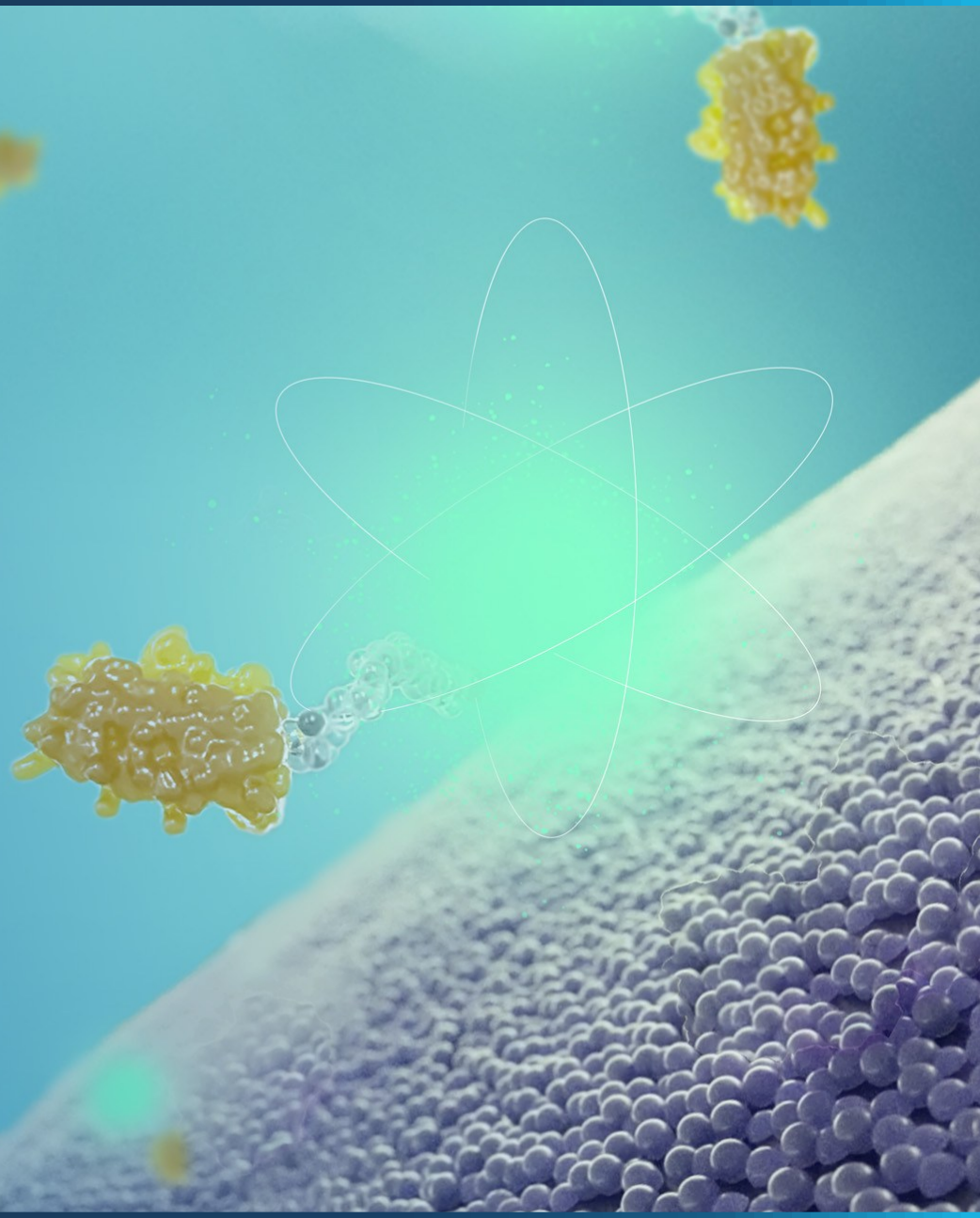
MOLECULAR partners

DARPins 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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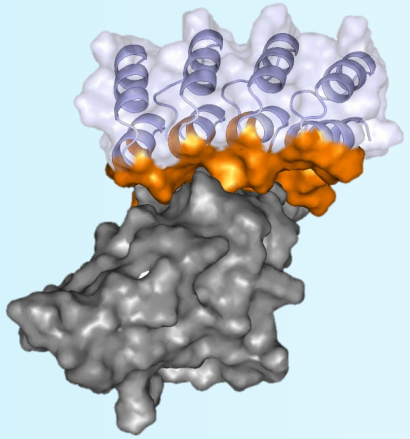
The DARPin Modality and Our Focus

DARPin
Designed Ankyrin Repeat Protein



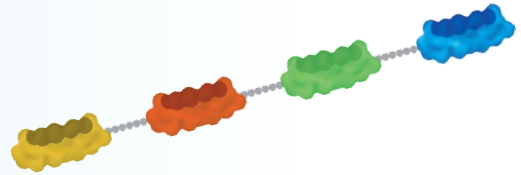
We pioneer DARPins as a new class of therapeutics

- 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

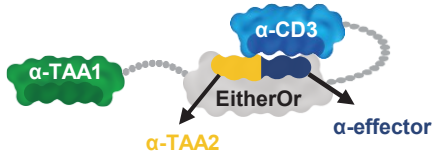
Our company focus

Radio-DARPin Therapeutics

Multi-specific immune cell engagers



Conditional “Switch” T cell engagers

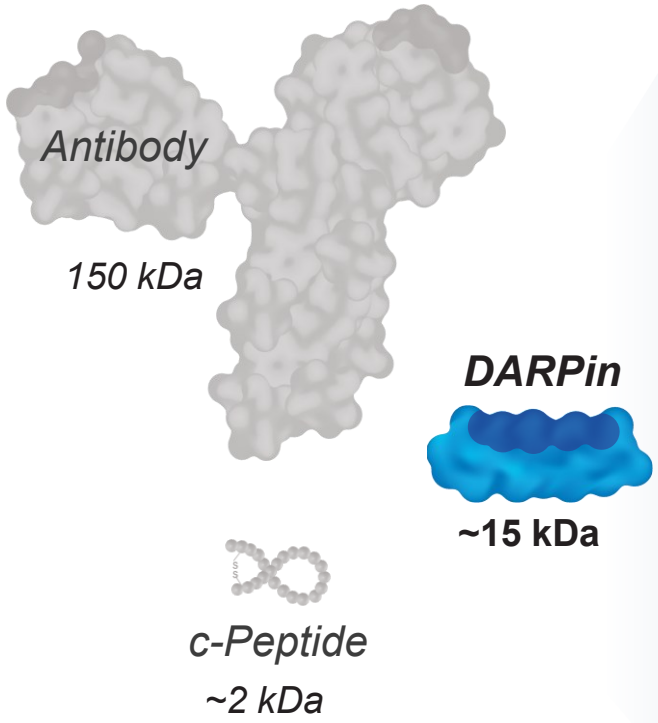


Our Pipeline – Differentiated Therapeutics for Patient Value

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

*The co-development agreement with Orano Med includes up to 10 targeted radiotherapy programs, including MP0712 and MP0726.
AML, acute myeloid leukemia; DLL3, Delta-like ligand 3; EpCAM, epithelial cell adhesion molecule; FAP, fibroblast activation protein; MDS, myelodysplastic syndrome; MSLN, mesothelin; NEC, neuroendocrine cancer; r/r, relapsed/refractory; SCLC, small cell lung cancer.

DARPin Features for Tumor Targeting of Radionuclides

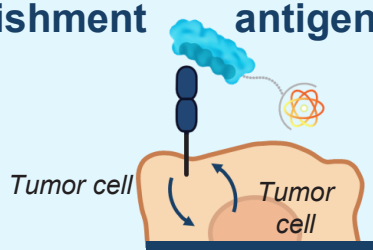


DARPins are small binding proteins derived from natural ankyrin repeat proteins

DARPin key features

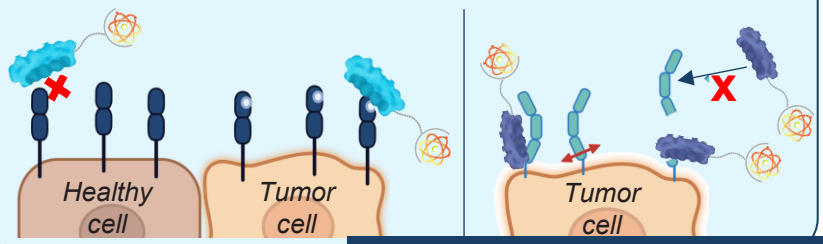
- ✓ **Small size** (~15 kDa)
  - → *Deep tumor penetration*
  - → *Short systemic half-life*
- ✓ **Broad target range** (100's)
  - → *Opening indications*
- ✓ **High affinity** (low pM range)
  - → *Long tumor retention*
- ✓ **High selectivity**
  - → *Low normal tissue*
- ✓ **High stability**
  - →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

Low density – rapid internalization & replenishment antigens



MP0712 (^{212}Pb x DLL3)

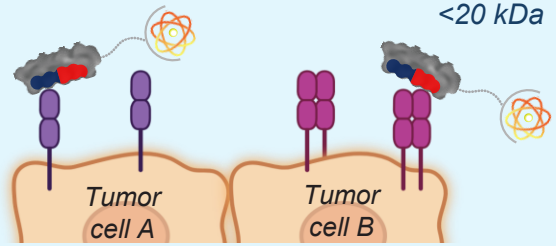
High selectivity to tumor antigens



MP0726 (^{212}Pb x MSLN)

Small bi-specific DARPins (*2in1 DARPin*)

<20 kDa



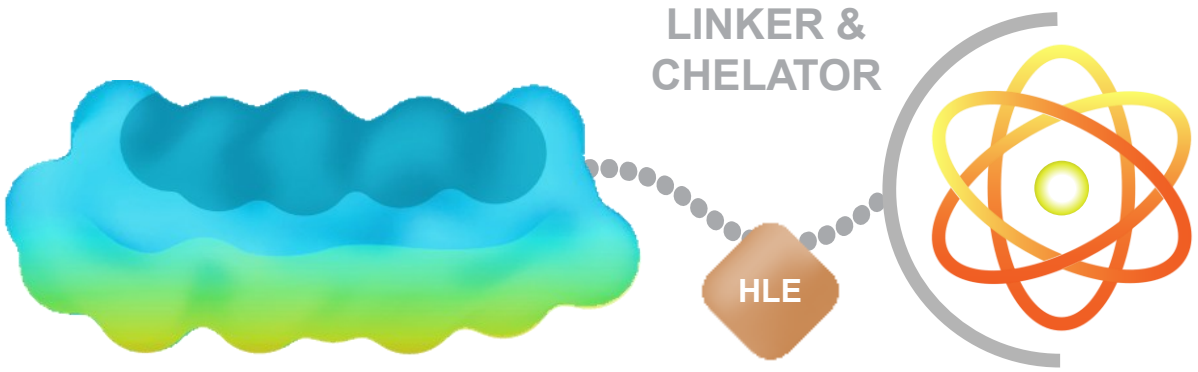
DARPin: Designed Ankyrin Repeat Protein
Binz HK. et al, *J Mol Biol*, 2003

