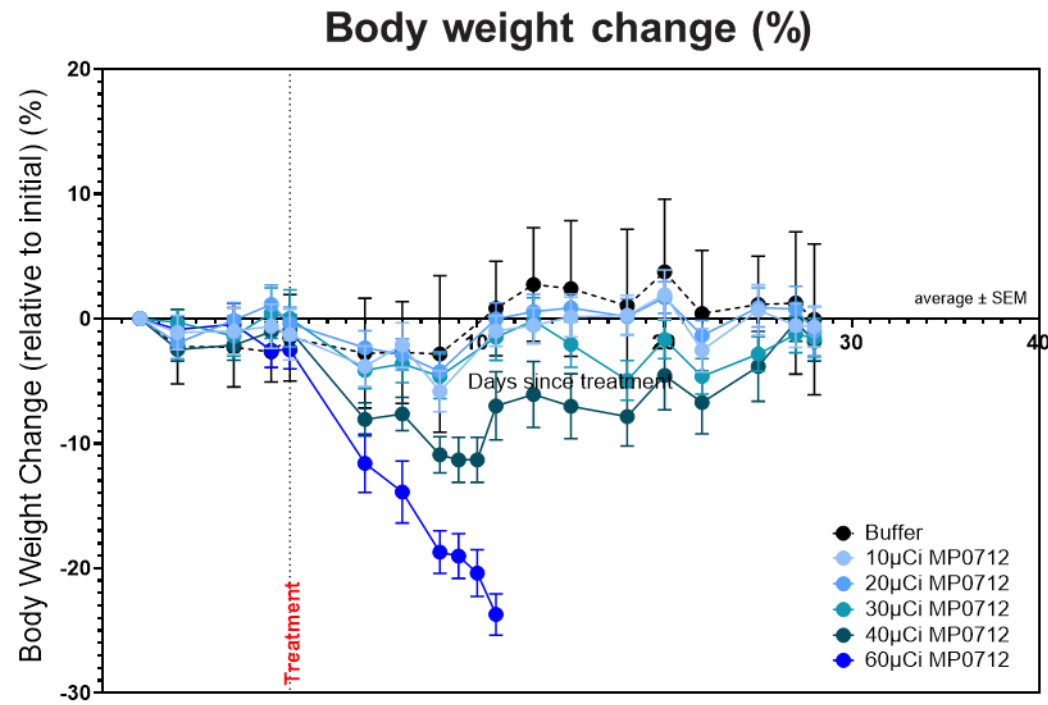


1x 200 MBq ²¹²Pb



- At Phase 1 starting dose (75 MBq) and at highest anticipated single dose (200 MBq) all healthy organs are within EBRT limits
- Monitor hematologic recovery to guide repeated dosing strategies

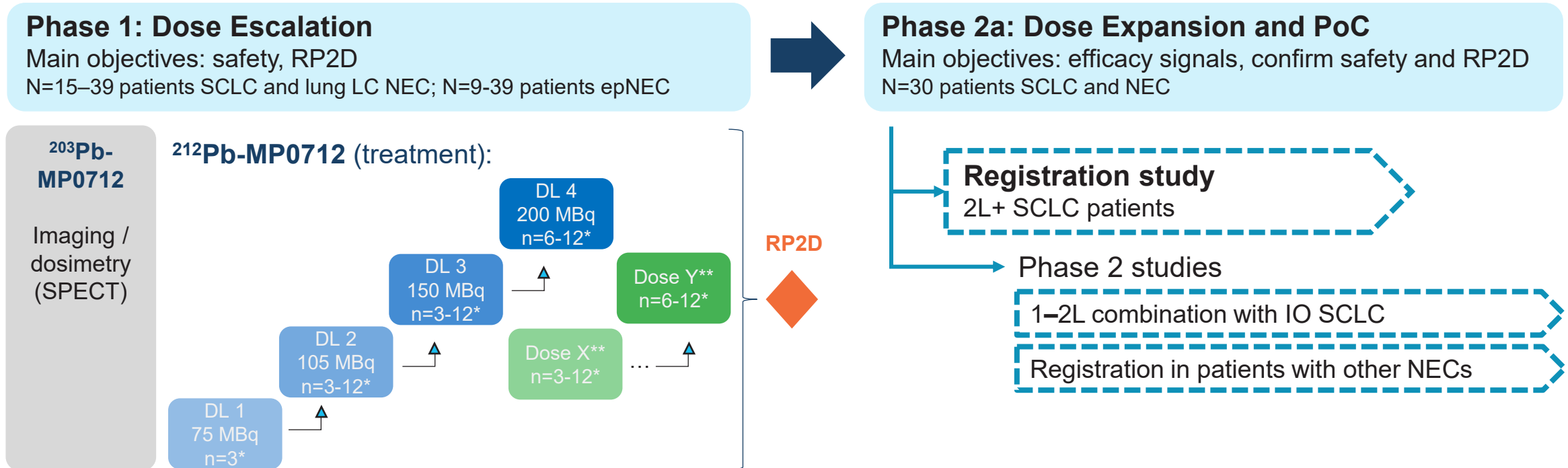
MP0712 Preclinical Safety Data Support Heme Recovery Hypothesis



