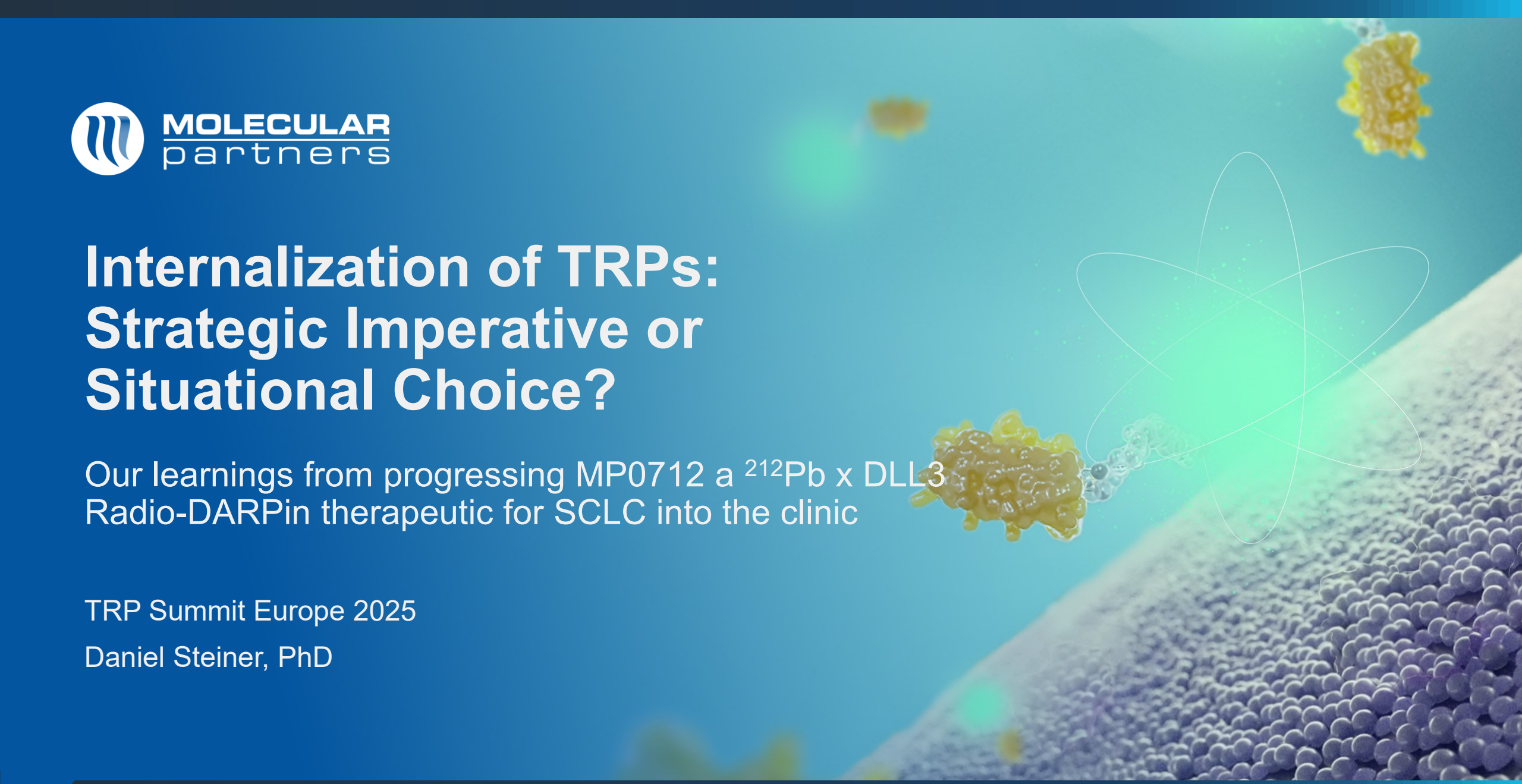
MOLECULAR partners

Internalization of TRPs: Strategic Imperative or Situational Choice?

Our learnings from progressing MP0712 a ^{212}Pb x DLL3 Radio-DARPin therapeutic for SCLC into the clinic



TRP Summit Europe 2025

Daniel Steiner, PhD

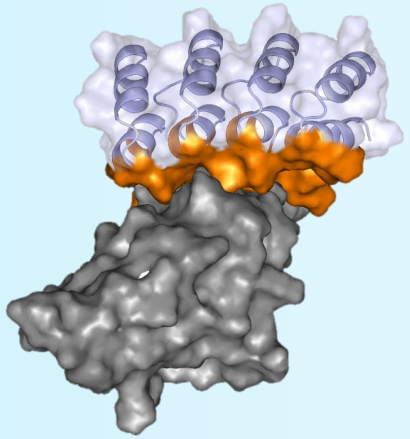
Disclaimer

This presentation contains forward looking statements. Any statements contained in this presentation that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, as amended, including without limitation: implied and express statements regarding the clinical development of Molecular Partners' current or future product candidates; expectations regarding timing for reporting data from ongoing clinical trials or the initiation of future clinical trials; the potential therapeutic and clinical benefits of Molecular Partners' product candidates and its RDT and Switch-DARPin platforms; the selection and development of future programs; Molecular Partners' collaboration with Orano Med including the benefits and results that may be achieved through the collaboration; and Molecular Partners' expected business and financial outlook, including anticipated expenses and cash utilization for 2025 and its expectation of its current cash runway and the expected use of proceeds from the October 2024 offering. These statements may be identified by words such as "aim", "anticipate","expect", "guidance", "intend", "outlook", "plan", "potential", "will" and similar expressions, and are based on Molecular Partners' current beliefs and expectations. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Some of the key factors that could cause actual results to differ from Molecular Partners' expectations include its plans to develop and potentially commercialize its product candidates; Molecular Partners' reliance on third party partners and collaborators over which it may not always have full control; Molecular Partners' ongoing and planned clinical trials and preclinical studies for its product candidates, including the timing of such trials and studies; the risk that the results of preclinical studies and clinical trials may not be predictive of future results in connection with future clinical trials; the timing of and Molecular Partners' ability to obtain and maintain regulatory approvals for its product candidates; the extent of clinical trials potentially required for Molecular Partners' product candidates; the clinical utility and ability to achieve market acceptance of Molecular Partners' product candidates; the potential that Molecular Partners' product candidates may exhibit serious adverse, undesirable or unacceptable side effects; the impact of any health pandemic, macroeconomic factors and other global events on Molecular Partners' preclinical studies, clinical trials or operations, or the operations of third parties on which it relies; Molecular Partners' plans and development of any new indications for its product candidates; Molecular Partners' commercialization, marketing and manufacturing capabilities and strategy; Molecular Partners' intellectual property position; Molecular Partners' ability to identify and in-license additional product candidates; unanticipated factors in addition to the foregoing that may cause Molecular Partners' actual results to differ from its financial and business projections and guidance; and other risks and uncertainties set forth in Molecular Partners' Annual Report on Form 20-F for the year ended December 31, 2024 and other filings Molecular Partners makes with the SEC from time to time. These documents are available on the Investors page of Molecular Partners' website at www.molecularpartners.com. In addition, this presentation contains information relating to interim data as of the relevant data cutoff date, results of which may differ from topline results that may be obtained in the future.

Any forward-looking statements speak only as of the date of this presentation and are based on information available to Molecular Partners as of the date of this release, and Molecular Partners assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

The DARPin Modality and Our Focus

DARPin
Designed Ankyrin Repeat Protein



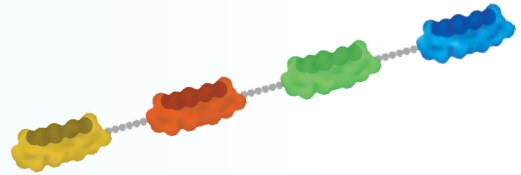
We pioneer DARPins as a new class of therapeutics

- 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

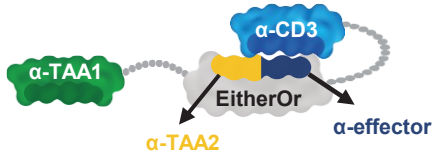
Our company focus

Radio-DARPin Therapeutics

Multi-specific immune cell engagers



Conditional “Switch” T cell engagers



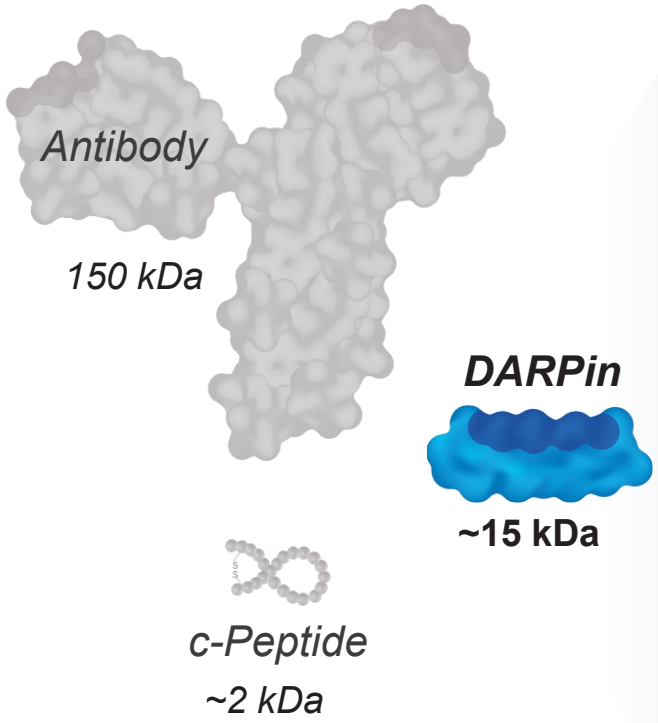
Our Pipeline – Targeted DARPin Therapeutics for Patients

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**				
Next-Gen Immune Cell Engagers	**MP0533**	**r/r AML and AML/MDS** *CD33 x CD123 x CD70 x CD3*				
	Switch-DARPin T Cell Engager	*CD3 x costim x TAAs*				
	MP0621 (Switch-DARPin)	**HSCT** *cKit x CD16a x CD47*				
	MP0317	**Advanced Solid Tumors** *FAP x CD40*				

MOLECULAR partners

*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; HSCT, hematopoietic stem cell transplant; MDS, myelodysplastic syndrome; MSLN, mesothelin; NEC, neuroendocrine cancer; r/r, relapsed/refractory; SCLC, small cell lung cancer; TAA, tumor-associated antigen.