Created in part with BioRender.com

Radio DARPin Platform for Therapeutic Candidates

DARPin: IDEAL VECTOR FOR RADIOPHARMACEUTICALS

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



ALPHA-EMITTING THERAPEUTIC ISOTOPES

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

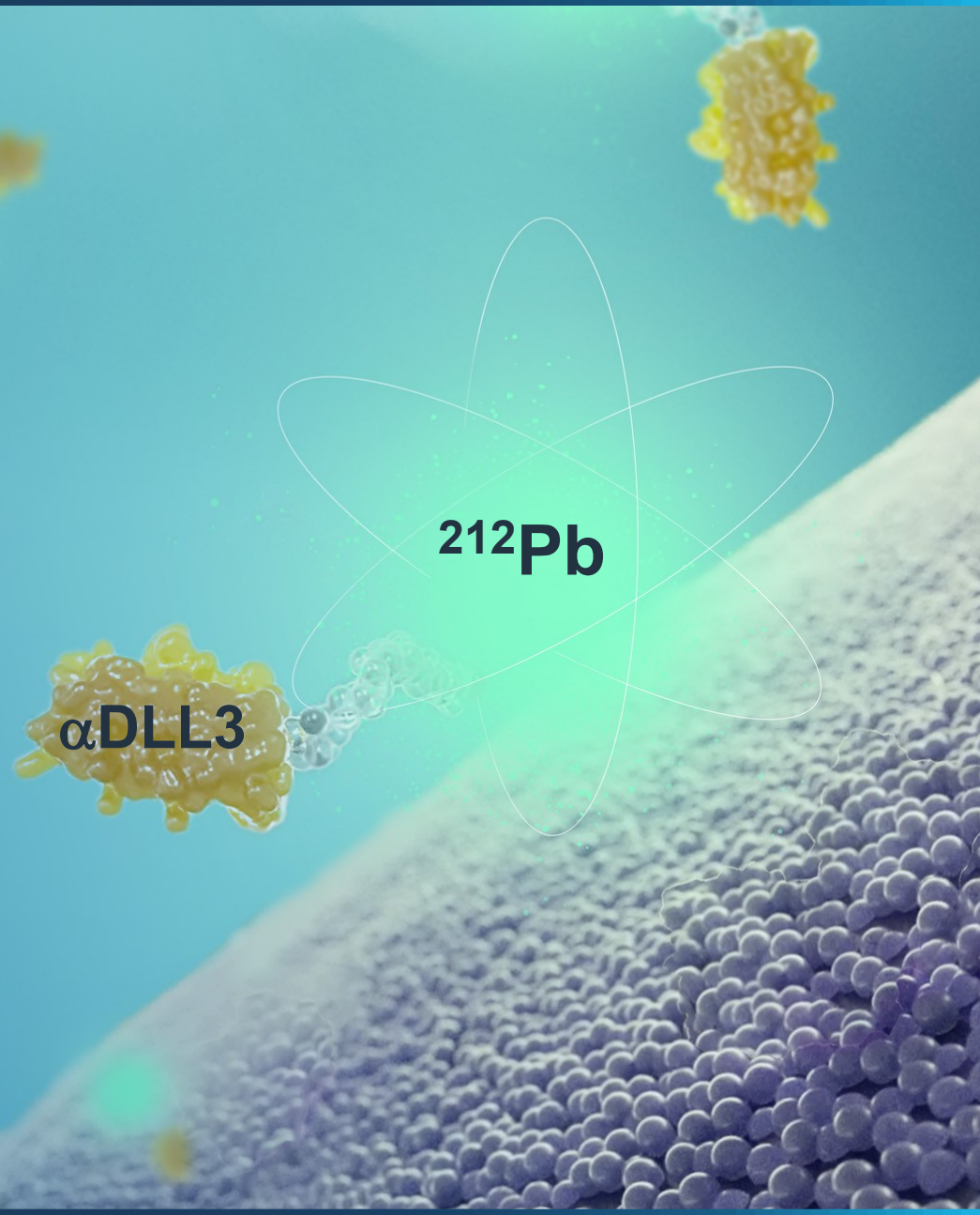
SURFACE ENGINEERING

- Enabled by high stability
- Reduce kidney accumulation

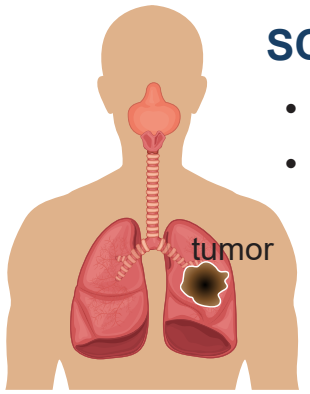
HALF-LIFE EXTENDER

- Tailored systemic exposure
- Promote tumor uptake

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]

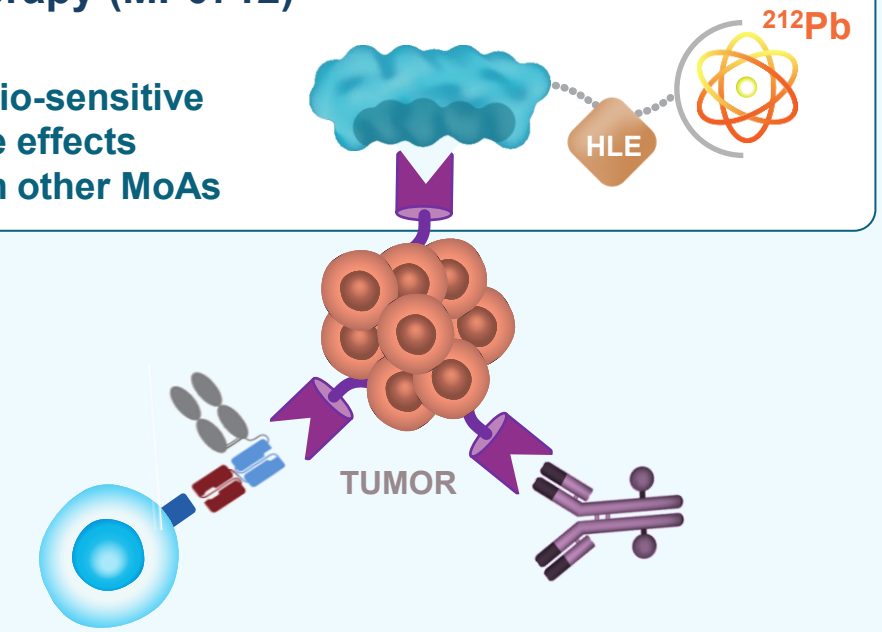
DLL3

DLL3: validated target

- Expressed in >85% of patients with SCLC[3]
- Expression in multiple neuroendocrine cancers (e.g., LC, Bladder, GEP)
- No expression in healthy tissues
- Tumor-targeting shown with DLL3 radio-diagnostic mAb (^{89}Zr-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

1. Treatment of R/R SCLC, UpToDate; 2. SEER; 3. Rojo et al., Lung Cancer 2020; 4. Tendler et al., Lancet Oncol 2024; 5. Thummalapalli et al., JCO Precis Oncol 2025; 6. Phase 2 DeLLphi-301 study (NCT05060016); 7. Dy et al., AACR-NCI-EORTC 2025.

2L, 2nd line; ADC, antibody-drug conjugate; DoR, duration of response; GEP, gastroentero-pancreatic; LC, large cell; MoA, mechanism of action; mPFS, median progression-free survival; OS, overall survival; RR, response rate; SCLC, small cell lung cancer.

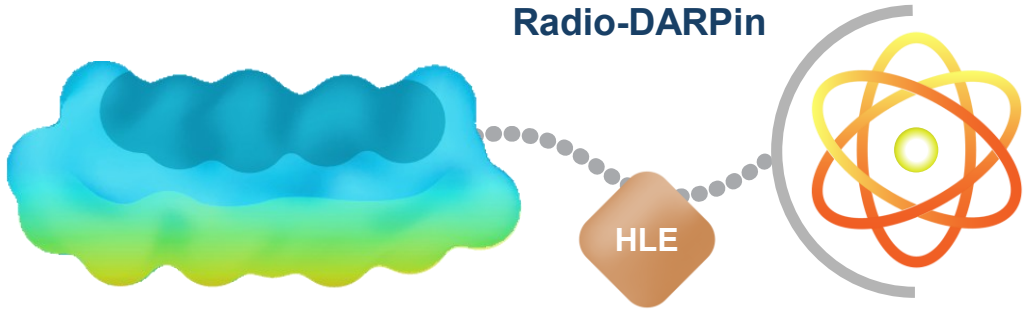
Making Alpha Therapies a Reality with DARPins and ^{212}Pb

MOLECULAR PARTNERS

PIONEERS of DARPIN THERAPEUTICS

ORANO MED

PIONEERS of TARGETED ALPHA THERAPY



FULL VALUE CHAIN PARTNERSHIP:

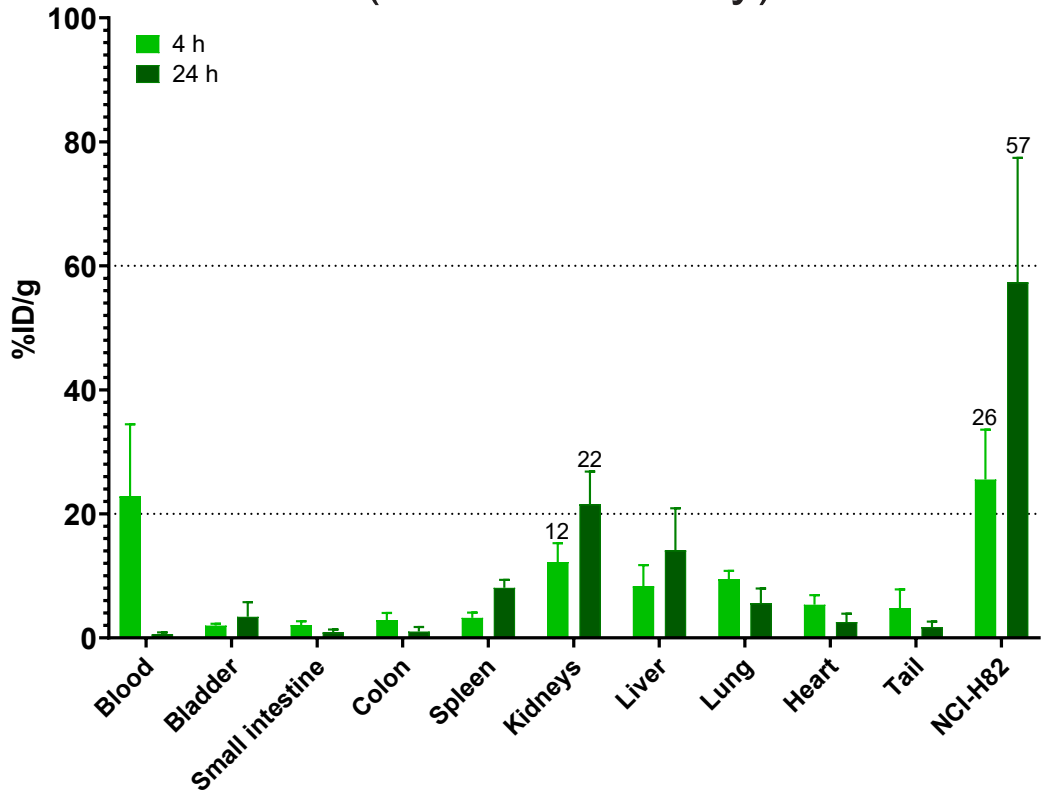
- ✓ **World class technologies & capabilities combined**
- ✓ **DARPins as well-suited vectors for radiopharmaceuticals**
- ✓ **^{212}Pb as potent therapeutic payload, proven clinical efficacy**