- Complete recovery of body weight loss after 10 days
- Complete recovery of hematologic profile after 28 days
- MP0712 treatment up to 30 μ Ci / 1.11 MBq well tolerated

MP0712 Phase 1/2a Study for SCLC and other NECs

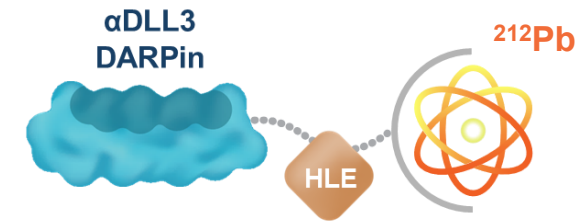
- First-in-Human, US multicenter, Phase 1/2a study of MP0712 monotherapy (NCT07278479)
- Patients with small cell lung cancer (SCLC) and other neuro-endocrine cancers (NECs)
 - Every patient will be imaged (^{203}Pb) before treatment (^{212}Pb)
 - Patient pre-selection on DLL3 expression: not planned for SCLC and LC NEC of lung, foreseen for epNEC



* Evaluable patients (Bayesian Logistic Regression Model guided dose escalation)

MP0712 Conclusions

²¹²Pb x DLL3 Radio-DARPin candidate for SCLC and other NECs



Conclusion

- **First patient ^{203}Pb imaging data:** initial proof-of-principle for Radio-DARPins in humans in line with preclinical observations
- **Robust tumor uptake and retention,** molecule design leveraging DLL3 internalization
- **Favorable biodistribution and dosimetry on healthy organs** support Phase 1 design to establish MP0712 safety profile

Outlook

- **MP0712 Phase 1/2a study open** in the US, patient screening ongoing
- Initial **safety data anticipated in H1 2026**, initial **activity in H2 2026**