DARPin Features for Tumor Targeting of Radionuclides

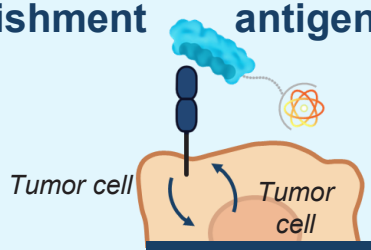


DARPins are small binding proteins derived from natural ankyrin repeat proteins

DARPin key features

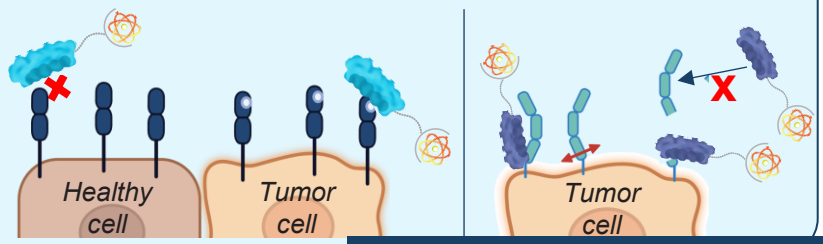
- ✓ **Small size** (~15 kDa)
  - → *Deep tumor penetration*
  - → *Short systemic half-life*
- ✓ **Broad target range** (100's)
  - → *Opening indications*
- ✓ **High affinity** (low pM range)
  - → *Long tumor retention*
- ✓ **High selectivity**
  - → *Low normal tissue*
- ✓ **High stability**
  - →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

Low density – rapid internalization & replenishment antigens



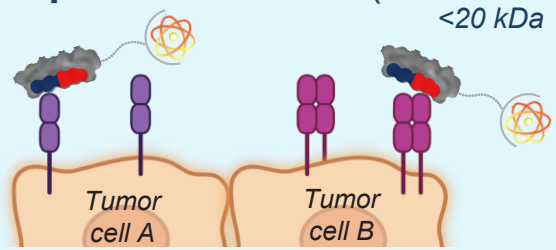
MP0712 (^{212}Pb x DLL3)

High selectivity to tumor antigens



MP0726 (^{212}Pb x MSLN)

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



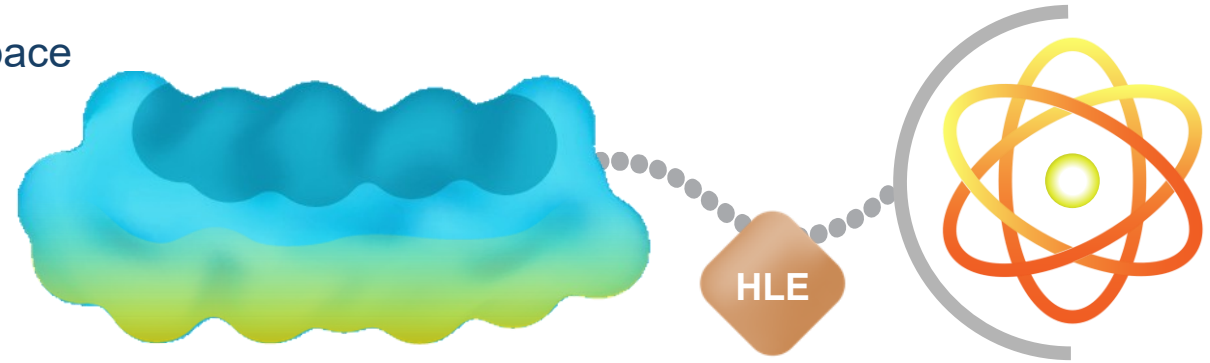
DARPin: Designed Ankyrin Repeat Protein
Binz HK. et al, *J Mol Biol*, 2003

Created in part with BioRender.com

Radio DARPin Platform Versatile Therapeutic Candidates

INTRINSIC DARPin PROPERTIES FOR RADIOPHARMACEUTICALS

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



THERAPEUTIC ISOTOPEs

- Matching tumor type, target biology and vector properties

SURFACE ENGINEERINGs

- Enabled by high stability
- Reduce kidney accumulation

HALF-LIFE EXTENDERs

- Tailored systemic exposure
- Promote tumor uptake

BioD, biodistribution; HLE, half-life extender

Our Development Engine for Radio-DARPin Candidates

4th Gen Library
Designed for low kidney and low immunogenicity

Display Technology
DARPin selection from large libraries (10^{12})

Deep Sequencing
NGS processes tailored to DARPins

Data Mining
Select best hit panel from millions of options

In Silico Design
De novo computational design of DARPins

Surface Engineering
Candidate optimization for low kidney

Developability
Assess developability & immunogenicity

Radio DARPin hit panel
High affinity and diversity

Established Databases for AI-Driven Learning Loops
Integration of learnings from >2500 treated patients, BioD studies, biophysical assessments, NGS… into libraries and DARPin generation processes

— *Parallel* —

KDXXGXTP
VL I
AI S
WF T
ML D

Screening BioD
BioD studies to assess tumor accumulation and retention in vital organs

Lead Optimization
High throughput Mini-library & AI/ML-driven evolution process for all candidates

Combined Data-Driven Lead Selection
Expeditious data-driven identification & optimization of best performing candidates (minimize time-consuming cycles)

Modulators & Isotopes

Radio-Isotope
Radio isotope matching exposure and BioD

Linker
Various linker chemistries matching need

HLE

Half-Life Extension
Toolbox with different strengths & properties

Chelator
Different chelator options matching radio-isotope

AI / ML, artificial intelligence / machine learning;
BioD, biodistribution; NGS, next generation sequencing.

Rationale for Developing ^{212}Pb-based RDTs

oranomed
^{212}Pb for Targeted Alpha Therapy

^{212}Pb has beneficial properties as radioisotope [1]

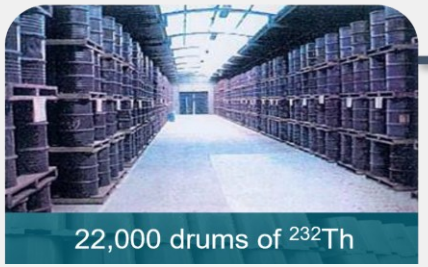
1) **Efficacy** – short decay half-life is leading to high energy deposition on tumor in short time frame, spares infiltrating immune cells and might be beneficial for early combination with immunotherapy
2) **Safety** – clean decay chain – ^{212}Pb is an alpha precursor with limited release of free daughter radionuclides
3) **Waste management** – less problematic thanks to short half-life

Orano Med as leader in ^{212}Pb targeted α-therapies

- Independent, unlimited supply of ^{212}Pb
- Regional manufacturing capabilities to commercial
- Clinical capabilities demonstrated with ^{212}Pb and AlphaMedix™ in Phase 2 study in collaboration with RadioMedix

Strategic collaboration between MP / OM since 2023

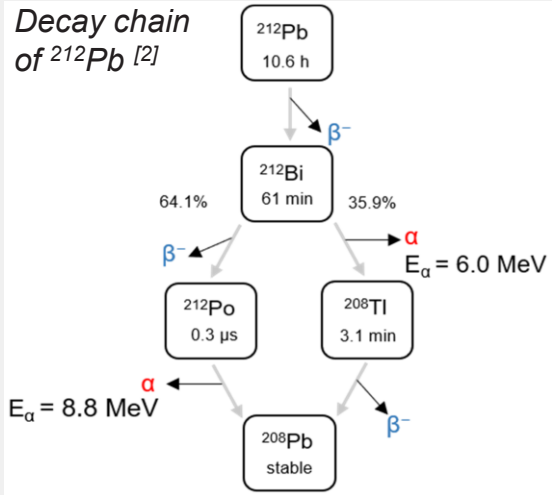
- Global partnership to develop ^{212}Pb Radio-DARPin Therapeutics
- Deep complementary capabilities and expertise
- Pipeline of 10 programs to co-develop



^{232}Th
14 Bn years
↓
^{228}Ra
5,7 years
↓
^{228}Th
1,9 years
↓
^{224}Ra
3,6 days
↓
^{212}Pb
10,6 hours

Lead-212 is obtained **chemically** by **successive extractions and purifications** of the descendants of thorium-232

Decay chain of ^{212}Pb [2]



1. Zimmermann, *J Nucl Med*, 2023.
2. Li et al., *Materials* 2021.

Strong Emerging Clinical Data Supports ^{212}Pb as Therapeutic Isotope

BERLIN 2025 ESMO congress
BERLIN GERMANY
17-21 OCTOBER 2025

"Sustained and clinically meaningful responses (60% ORR) across both RLT-naïve and RLT-exposed patients with unresectable or metastatic GEP-NETs"

TRP presentation Wed 4pm

Volker Wagner
Chief Medical Officer
Oranomed

Perspective Therapeutics Presents Updated Interim Data from its Ongoing Phase 1/2a Clinical Trial of [212Pb]VMT-α-NET at the ESMO Congress 2025

PERSPECTIVE THERAPEUTICS

"[212Pb]VMT-α-NET continues to demonstrate durable anti-tumor activity and excellent tolerability"