MP0712: Favorable Biodistribution and Potent Efficacy

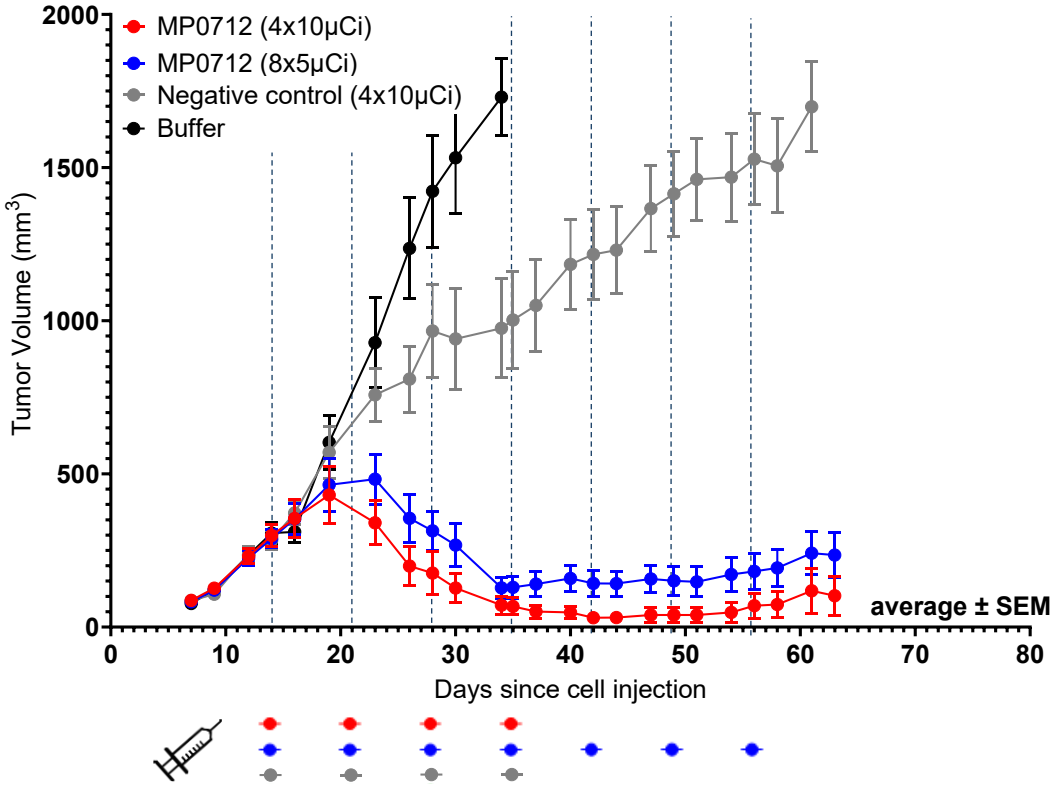
In mouse models matching the low DLL3 expression levels of patients

High Tumor Accumulation

(Tumor > Kidney)



Reduction of Established Tumors



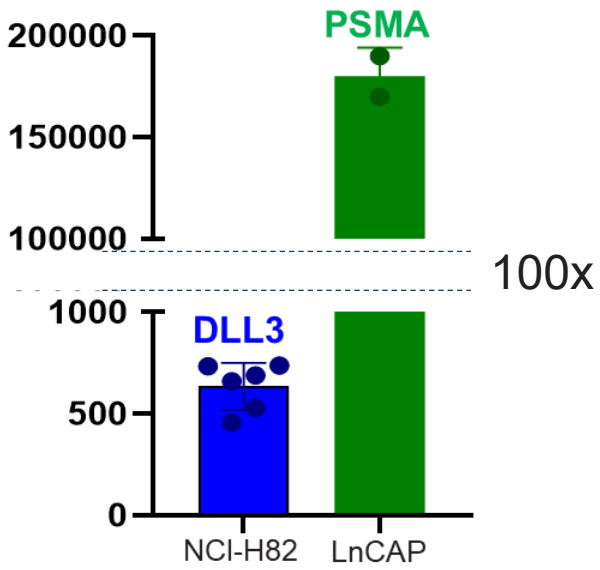
Steiner et al., TRP 2024;
Croset et al., EANM 2024;
Lizak et al., SNMMI 2024.

BioD study in NCI-H82 i.v. model. Dose: 10 µCi of ^{212}Pb at 0.01 mg/kg of DLL3 DARPin.
Efficacy study in NCI-H82 s.c. model / MP0712 and negative control injected 4x 10 µCi at 0.01 mg/kg or 8x 5 µCi at 0.01mg/kg every week; 10 µCi = 370 kBq.

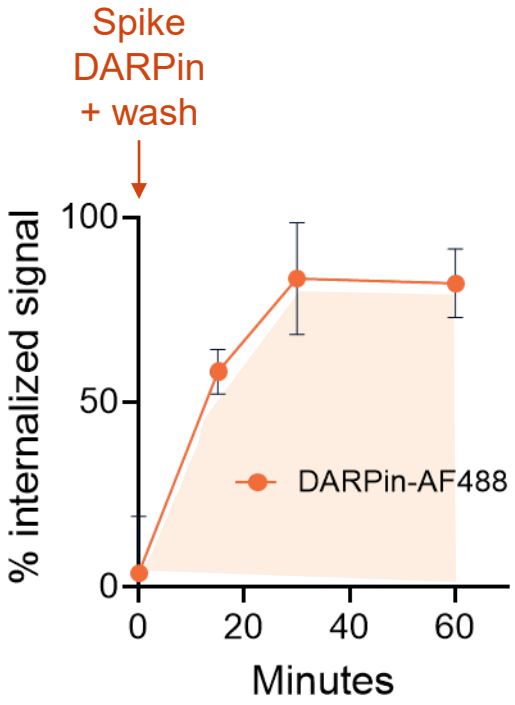
MP0712: Rapid Internalization and Accumulation in Cells

Very low DLL3 copy number

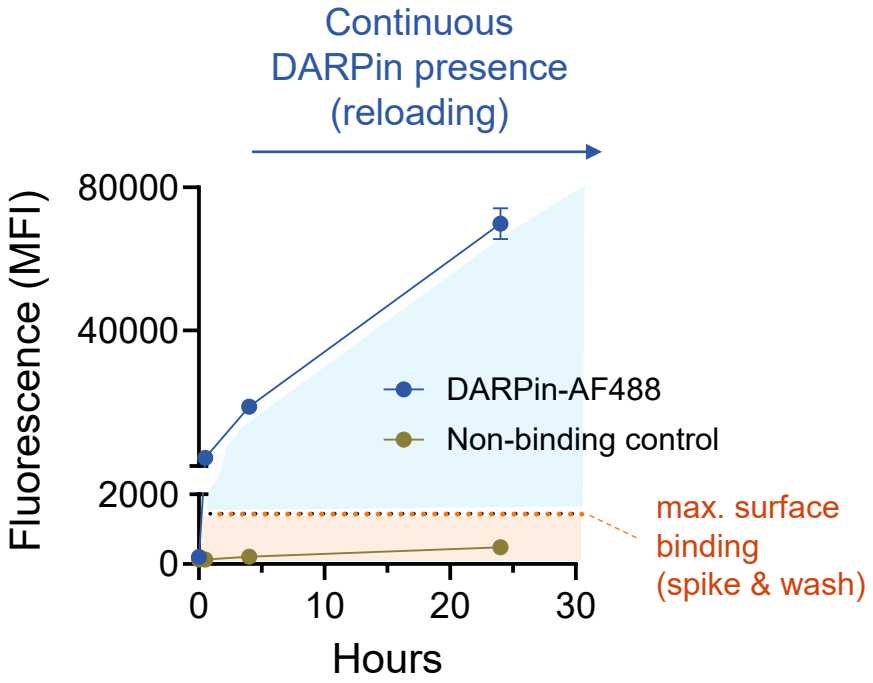
DLL3: <1000 receptors/cell
PSMA: >100'000 receptors/cell



DLL3 DARPin is rapidly internalized*…

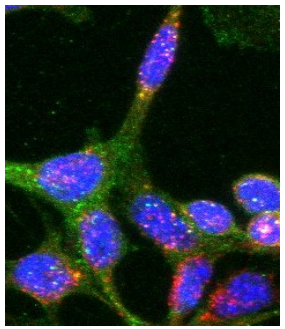


… and accumulates over time in cells**

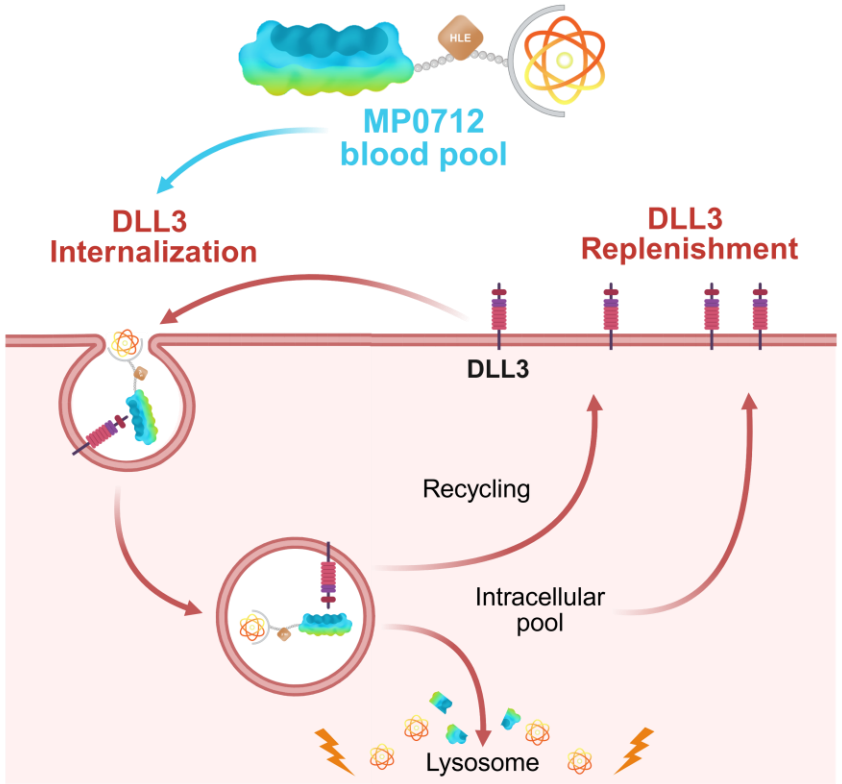


PSMA: Lückerath et al., JNM 2018; Kwon et al, Journal of Biomedical Optics 2023. DLL3 quantification carried out in-house, on NCI-H82 tumors, n=6.
Internalization of DARPins labelled with anti-DARPin Fab-Alexa 488 conjugate into *SHP-77 human SCLC cells, into **hDLL3-HEK cells.
MFI, Mean Fluorescence Intensity; PSMA prostate-specific membrane antigen.