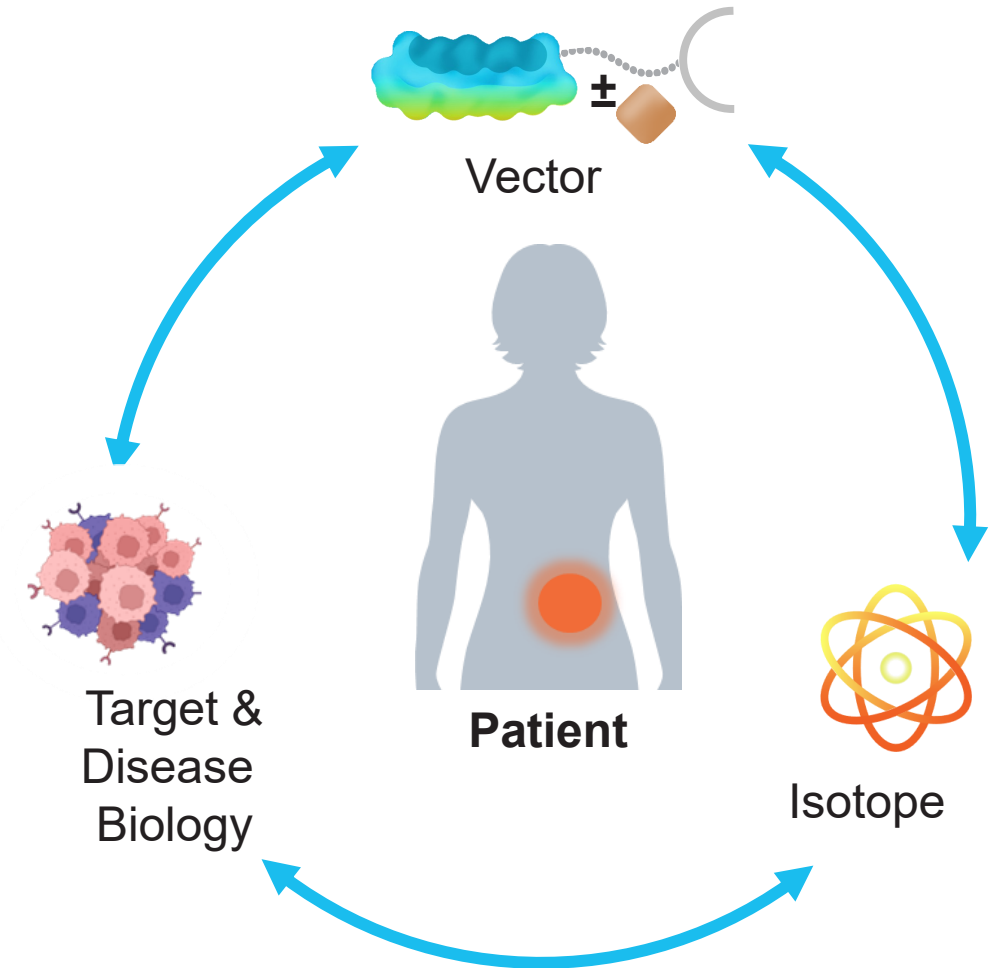
Outlook

- Vector, Chelator and Isotope Flexibility for Next Radio-DARPin
- Building a Diverse Radiotherapeutics Pipeline

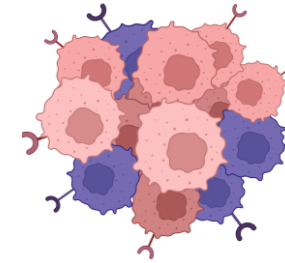
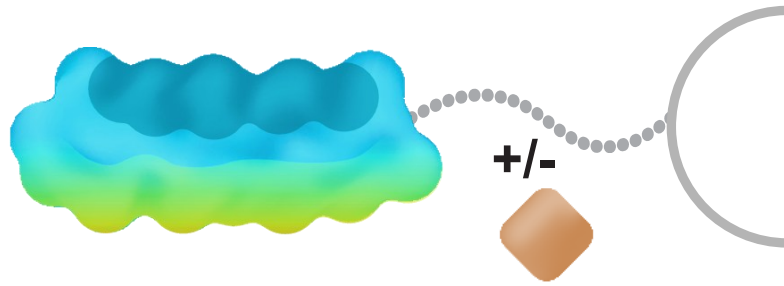


Learnings for Designing Radio-DARPin Therapeutics for Patients

- (1) Deep understanding of disease & target biology
- (2) Versatility in vector design that address biology
- (3) Optionality to select isotope that best matches vector characteristics and biology
- (4) Rapid, iterative empirical testing to identify the most effective solution



Radio-DARPin Flexibility to Address Target & Disease Biology



Vector



Mono



2-in-1



Multi

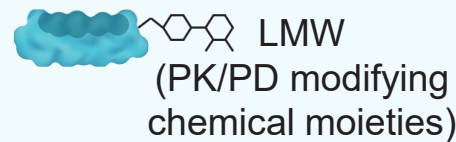


+

Modifier



(e.g. half-life extension)