TRP presentation Mo 9:30am

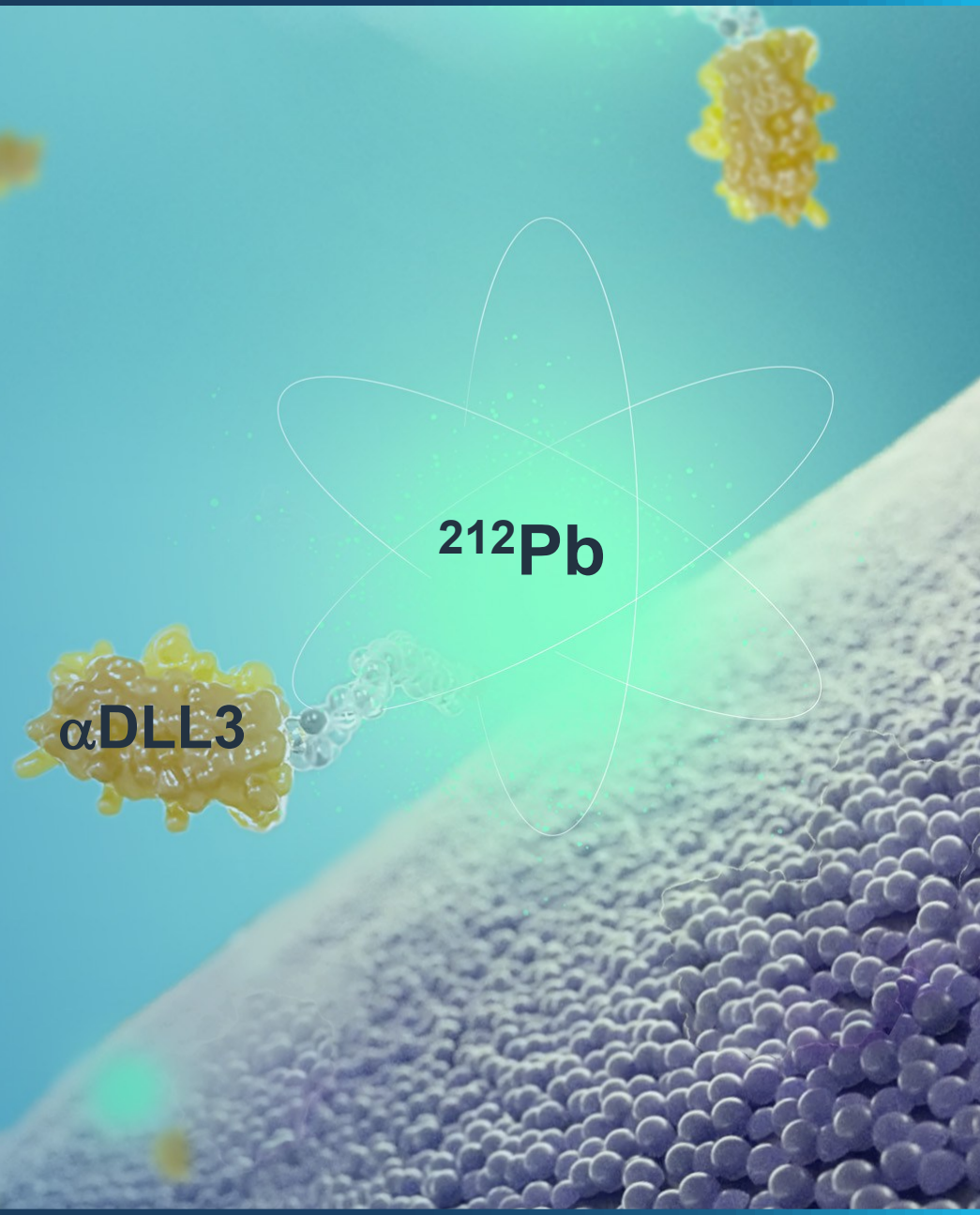
Thijs Spoor
Chief Executive Officer
Perspective Therapeutics

"100% ORR in prostate cancer patients with RECIST-measurable lesions, including two complete responses"

GEP-NET, gastroenteropancreatic neuroendocrine tumor; ORR, overall response rate; RECIST, response evaluation criteria in solid tumors; SSTR2, somatostatin receptor 2.

MOLECULAR partners

Our learnings from progressing MP0712 (^{212}Pb x DLL3) Radio-DARPin therapeutic for SCLC into the clinic



MP0712, the first ^{212}Pb x DLL3 Targeted Radiotherapeutic for SCLC

SCLC: critical unmet need, limited treatment options

- Median progression free survival (mPFS) ~3 months[1,2]
- 5-year overall survival (OS) ~3%[1,2]

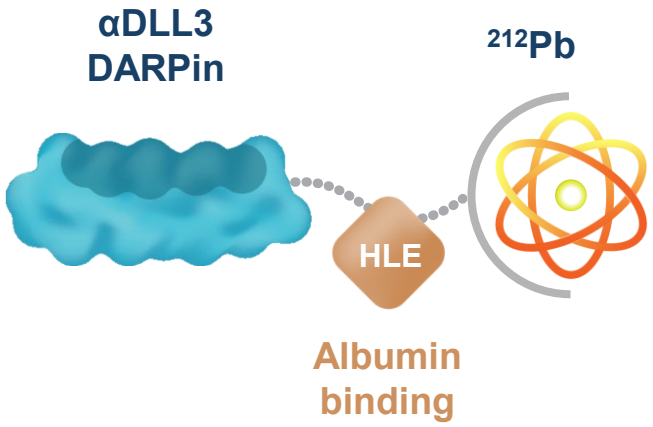
DLL3: a validated target for SCLC

- Expressed in >85% of SCLC patients[3] and in neuroendocrine cancers
- No expression in healthy tissues
- Tarlatamab[4], approved DLL3 targeting drug (T cell engager)
  - ORR ~40%, DOR 9.7 months, PFS 4.3 months
- ZL-1310[5], DLL3 ADC, Ph 1: ORR 68%* in 2L, DOR 6.1 months

MP0712: targeted delivery of alpha radiation

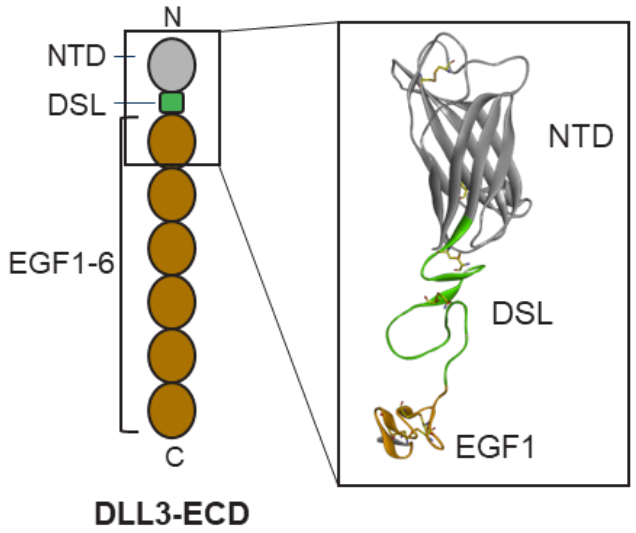
- Specific binding with high affinity & good developability
- Affinity to hDLL3: 0.2 nM by SPR
- Human cell binding: ~2nM on NCI-H82 ± HSA

MP0712 product composition



1.Treatment of refractory and relapsed small cell lung cancer, UpToDate; 2. SEER; 3. Rojo et al., Lung Cancer 2020; 4. Phase 2 DeLLphi-301 study (NCT05060016); 5. Grace K. Dy et al., AACR-NCI-EORTC 2025; *includes 10% unconfirmed reponses; DOR, duration of response; HLE, half-life extension; ADC, Antibody Drug Conjugate; HSA, human serum albumin, ORR, overall response rate; SCLC, small cell lung cancer; SPR Surface Plasmon Resonance.

DLL3 is a Close to Ideal Tumor Target for Radioligand Therapy

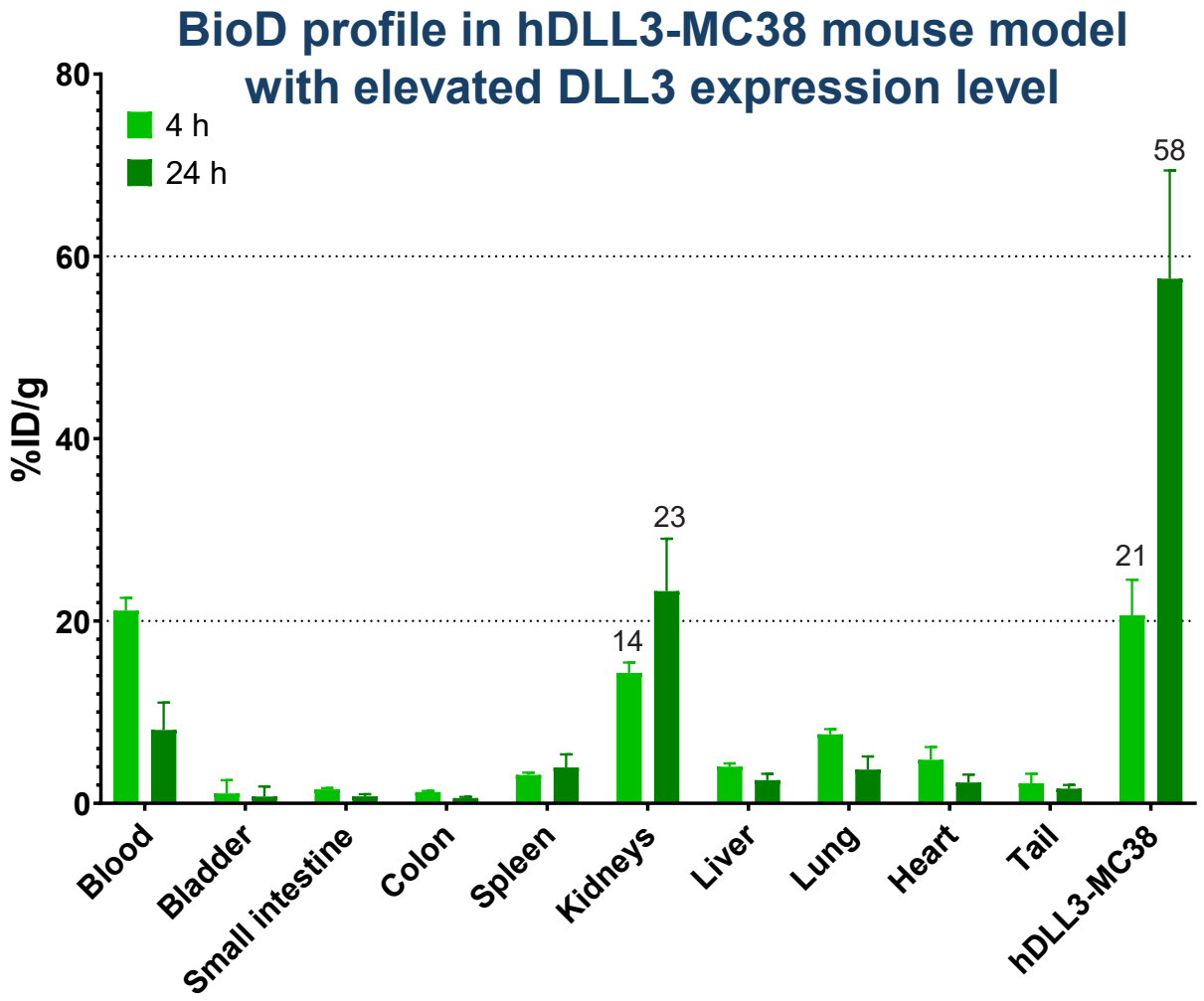


Schematic representation of the extra-cellular domain of DLL3 (DLL3-ECD), and structural model of the NTD, DSL and EGF1 domain

Ideal RLT Target Hallmarks	DLL3 in SCLC & NEC
Drugability shown by TCEs and ADCs	✓✓✓
Low expression in healthy tissue	✓✓✓
Homogenous target expression in tumors	✓✓
High prevalence in disease	✓✓✓
Low amount of shed – soluble target	✓✓✓
Critical role in disease pathogenesis	✓
Maintained expression in metastases	✓✓✓
Maintained in later treatment lines	✓✓✓

DLL3, delta-like ligand 3; NEC, neuroendocrine cancer; RLT, radioligand therapy; SCLC, small cell lung cancer. NTD, N-terminal domain; DSL, Delta/Serrate/Lag-2 domain, EGF1, EGF-like 1 domain

Identification of ^{212}Pb x DLL3 Candidates with Attractive BioD Profile



- Candidate screening and optimization in hDLL3-MC38 model
- High tumor uptake & encouraging BioD profile with **T:K Ratio >2**
- **MP0712 selected as Lead Candidate** for ^{212}Pb x DLL3 Radio-DARPin Therapy

Lizak et al, SNMMI 2024 (oral presentation)

Mice xenografted s.c. with hDLL3-MC38 (Biocytogen)
Dose: 10 µCi of ^{212}Pb at 0.01 mg/kg of DLL3 DARPin
BioD, biodistribution; T:K, tumor to kidney ratio.