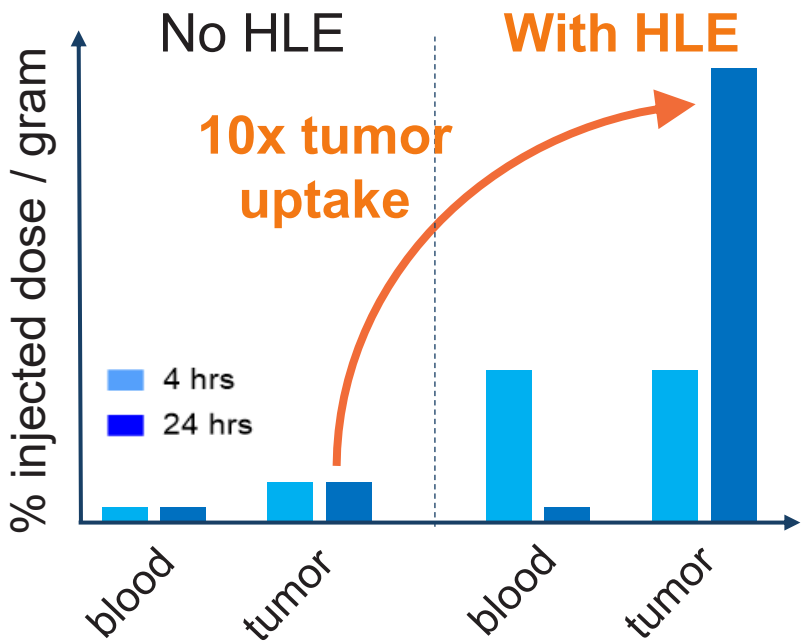
MP0712: High Tumor Uptake via DLL3 Internalization - Replenishment and Half-Life Engineering



- DARPin
- Nucleus
- Endosome



Optimal half-life for tumor uptake of MP0712

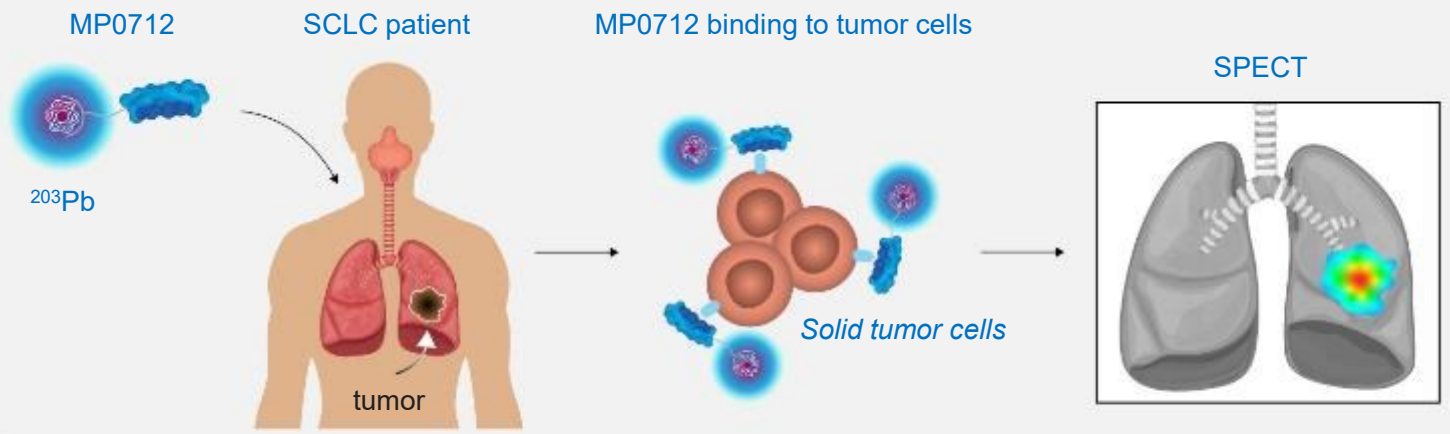


DARPin half-life optimization allows to leverage rapid internalization & replenishment of DLL3 for high MP0712 accumulation in tumors

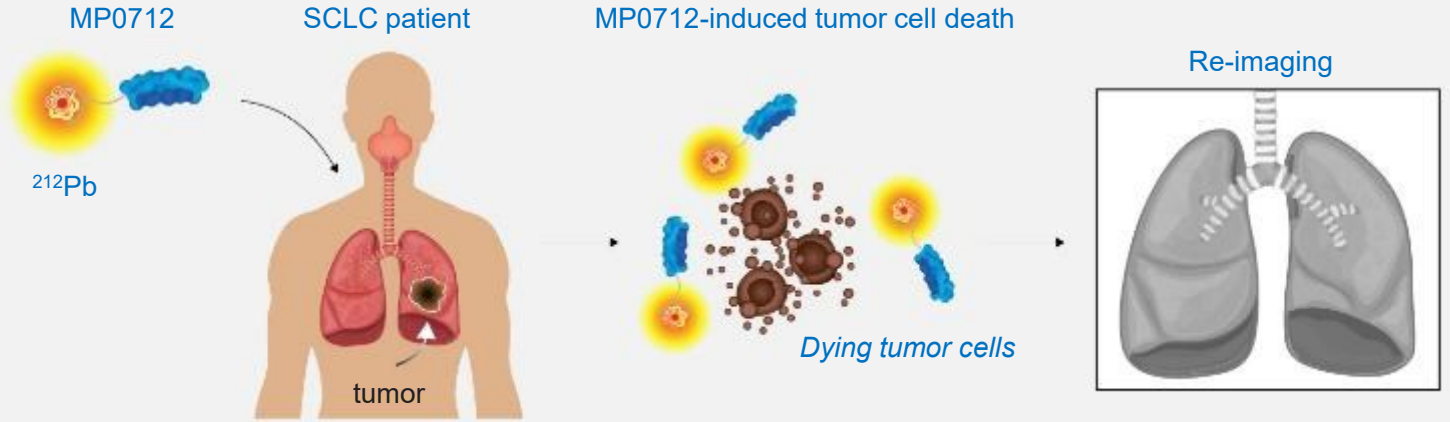
Immunofluorescence co-staining of anti-DARPin antibody, an early endosomal marker (EEA1) and cell nucleus marker (DAPI) after 3 h incubation. Schematic for uptake in blood and tumors with and without HLE in mice – data presented at multiple conferences in 2024.

MP0712 Development Pathway

1. Imaging



2. Treatment



Named Patient Access Program:

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

*Request from NuMeRI, Pretoria, South Africa**

Phase 1/2a Study:

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

NuMeRI, Nuclear Medicine Research Infrastructure; SCLC, small cell lung cancer; SPECT, single-photon emission computed tomography.