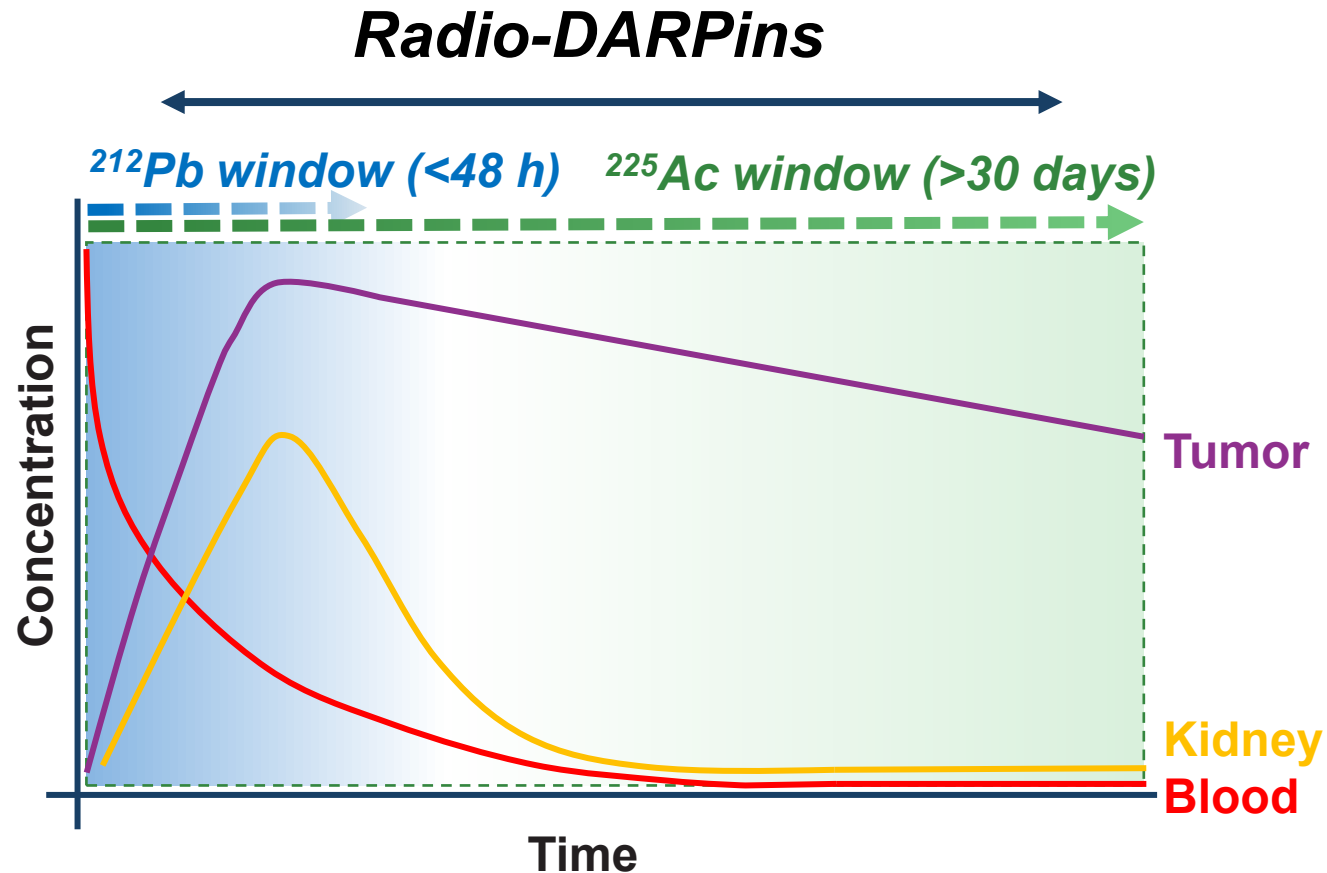
Tailored

Target & Disease Biology

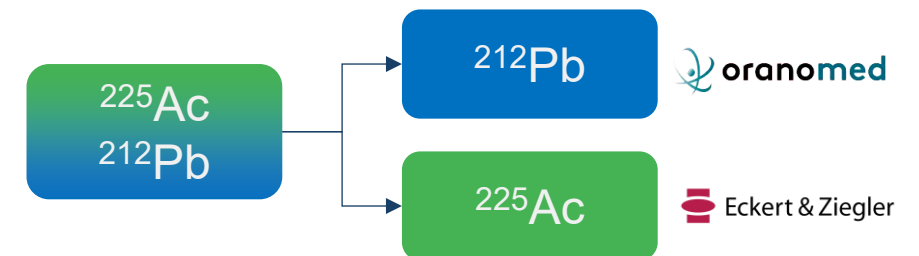
Many parameters to consider:

- Target density on tumor (e.g., DLL3)
- Shed/soluble target sink (e.g., MSLN)
- Heterogeneity: inter-patient, inter-lesion, intra-tumor
- Target off-tumor expression
- ...