DLL3 is a Close to Ideal Tumor Target for Radioligand Therapy

However, low cell surface density on tumor cells is a challenge

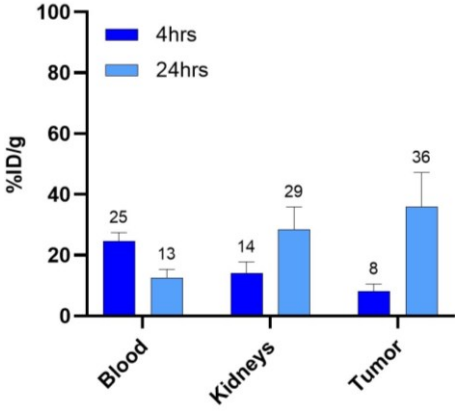
Target density on tumor cell [receptors / cell]	
HER2+ BC	**DLL3 SCLC**
max values in the **millions range**	max values in the **thousands range**

Ideal RLT Target Hallmarks	DLL3 in SCLC & NEC
Drugability shown by TCEs and ADCs	✓✓✓
Low expression in healthy tissue	✓✓✓
High target density on tumor cell surface	×
Homogenous target expression in tumors	✓✓
High prevalence in disease	✓✓✓
Low amount of shed – soluble target	✓✓✓
Critical role in disease pathogenesis	✓
Maintained expression in metastases	✓✓✓
Maintained in later treatment lines	✓✓✓

BC, breast cancer; DLL3, delta-like ligand 3; HER2, human epidermal growth factor receptor; NEC, neuroendocrine cancer; RLT, radioligand therapy; SCLC, small cell lung cancer.

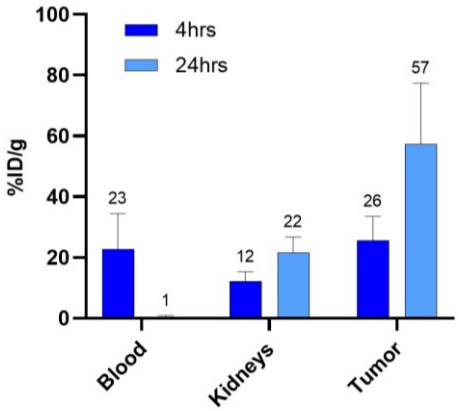
MP0712 Shows Favorable Biodistribution and Tumor Specificity

*R2G2 mice xenografted **s.c.** with* ***NCI-H82***



T:K at 4h = 0.6 / at 24h = 1.2

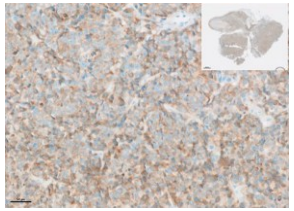
*R2G2 mice xenografted **i.v.** with* ***NCI-H82***



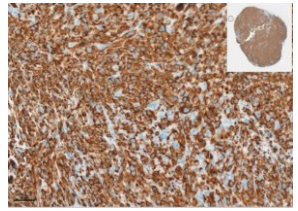
T:K at 4h = 2.1 / at 24h = 2.6

DLL3 expression & distribution by IHC

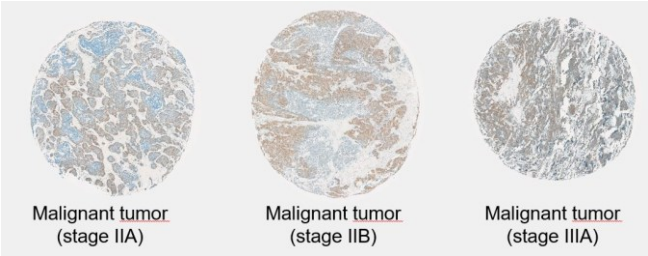
NCI-H82 tumors



hDLL3-MC38 tumors



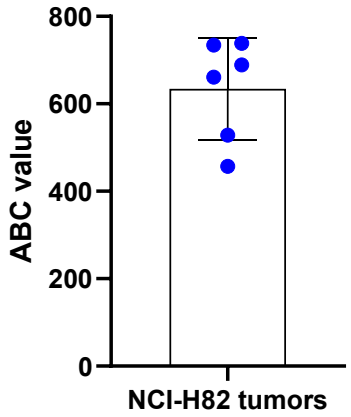
Malignant human SCLC tumors

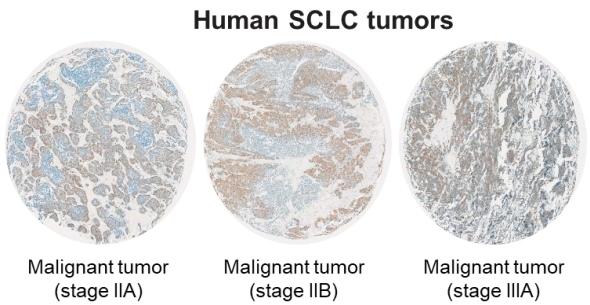


- **MP0712 reaches T:K ratios > 2 in mouse model matching clinically relevant DLL3 expression levels**

High MP0712 Tumor Uptake, Despite low DLL3 Copy Number

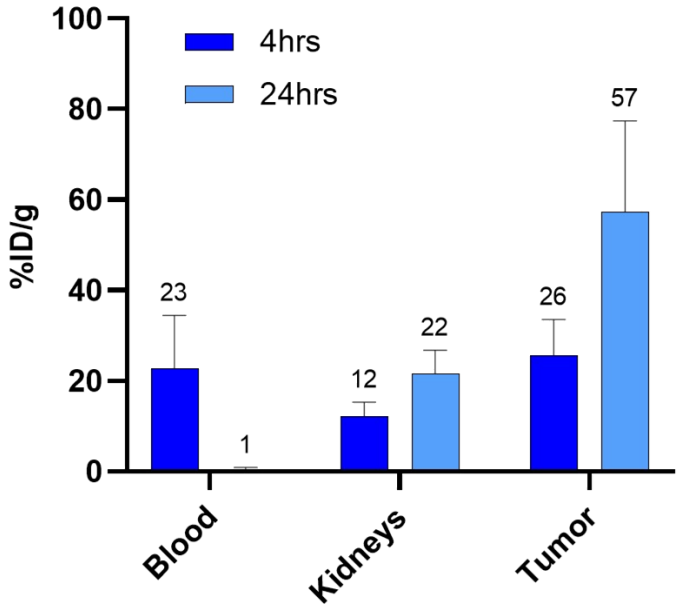
Low DLL3 density on tumor cells
(of <1000 receptors/cell)





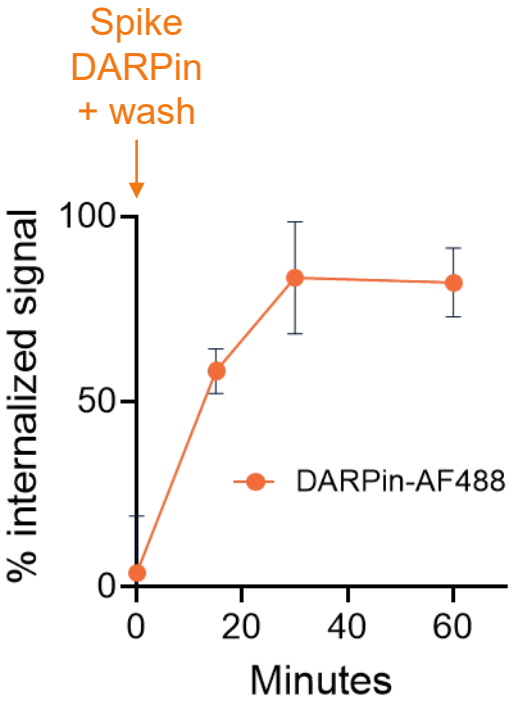
?