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

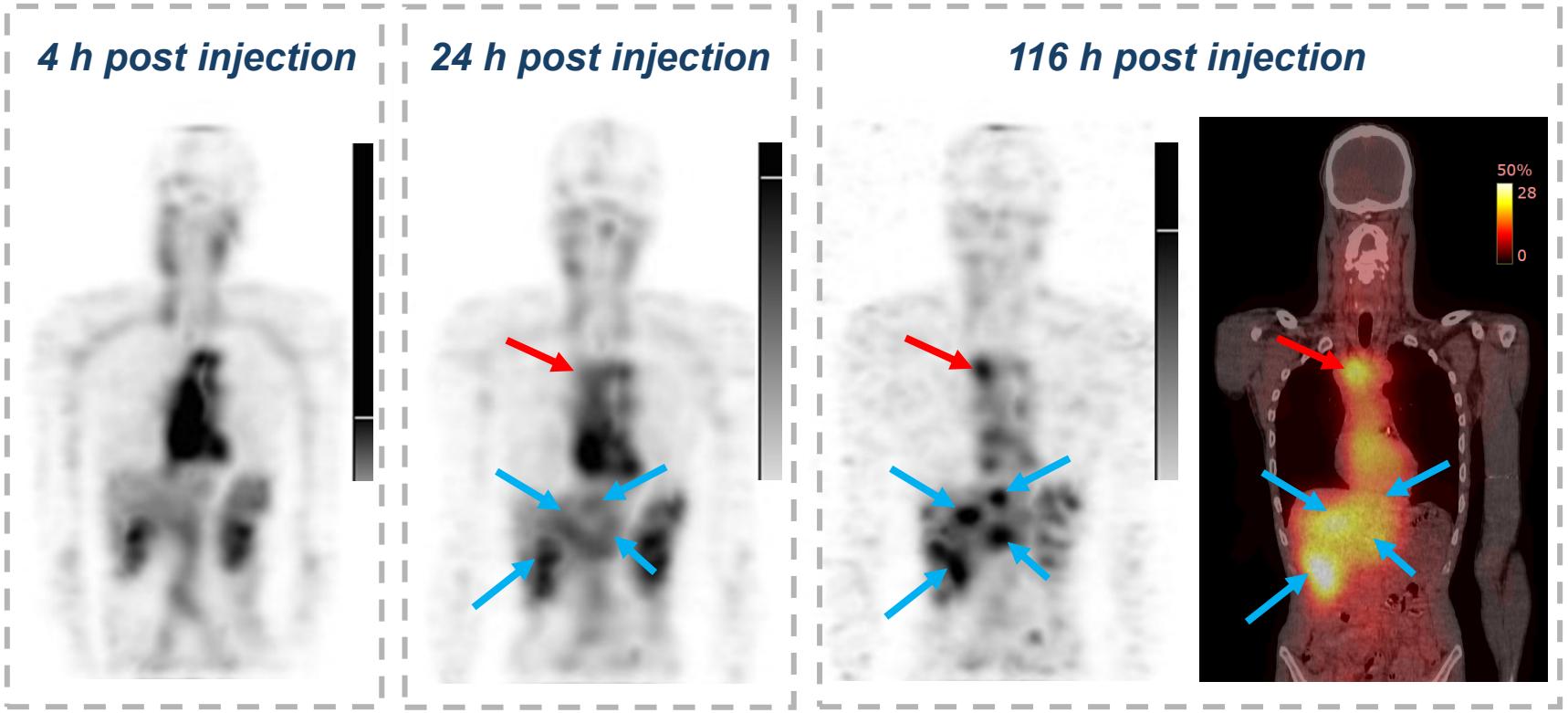
- Radio- & chemotherapy

Dosing

- 185 MBq of ^{203}Pb-MP0712

Result

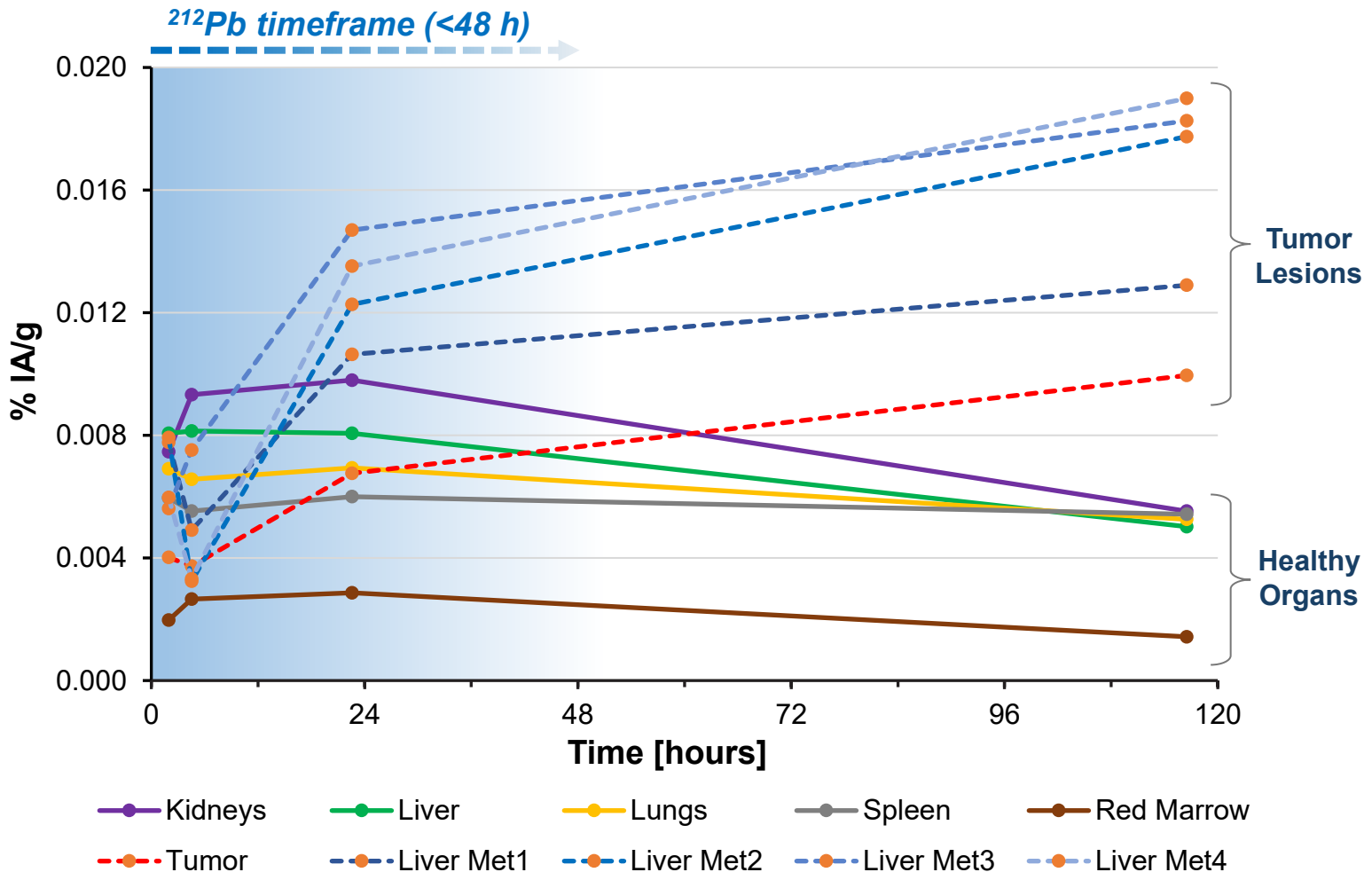
- Stage IV by MP0712 - SPECT with 4 liver mets



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

Patient imaged as part of a Named Patient Access Program at NuMeRI, Pretoria, South Africa.
Example of patient case series presented with courtesy of Prof. Dr. M. Sathekge.
Complete SPECT/CT imaging data set presented at TWC 2026 by Dr. Joseph Kabunda (Abstract-ID 207).

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

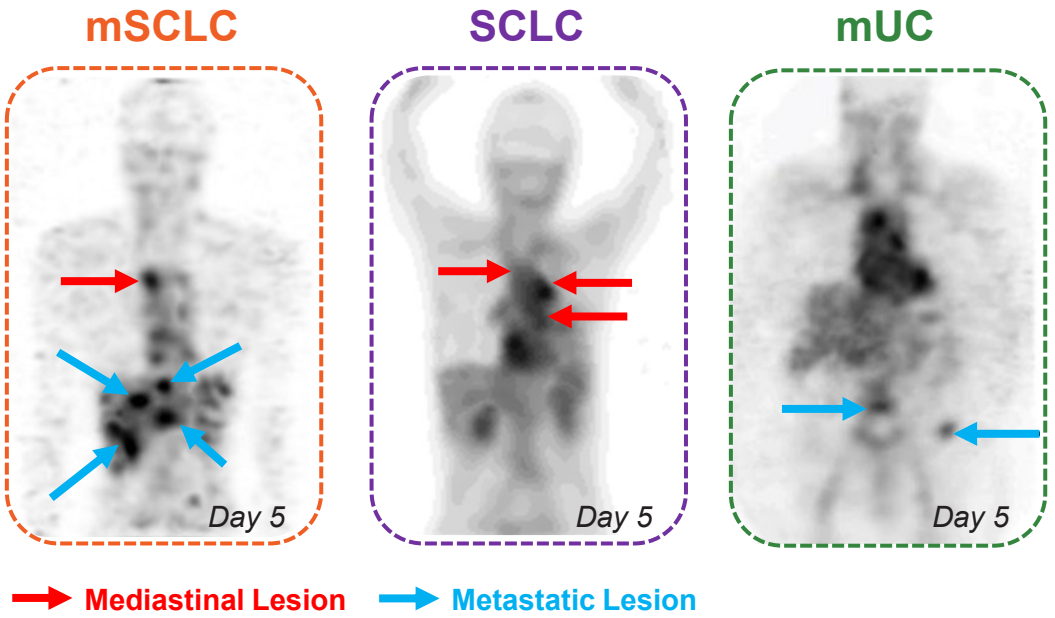


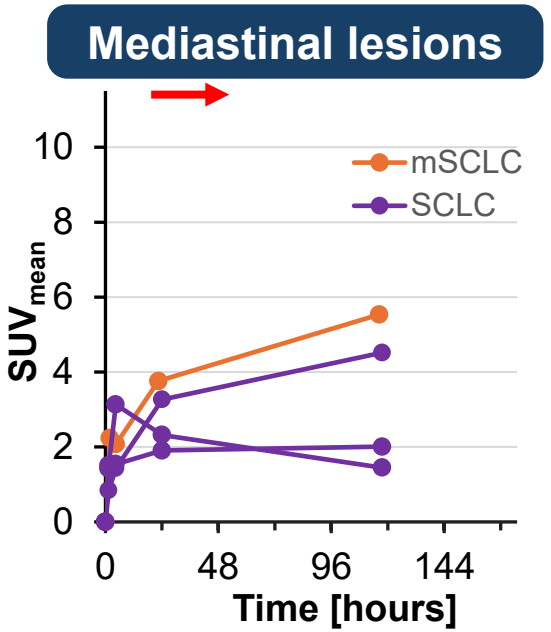
- **Continued tumor uptake** during imaging period (up to 116 h)
- **Higher uptake in liver metastases** as compared to primary lesion
- **Washout from healthy organs** visible from 24 h onwards
- Healthy organ profile consistent with profile observed in other patients

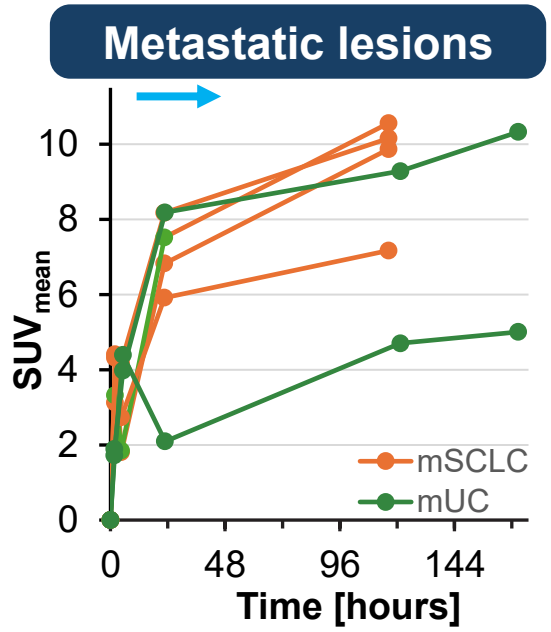
Lizak et al. TWC 2026.

Quantitative image analysis performed by RAPID, LLC.
mSCLC, metastatic small cell lung cancer.

^{203}Pb-MP0712 Uptake in Tumor Lesions







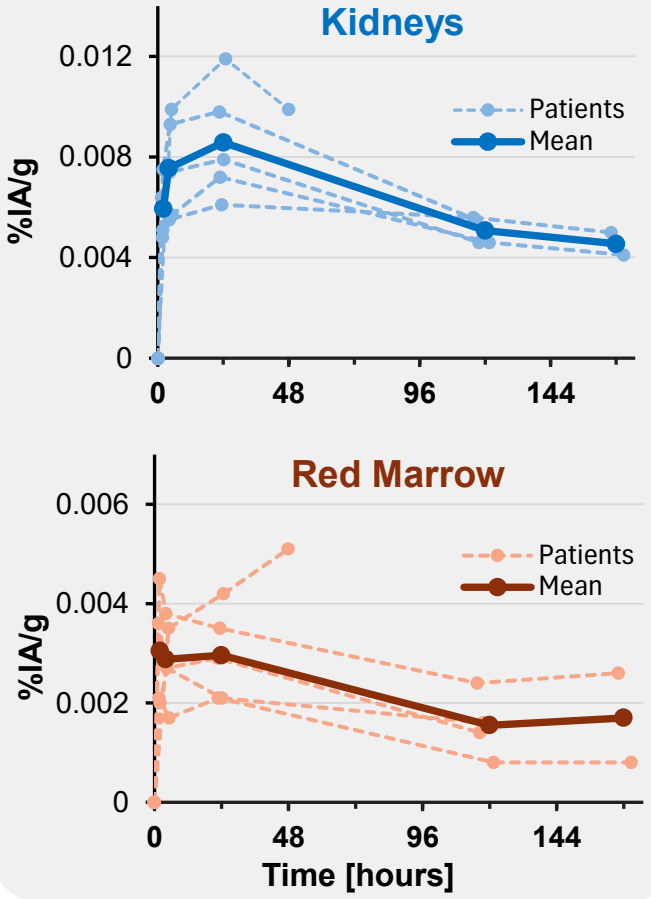
- **Progressive uptake** of MP0712 across different tumor types
  - ~80% of uptake reached at 24 h
  - **Strong tumor retention** with continued uptake during imaging period (up to 7 days)
- **Preferential uptake in metastatic lesions**
  - ➢ **Phase 1 study** in US expected to enroll **metastatic SCLC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

Complete SPECT/CT imaging data set presented at TWC 2026 by Dr. Joseph Kabunda (Abstract-ID 207).
Quantitative image analysis performed by RAPID, LLC.
* SPECT imaging with ^{203}Pb does not allow reliable SUV_{max} determination.

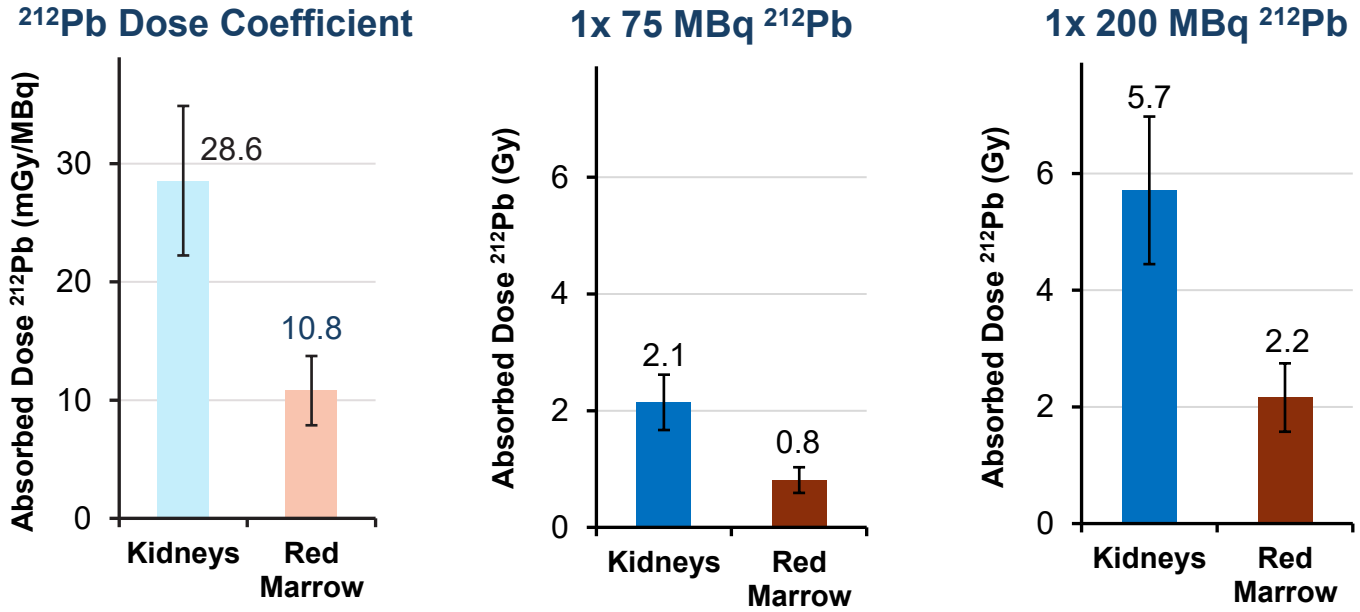
mUC, metastatic urothelial bladder cancer; SUV, standard uptake volume.