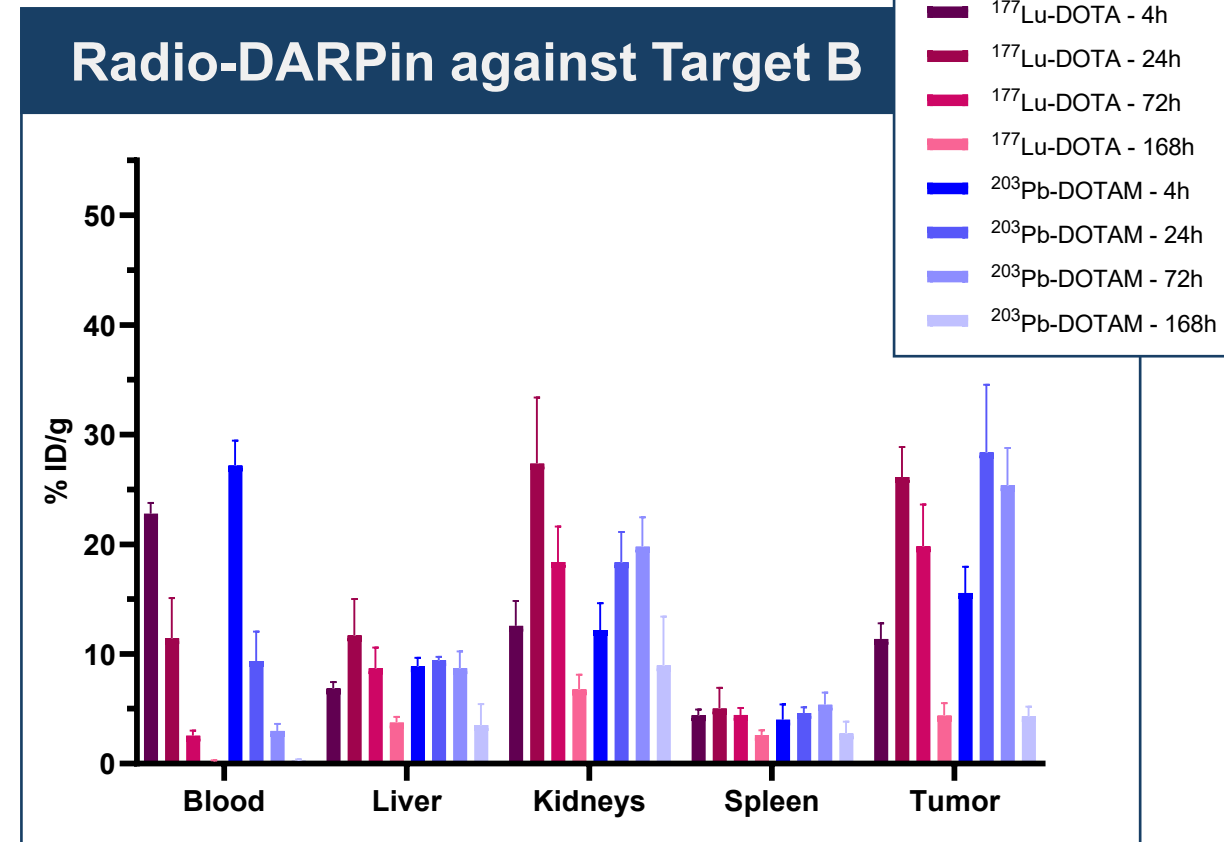
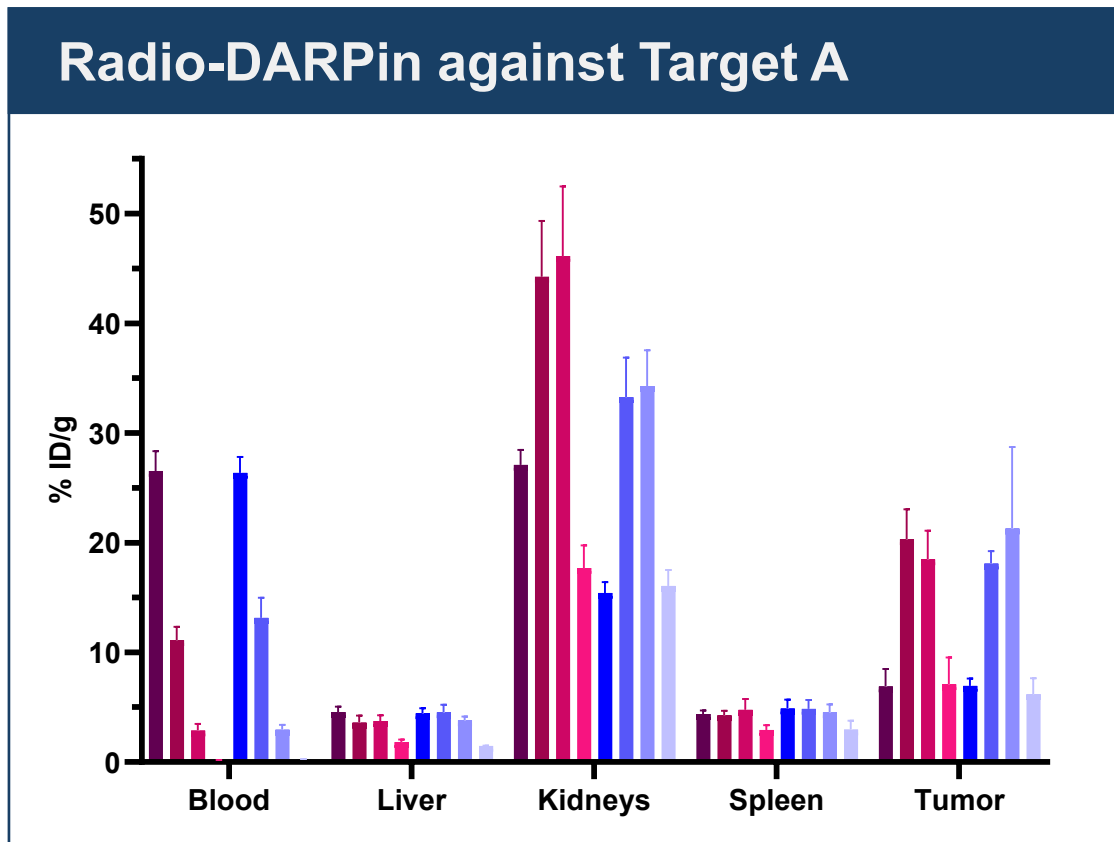
Long Tumor Retention Make DARPinS Alpha-Agnostic