High Tumor Accumulation
(MP0712: Tumor > Kidney)

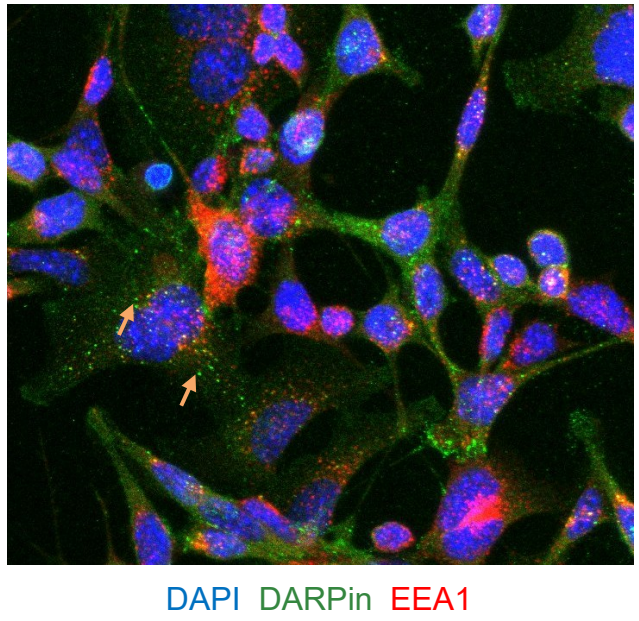


*R2G2 mice xenografted **i.v.** with **NCI-H82***

MP0712-DLL3 DARPin is Rapidly Internalized and Accumulates Intracellularly in DLL3-expressing Cells *in vitro*

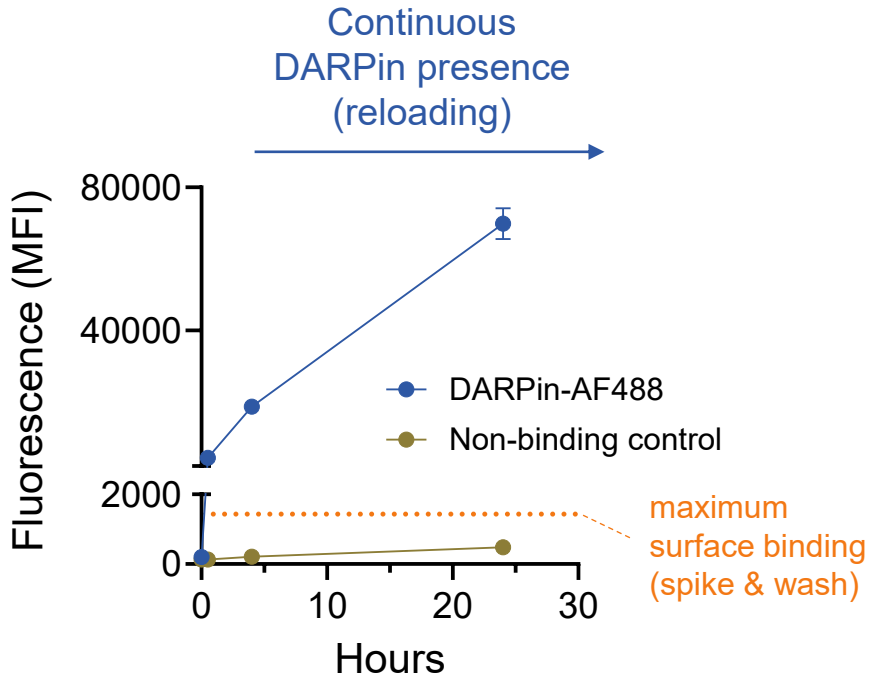


Surface-bound DLL3-DARPin is rapidly internalized into SHP-77 human SCLC cells*



DAPI DARPin EEA1

Internalized DLL3-DARPin shows significant co-localization to the endosomal compartment in HEK-hDLL3 cells**

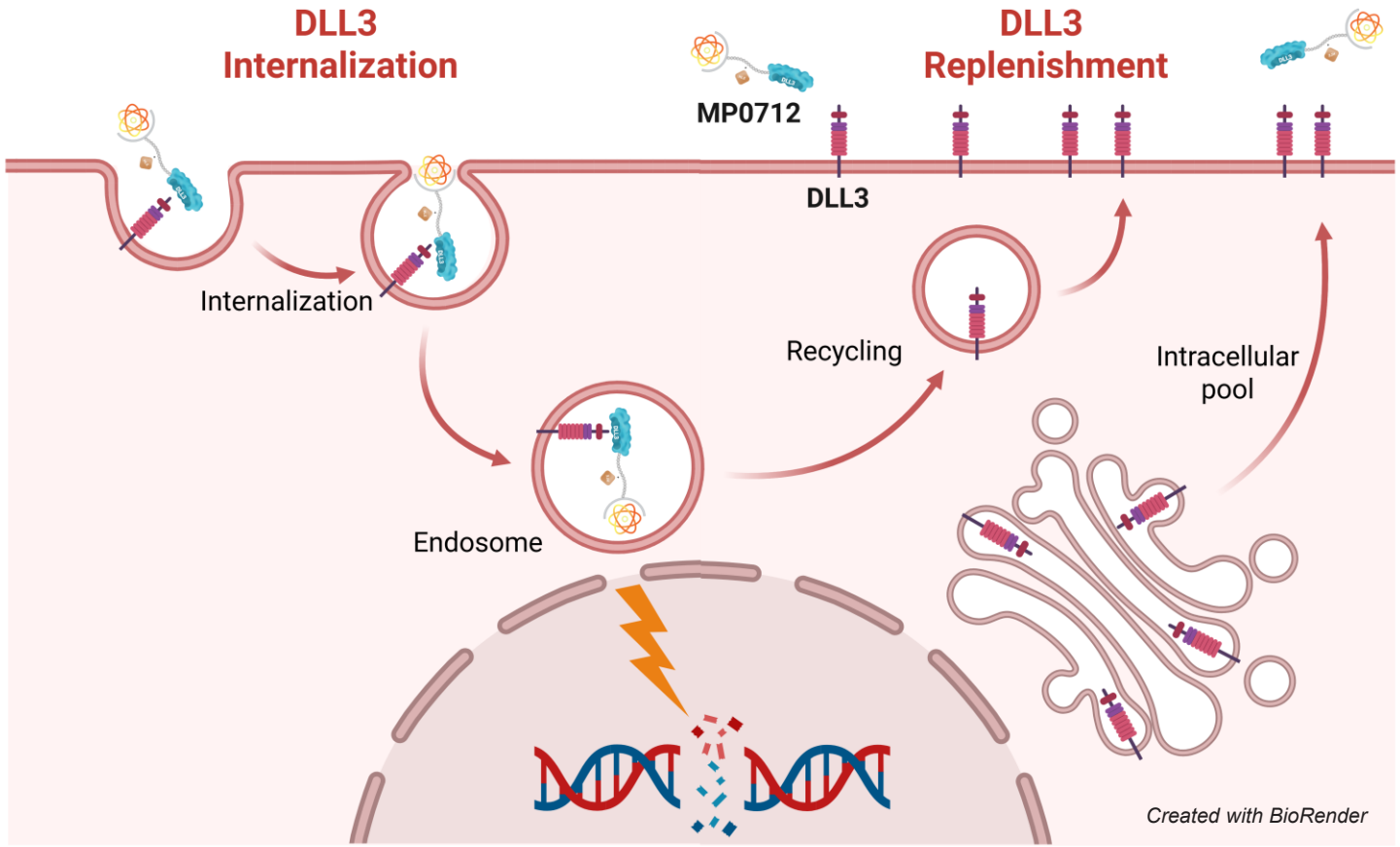


DLL3-DARPin accumulates in HEK-hDLL3 cells over time (beyond the bound fraction at saturation)*

MOLECULAR partners

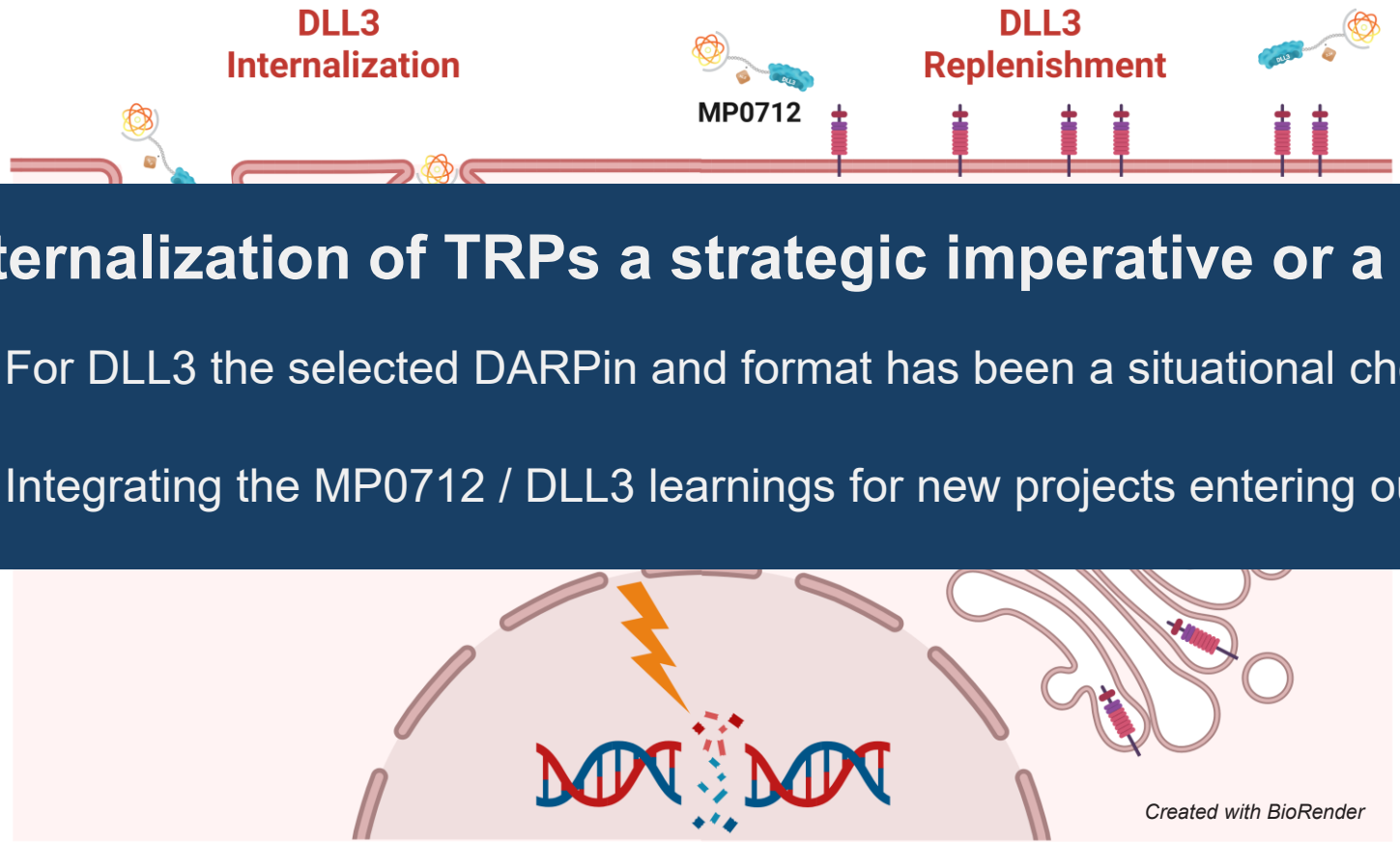
* Internalization of DARPins labelled with anti-DARPin Fab-Alexa 488 conjugate
** Immunofluorescence co-staining of anti-DARPin antibody, an early endosomal marker (EEA1) and cell nucleus marker (DAPI) after (3 h incubation)
MFI, Mean Fluorescence Intensity.