MP0712 Organ Dosimetry and Projection to Phase 1

^{203}Pb Time-activity curves



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



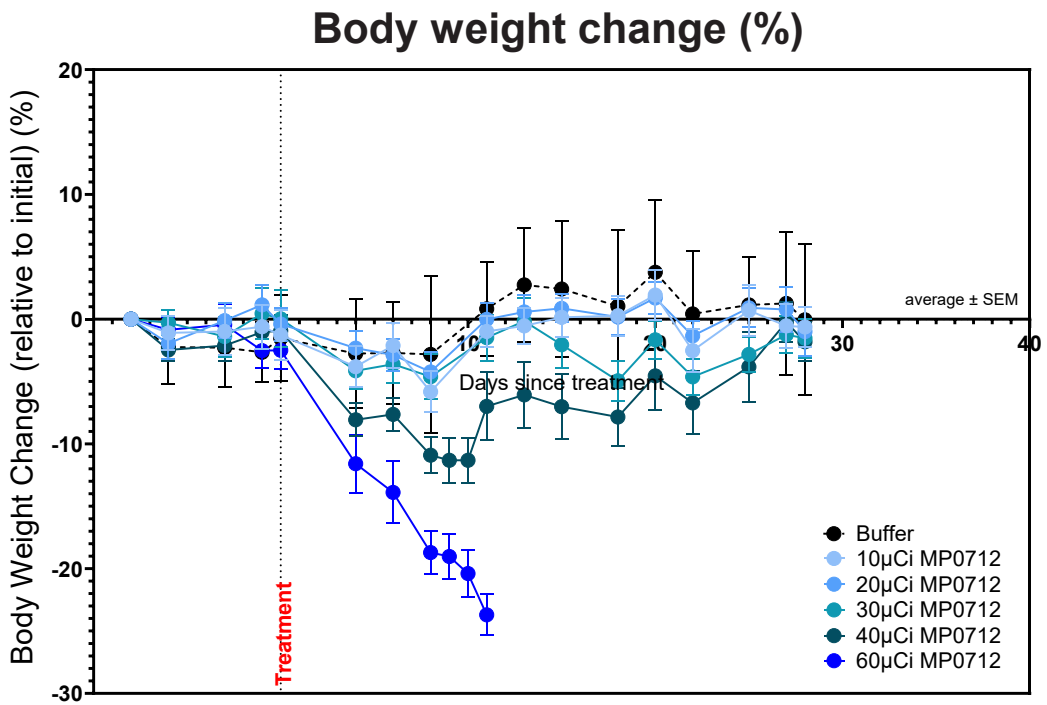
- At Phase 1 starting dose (75 MBq) and at highest anticipated single dose (200 MBq) all healthy organs are within EBRT limits

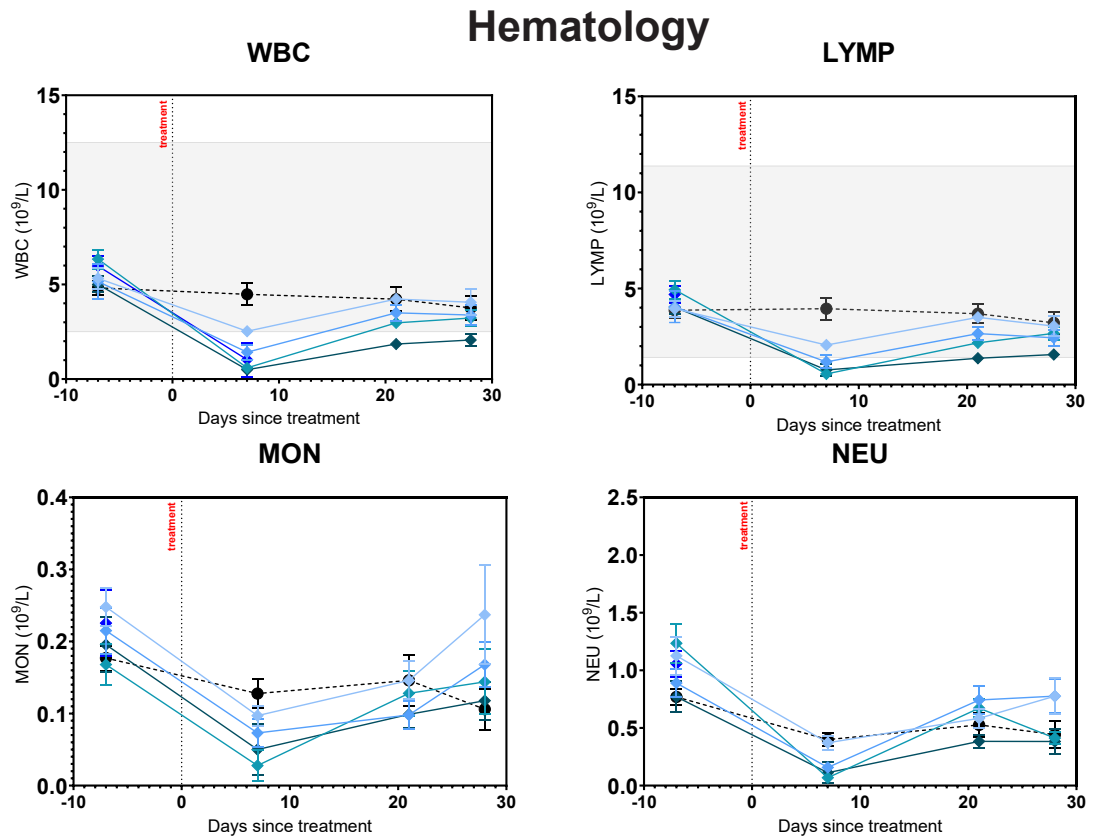
➢ Monitor hematologic recovery to guide repeated dosing strategies

Dosimetry calculations for ^{212}Pb performed by RAPID, LLC on 5 evaluable patients; RBE = 5.
Complete dosimetry dataset presented at TWC 2026 by Dr. Kamo Ramonaheng (Abstract-ID 260).

EBRT, external beam radiation therapy; RBE, relative biologic effectiveness.

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 µCi / 1.11 MBq well tolerated**

Croset A. et al. AACR 2025.

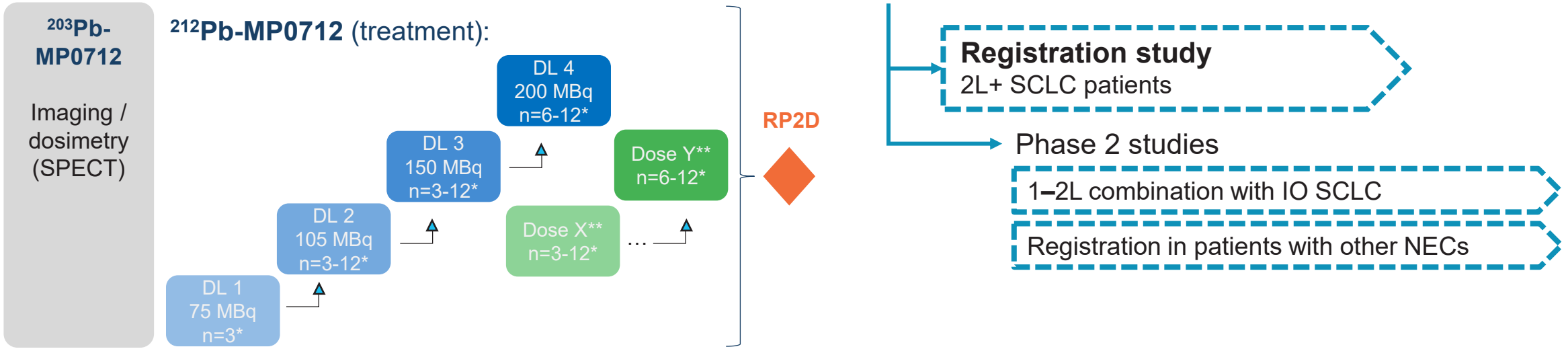
MP0712 DRF study done in WT mice
^{212}Pb-DOTAM-DARPin injected once from 10 to 60µCi.

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

Phase 1: Dose Escalation
Main objectives: safety, RP2D
N=15–39 patients SCLC and lung LC NEC; N=9-39 patients epNEC

Phase 2a: Dose Expansion and PoC
Main objectives: efficacy signals, confirm safety and RP2D
N=30 patients SCLC and NEC



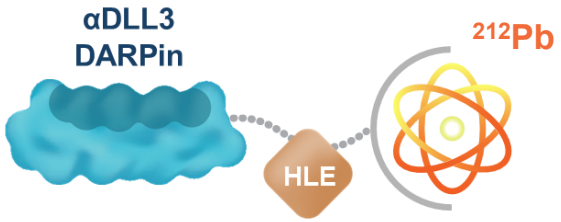
* Evaluable patients (Bayesian Logistic Regression Model guided dose escalation)

**epNEC to start at a dose level previously tested in SCLC or LC NEC of lung at which a first signal of pharmacological activity is detected. RP2D for epNEC is anticipated to be same as RP2D for SCLC/LC NEC of lung.

1/2 L, 1st/2nd line; DL, dose level; IO, immuno-oncology; LC NEC, large cell neuroendocrine cancer; PoC, proof-of-concept; RP2D, recommended phase 2 dose.