- Based on ^{203}Pb -MP0712 learnings DARPin profile can work for both ^{212}Pb and/or ^{225}Ac
- Opportunity to evaluate both isotopes in parallel and decide on the best isotope with data

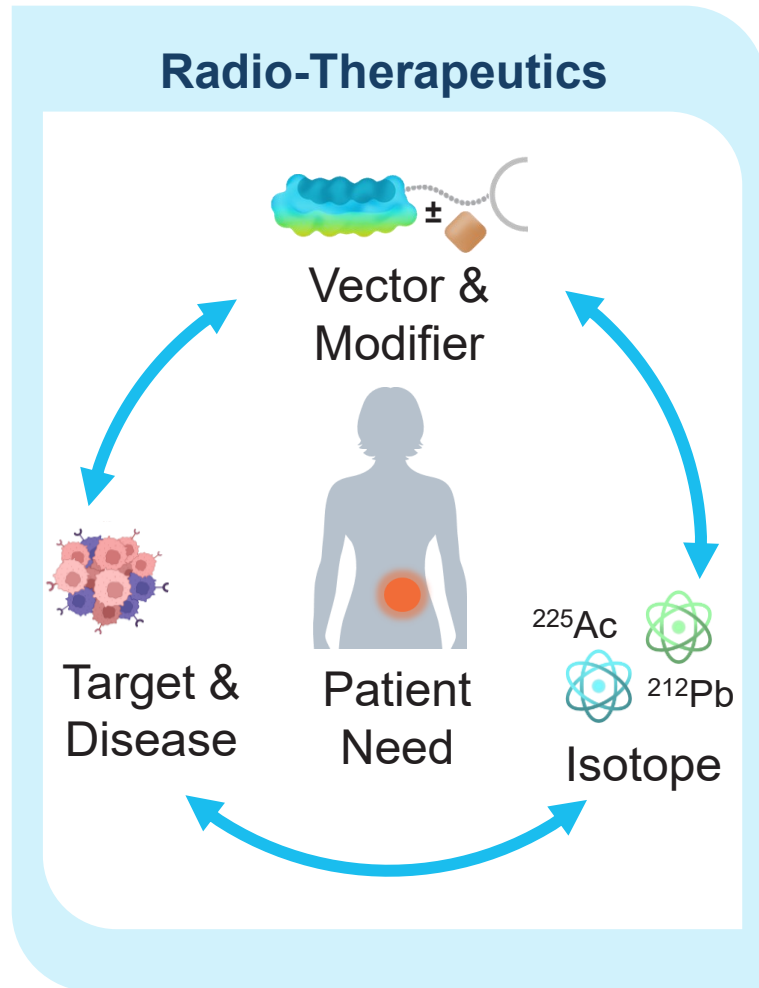


Radio-DARPin Enable Chelator and Isotope Flexibility



- Comparable BioD profile using ^{203}Pb -DOTAM and ^{177}Lu -DOTA with similar uptake and washout rates
- Assumption: ^{203}Pb -DOTAM and ^{177}Lu -DOTA can be used as surrogates for the therapeutic candidates (^{212}Pb / ^{225}Ac)
- Flexibility to select therapeutic isotope based on pre-clinical and/or early human imaging data

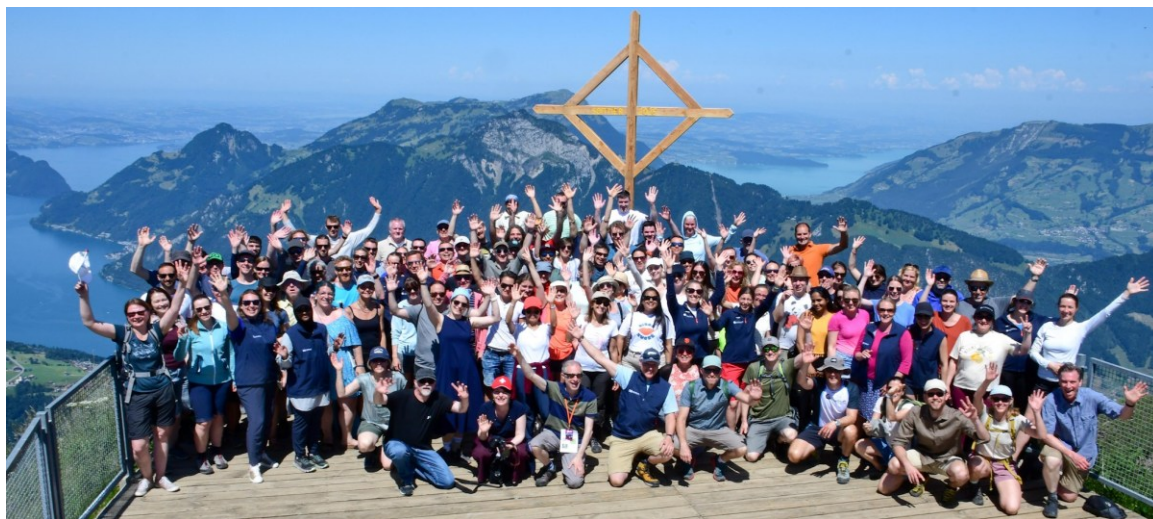
Building a Diverse Radiotherapeutics Pipeline



CANDIDATE	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2
MP0712	SCLC & NECs ^{212}Pb x DLL3		 Co-development*	Initial <u>PhI</u> data in 2026
MP0726	Ovarian Cancer ^{212}Pb x MSLN	 Co-development*	Progress MP0726 into FIH	
Undisclosed Programs (Solid Tumors)	Radio - C	^{212}Pb	Evaluate Radio-DARPin candidates in alpha-agnostic manner and nominate new RDT programs	
	Radio - D	^{225}Ac		
	Radio - E	^{225}Ac		
	Radio - F	^{225}Ac ^{212}Pb		

Acknowledgments

Team at Molecular Partners AG



NuMeRI Team

Mike Sathekge
Joseph Kabunda
Honest Ndlovu



Orano Med Team



Amal Saidi
Aaron Schatzmann
Tania Stallons
Amy Wong
Federico Rojas
Amanda Reyes
Jessica Johnson
Rob Chastain
Haley Sprague

Patients and their Families



Thank you for your interest!

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