Hypothesis: Free Surface DLL3 is Continually Replenished for Binding and Internalization of MP0712



DARPin binding properties and extended systemic half-life to exploit the rapid internalization & replenishment of DLL3 for radioisotope accumulation in SCLC cells

Hypothesis: Free Surface DLL3 is Continually Replenished for Binding and Internalization of MP0712

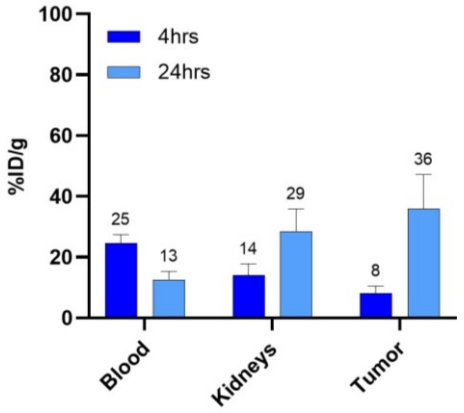


Internalization of TRPs a strategic imperative or a situational choice?

- For DLL3 the selected DARPin and format has been a situational choice matching target biology
- Integrating the MP0712 / DLL3 learnings for new projects entering our pipeline is a strategic imperative

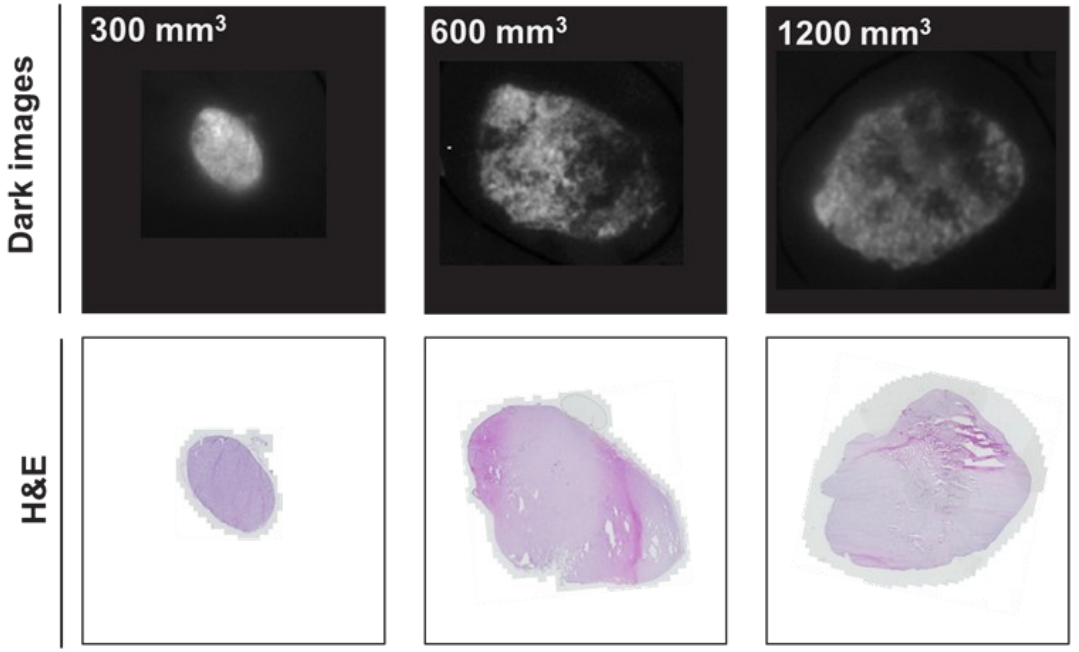
MP0712 Shows Homogeneous Distribution in Tumors

*R2G2 mice xenografted **s.c.** with*
NCI-H82



T:K at 4h = 0.6 / at 24h = 1.2

Sections of tumors with different size
(NCI-H82 s.c. model, alpha camera at 1h)

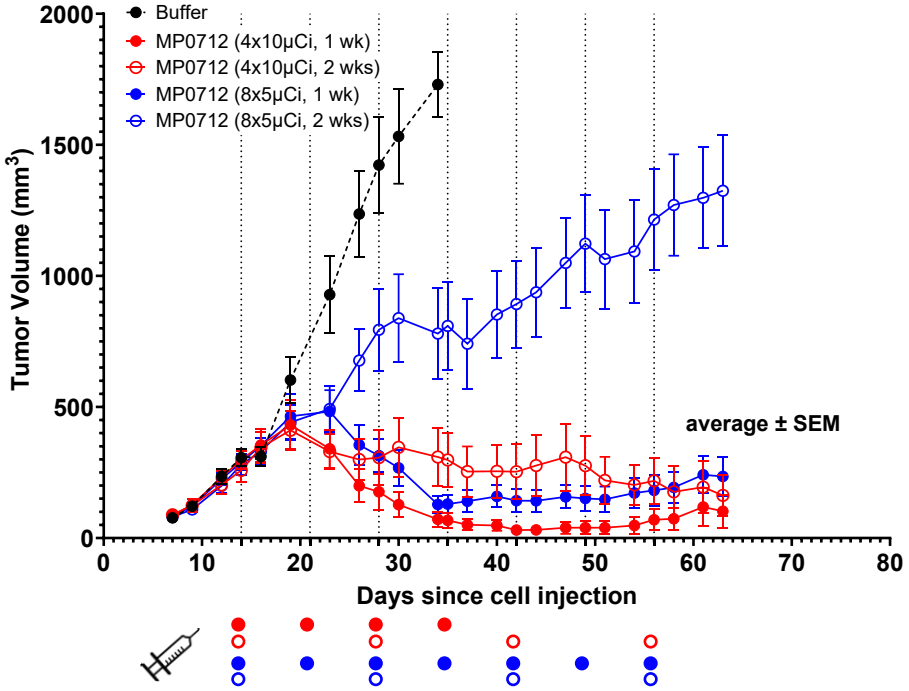


- **Imaging by alpha camera shows a homogeneous distribution of MP0712 in DLL3-low expressing tumors (NCI -H82) even at tumor sizes beyond 600 mm³**

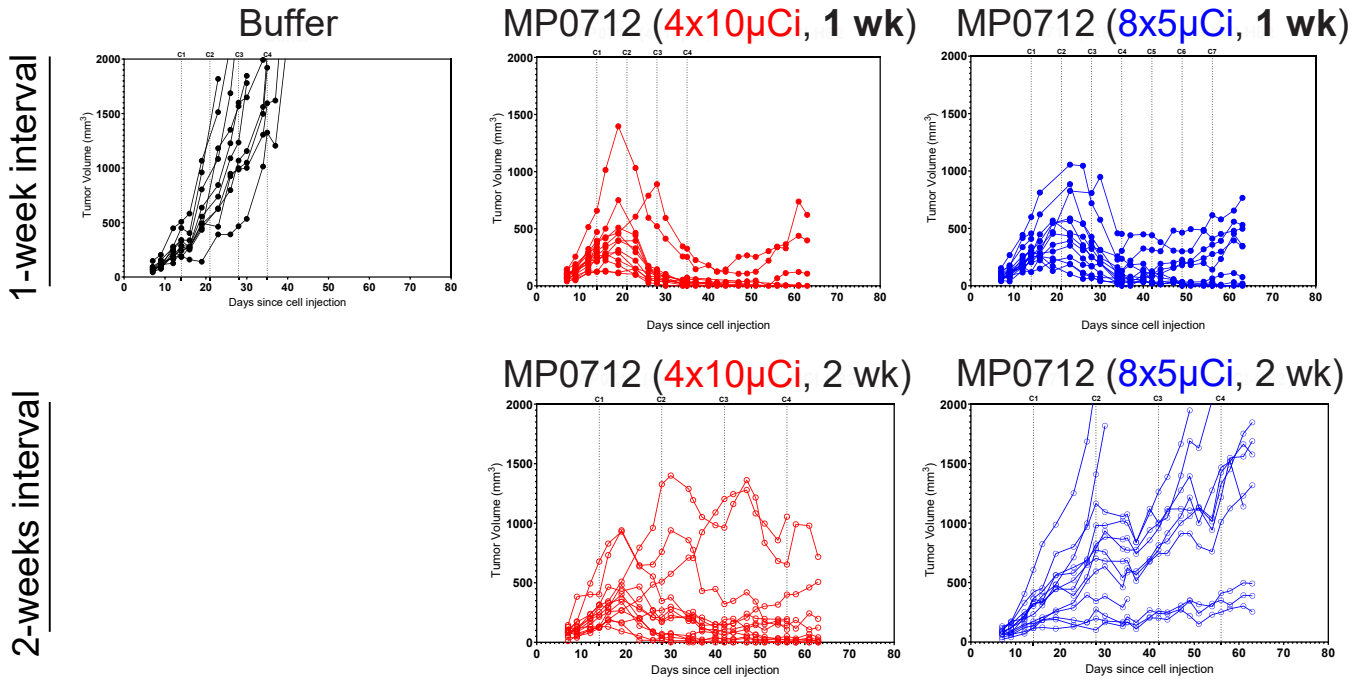
MP0712 biodistribution studies done in different mouse models expressing DLL3 / ^{212}Pb-DOTAM-DARPin injected 1 x 10µCi at 0.01mg/kg.
MP0712 imaging: DLL3 / ^{212}Pb-DOTAM-DARPin injected 1 x 100µCi at 0.01mg/kg.
Steiner D, et al. TRP Europe 2024 (oral presentation).