MP0712 Conclusions

^{212}Pb 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

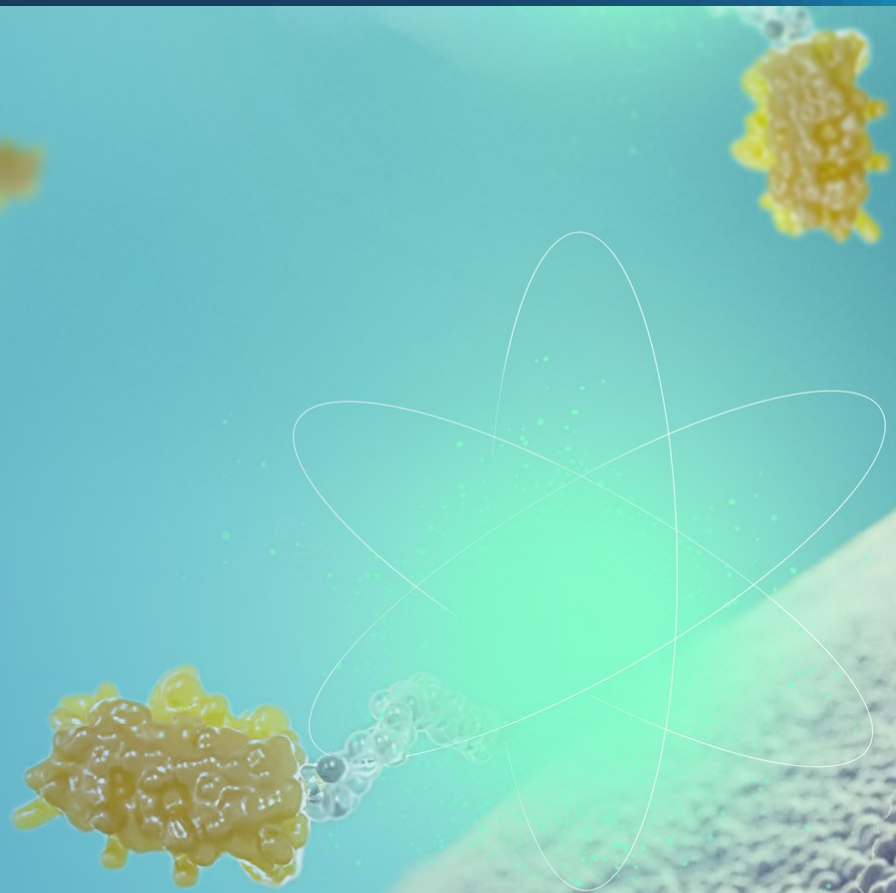
Outlook

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

MOLECULAR partners

Outlook

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



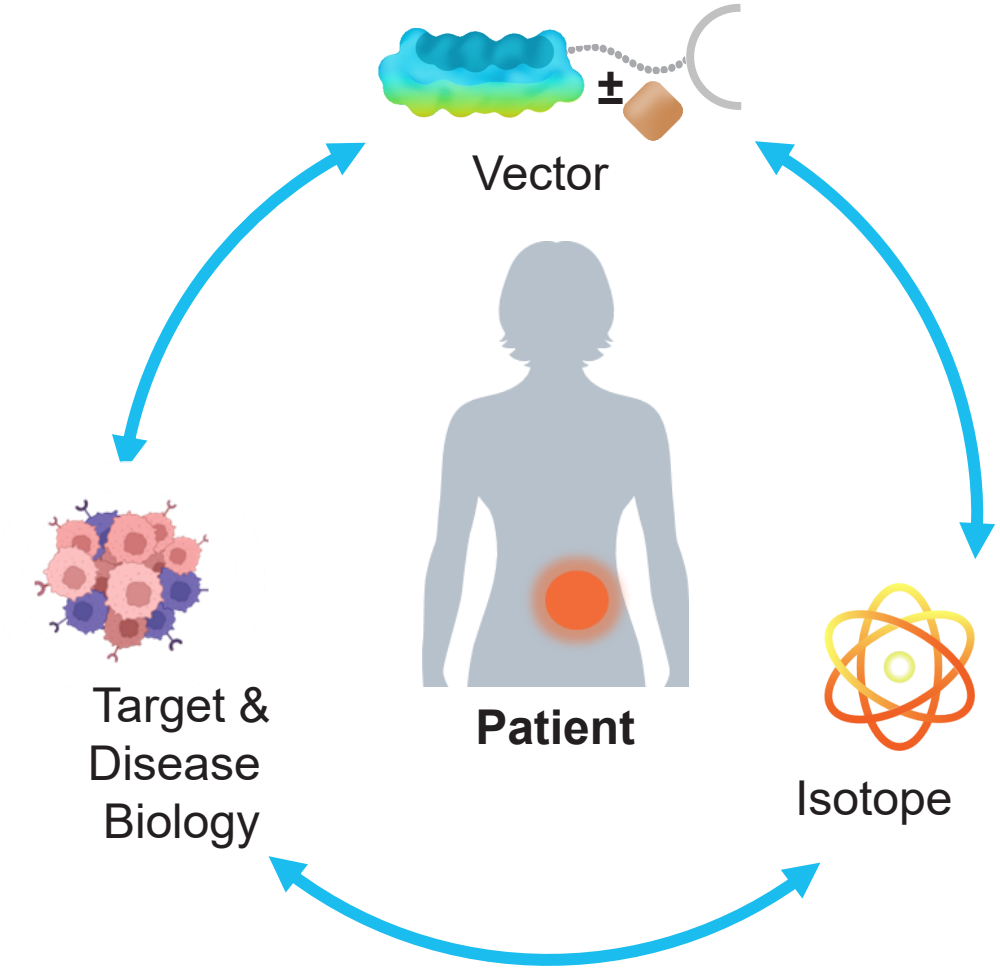
Learnings for Designing Radio-DARPin Therapeutics for Patients

(1) Deep understanding of disease & target biology

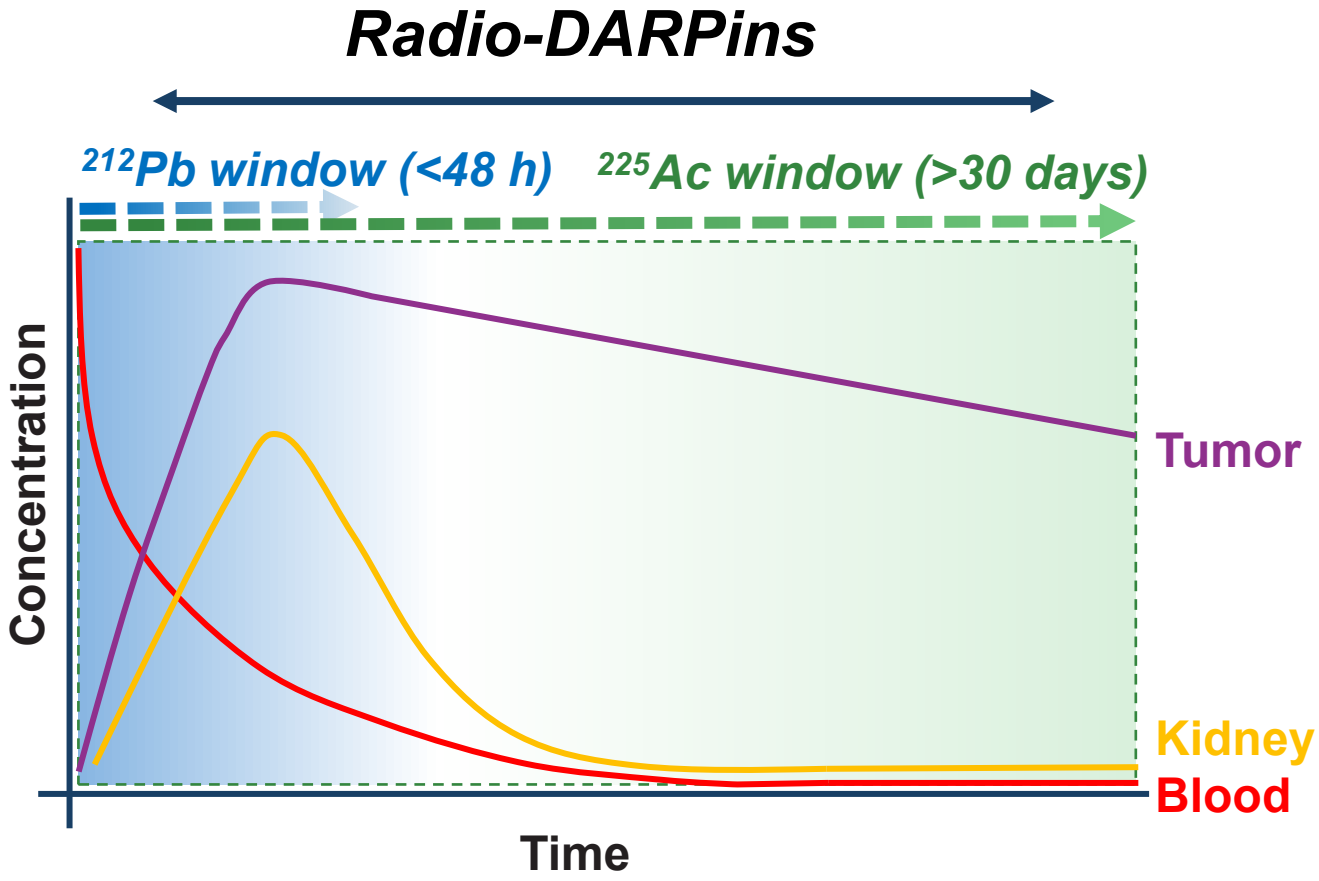
(2) Versatility in vector design that address biology

(3) Optionality to select isotope that best matches vector characteristics and biology

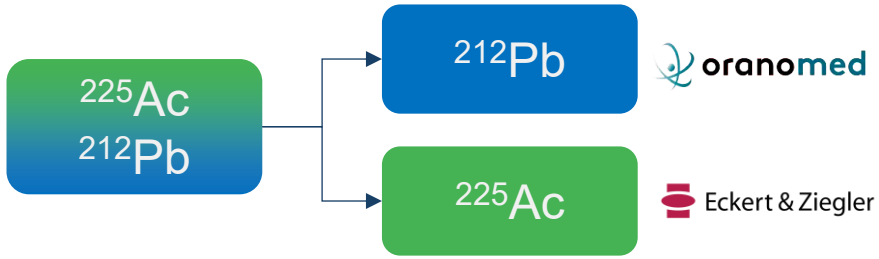
(4) Rapid, iterative empirical testing to identify the most effective solution



Long Tumor Retention Make DARPins Alpha-Agnostic

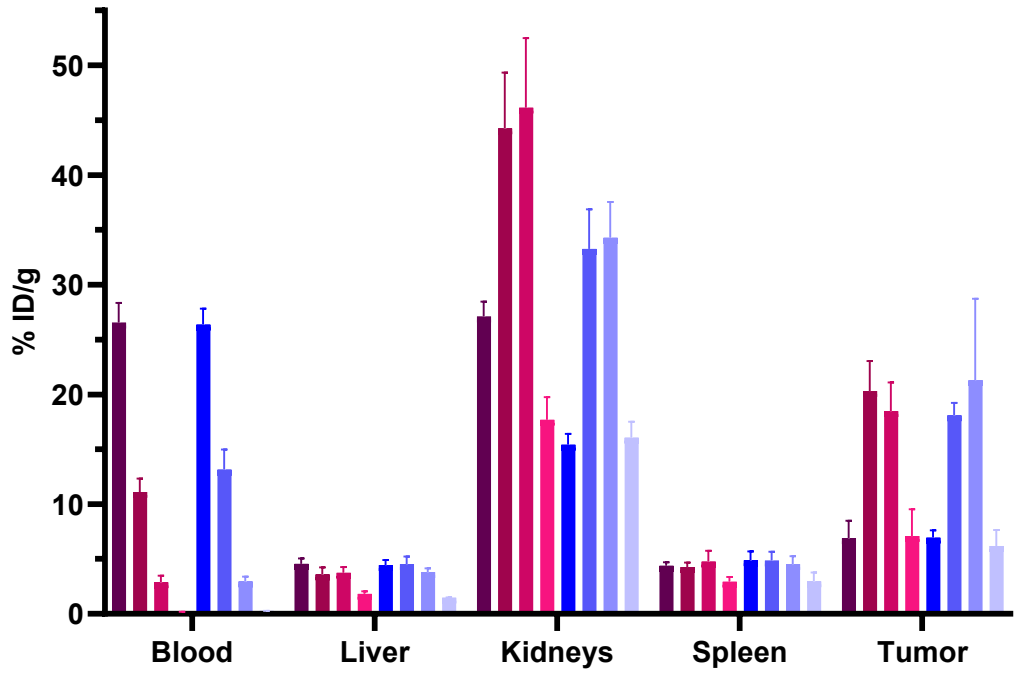


- Based on ^{203}Pb-MP0712 learnings DARPin profile can work for both ^{212}Pb and/or ^{225}Ac
- Opportunity to evaluate both isotopes in parallel and decide on the best isotope with data