MP0712: Potent Efficacy at Clinically-relevant Dose

*R2G2 mice xenografted **s.c.** with*
NCI-H82



Tumor growth curve for each animal

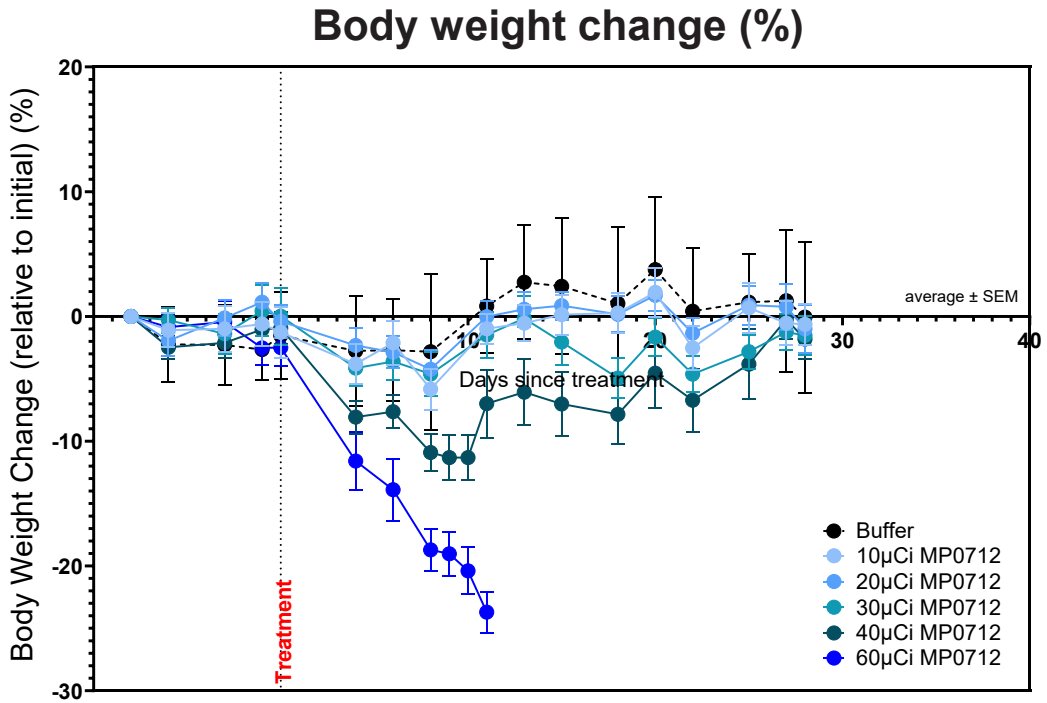


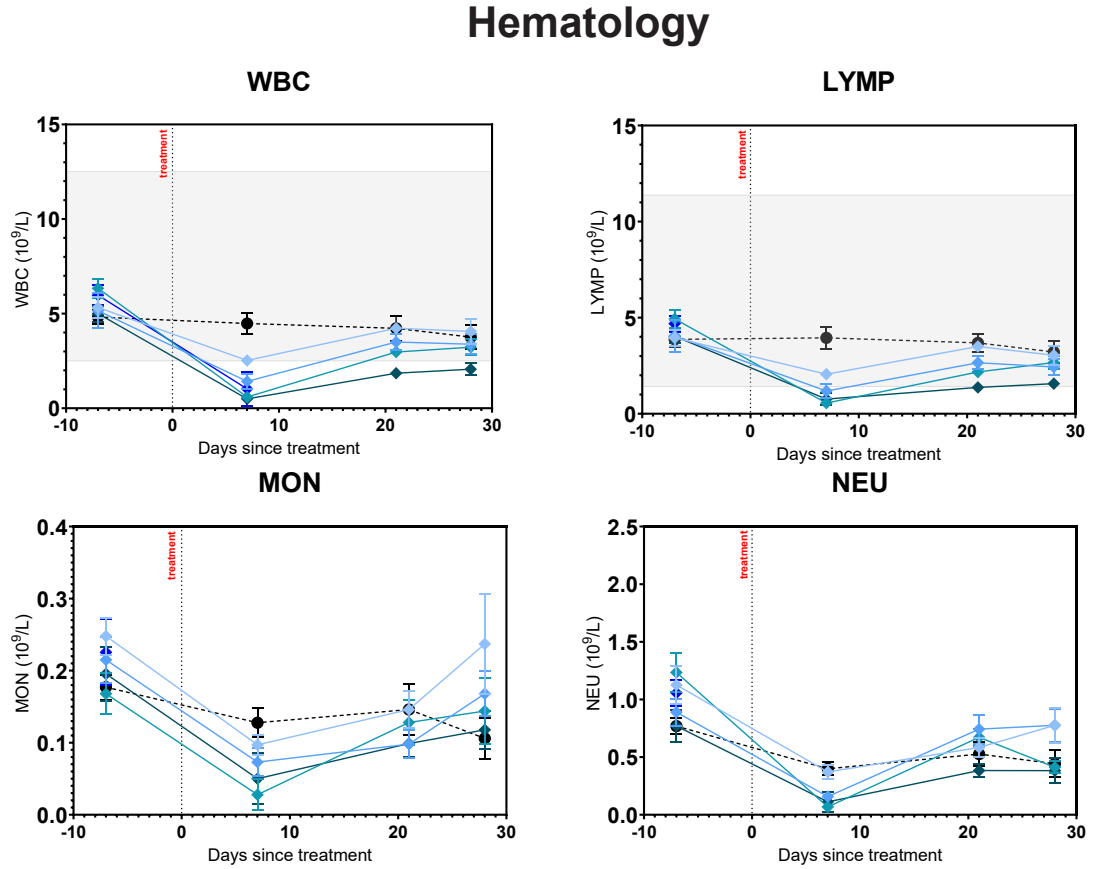
- **MP0712 induces complete tumor regression in NCI-H82 tumor model at 10 µCi injected every week**
- **At day 63, complete tumor regression is seen for ~70% of mice at 4 x 10 µCi weekly**

Croset A. et al. AACR 2025 (poster).

Efficacy study in NCI-H82 tumor model / MP0712 and negative control injected 4 x 10µCi or 8 x 5µCi at 1 HED every 1 or 2 weeks; 10 µCi = 370 kBq

MP0712 Shows a Favorable Safety Profile





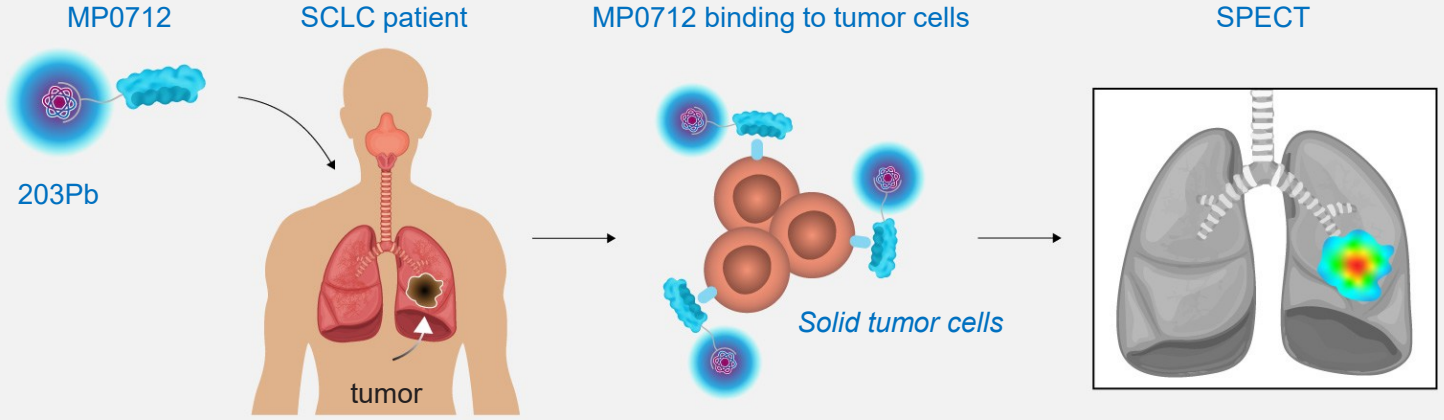
- **Complete recovery of body weight loss after 10 days**
- **Complete recovery of hematologic profile after 28 days**
- **MP0712 treatment up to 30 µCi / 1.11 MBq well tolerated**

Croset A. et al. AACR 2025 (poster).

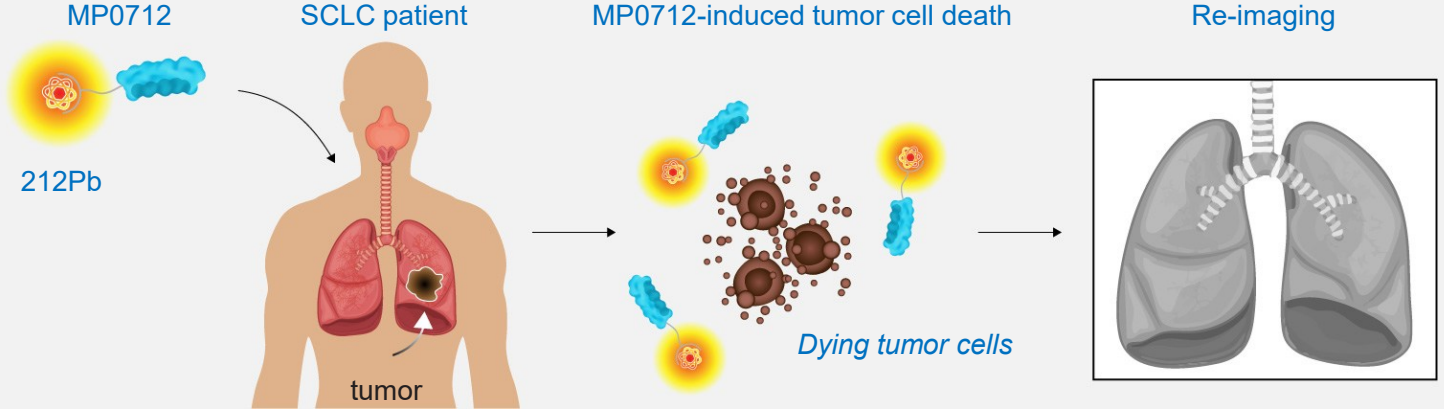
MP0712 DRF study done in WT mice
^{212}Pb-DOTAM-DARPin injected once from 10 to 60µCi.