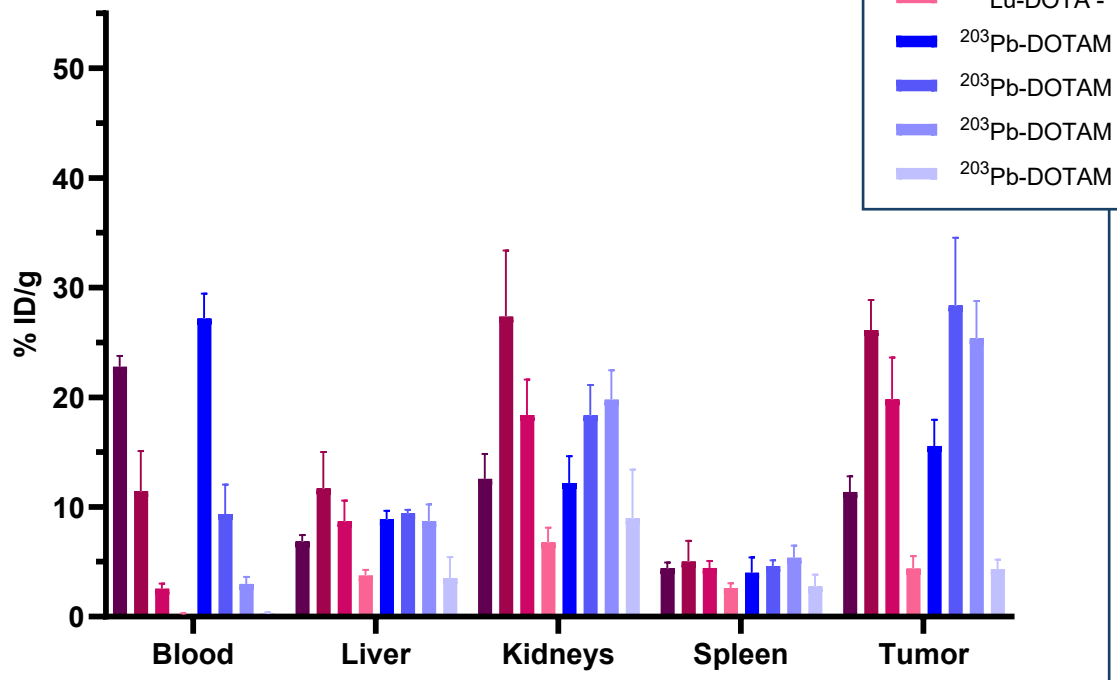


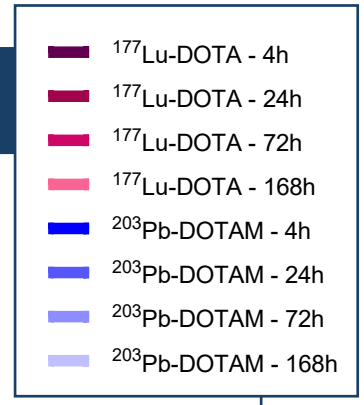
Radio-DARPins Enable Chelator and Isotope Flexibility

Radio-DARPin against Target A



Radio-DARPin against Target B



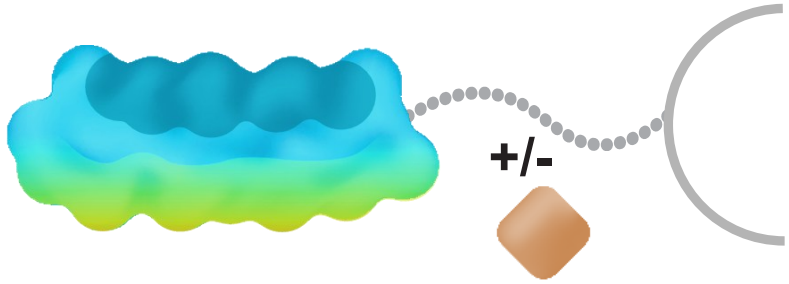


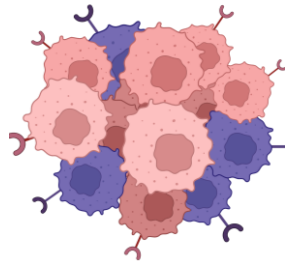
- Comparable BioD profile using ^{203}Pb-DOTAM and ^{177}Lu-DOTA with similar uptake and washout rates
- Assumption: ^{203}Pb-DOTAM and ^{177}Lu-DOTA can be used as surrogates for the therapeutic candidates (^{212}Pb / ^{225}Ac)
- Flexibility to select therapeutic isotope based on pre-clinical and/or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

MOLECULAR partners

Biodistribution (BioD) studies done in different mouse models expressing respective tumor target.
Target A: ^{203}Pb-DOTAM-DARPin injected 1 x 20mCi at 0.01mg/kg and ^{177}Lu-DOTA-DARPin injected 1 x 50µCi at 0.01mg/kg.
Target B: ^{203}Pb-DOTAM-DARPin injected 1 x 4mCi at 0.01mg/kg and ^{177}Lu-DOTA-DARPin injected 1 x 4µCi at 0.01mg/kg.

Radio-DARPin Flexibility to Address Target & Disease Biology





Vector + **Modifier**
(e.g. half-life extension)

Mono

2-in-1

Multi

Albumin-binding DARPin

LMW
(PK/PD modifying chemical moieties)

Naked
(no HLE)

Tailored

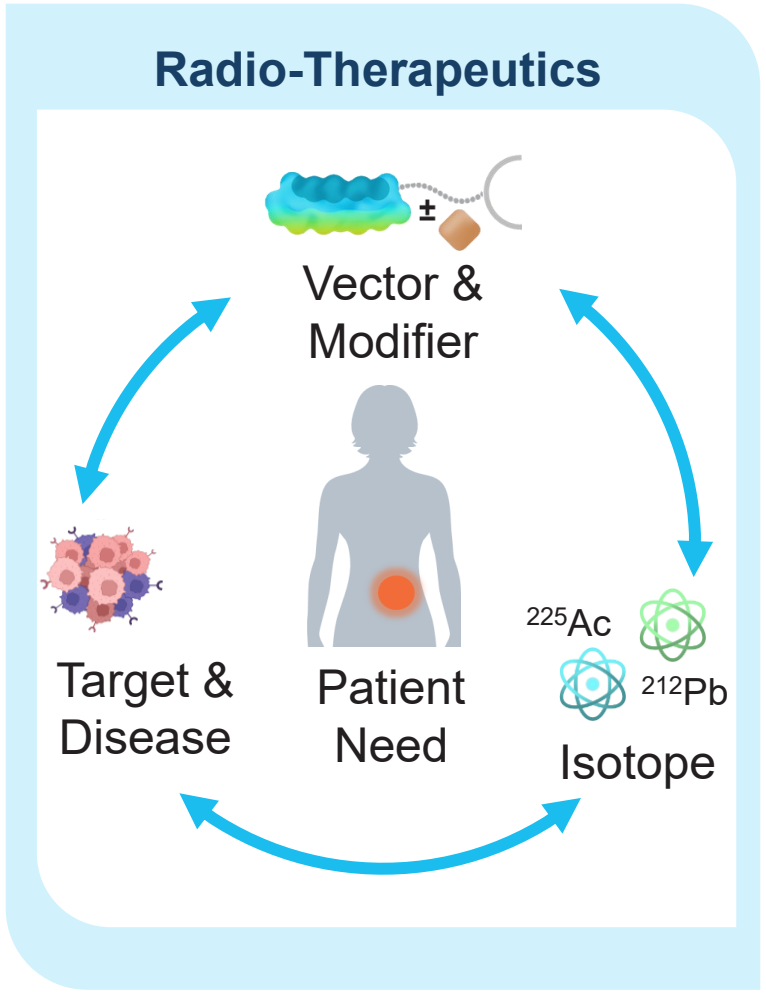
Target & Disease Biology

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
- …

HLE, half-life extension; LMW, low molecular weight; PK/PD, pharmacokinetics/pharmacodynamics.

Building a Diverse Radiotherapeutics Pipeline



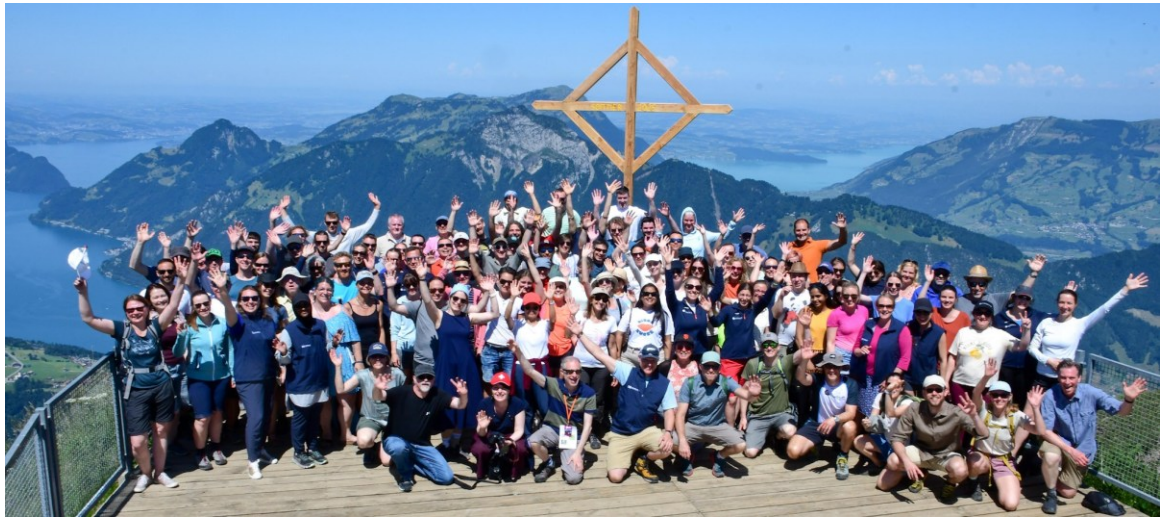
CANDIDATE	RESEARCH	PRE-CLINICAL	PHASE 1	PHASE 2
MP0712	**SCLC & NECs** *212Pb x DLL3*		oranomed *Co-development**	Initial PhI data in 2026
MP0726	**Ovarian Cancer** *212Pb x MSLN*		oranomed *Co-development**	Progress MP0726 into FIH
Undisclosed Programs (Solid Tumors)	**Radio - C**	212Pb		
	Radio - D	225Ac		
	Radio - E	225Ac 212Pb		
	Radio - F			

Evaluate Radio-DARPin candidates in alpha-agnostic manner and nominate new RDT programs

BioD, biodistribution; FIH, first in human; NEC, neuroendocrine cancer; PK, pharmacokinetic; SCLC, small cell lung cancer.

Acknowledgments

Team at Molecular Partners AG



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Patients and their Families

MOLECULAR partners

Thank you for your interest!

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