MP0712 Development Pathway

1. Imaging



2. Therapy



Named Patient Access Program:
Imaging and dosimetry with ^{203}Pb and option for treatment with ^{212}Pb

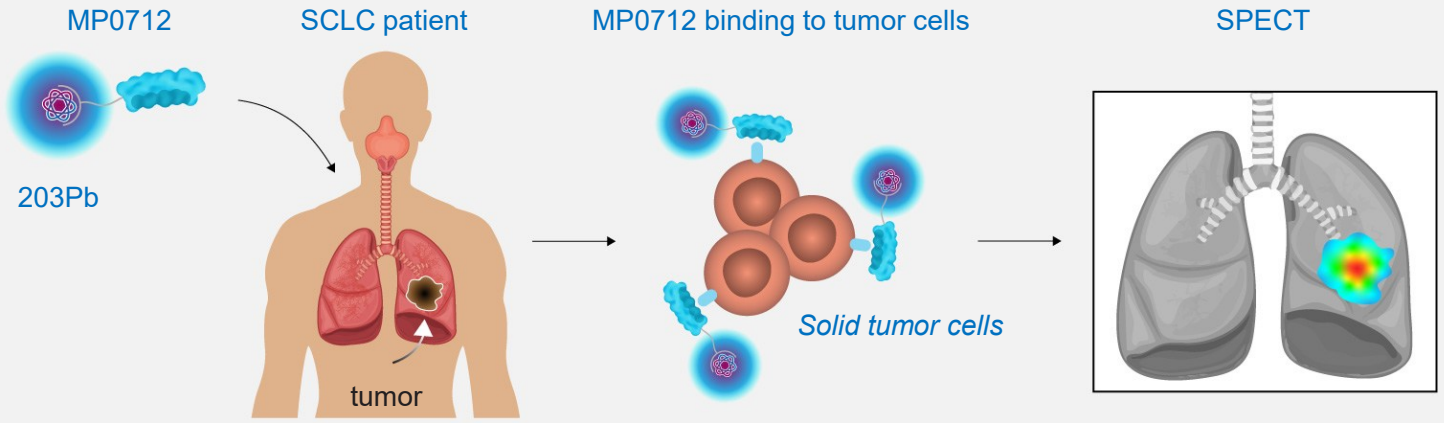
*Request from NuMeRI, Pretoria, South Africa**

Phase 1/2a study: Safety of ^{212}Pb and initial efficacy signals
Includes an imaging and dosimetry step with ^{203}Pb

*MP has accepted a request from Nuclear Medicine Research Infrastructure (NuMeRI) to provide MP0712 under the legal framework in South Africa for compassionate care (also referred to as Section 21 of the Medicines and Related Substances Act).

MP0712 Development Pathway

1. Imaging



Named Patient Access Program:

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

*Request from NuMeRI, Pretoria, South Africa**

- The aim of this type of program is to provide patients access to unregistered medicines outside of a controlled clinical study on an exceptional basis, where conventional therapies have been ruled out, have failed or are unavailable
- Patients are often included based on urgent need and thus can represent a heterogeneous population with advanced diseases and co-morbidities
- Therefore, these data can inform initial signals but can't be extrapolated to what you would expect from a pre-defined population of a clinical trial

*MP has accepted a request from Nuclear Medicine Research Infrastructure (NuMeRI) to provide MP0712 under the legal framework in South Africa for compassionate care (also referred to as Section 21 of the Medicines and Related Substances Act).

SPECT/CT Imaging of ^{203}Pb-MP0712 in SCLC: A Case Example from a Named Patient Access Program in SA (Patient #3)

Patient characteristics

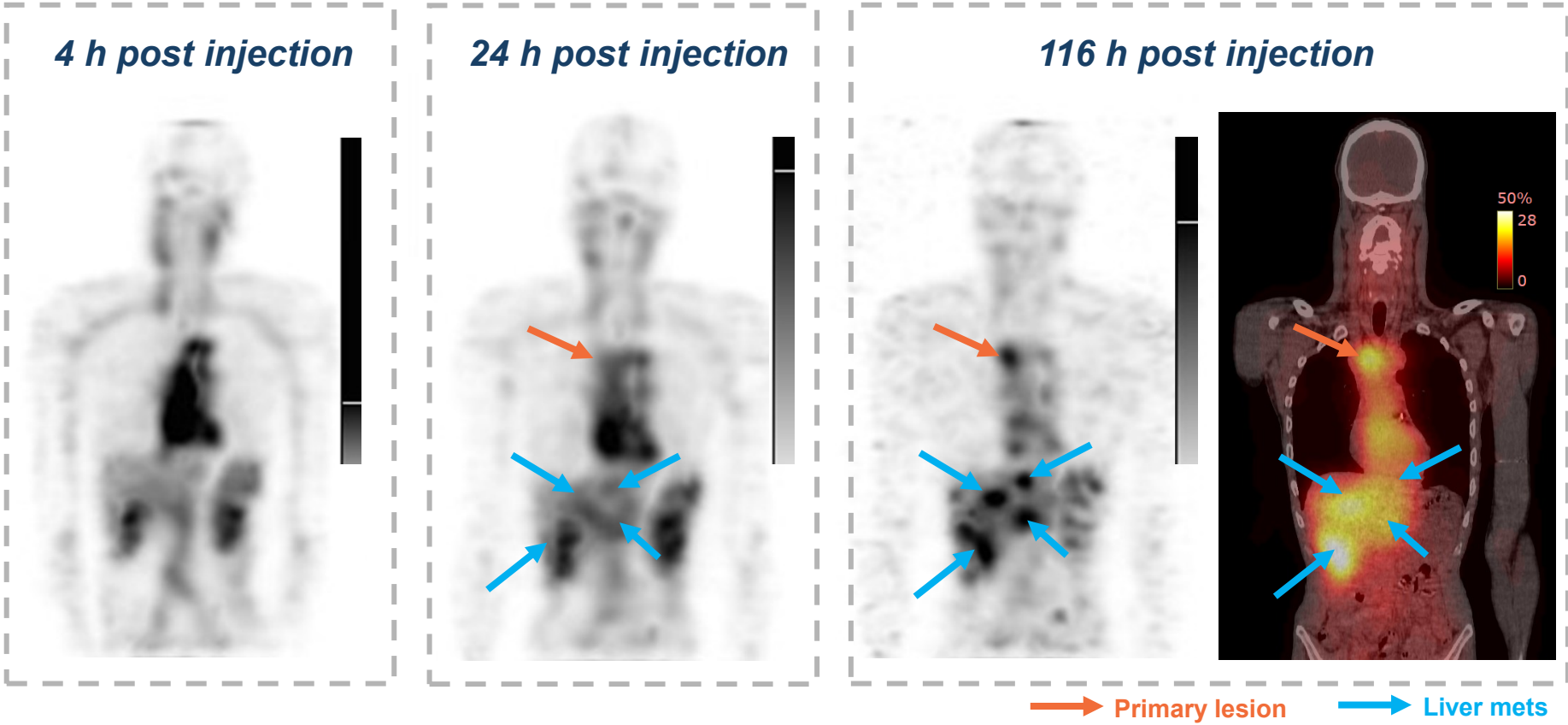
- 69-year-old male (smoker)
- Small cell neuroendocrine carcinoma of the lung
- Stage III at referral, primary tumor located at superior mediastinum

Treatment history

- Radiotherapy and chemotherapy

Dosing & Result

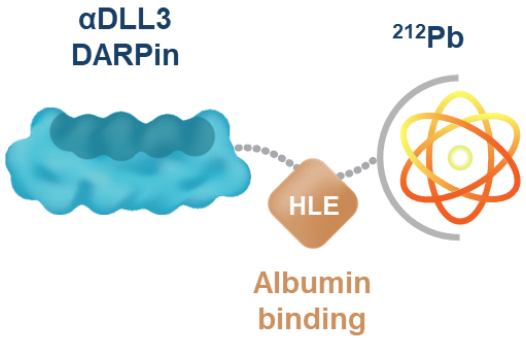
- 5.1 mCi of ^{203}Pb-MP0712
- Stage IV by MP0712 - SPECT with 4 liver mets



➢ **Initial high blood pool, followed by specific uptake in primary and metastatic lesions over time, and limited accumulation in healthy organs 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.
Full data are planned to be presented by the NuMeRI team at the Theranostics World Congress (TWC) 2026.

Conclusions & Outlook



MP0712: ^{212}Pb x DLL3 Radio-DARPin therapeutic candidate for SCLC

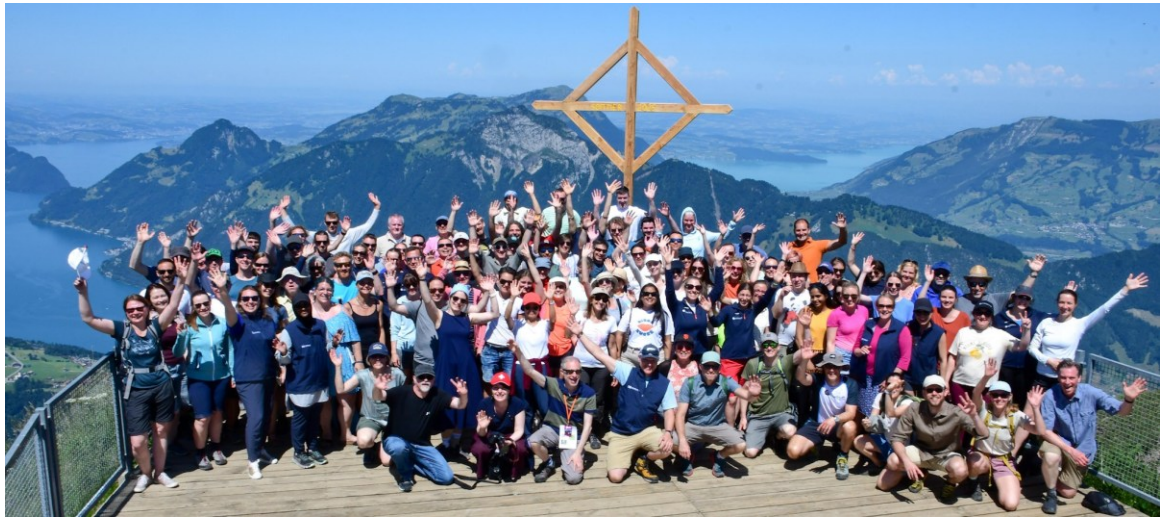
- Attractive BioD, good efficacy & favorable safety profile in pre-clinical models
- High tumor uptake despite low DLL3 density on tumor cell surface: situational choice for DARPin and format that works best for piggybacking on rapid internalization & replenishment of DLL3
- Initial ^{203}Pb-MP0712 imaging data from a patient case receiving compassionate care at NuMeRI indicates specific uptake in primary tumor & metastatic lesions supporting intended MP0712 MoA

Outlook

- Full ^{203}Pb-MP0712 compassionate care imaging & dosimetry data to be presented by NuMeRI at TWC 2026
- MP0712 Phase 1 IND application filed, study start expected before year end with initial data in 2026
- Plan to progress several programs in 2026, including MP0726 targeting mesothelin
- Target internalization & replenishment considerations as a strategic imperative for new projects

Acknowledgments

Team at Molecular Partners AG



Orano Med Team

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

NuMeRI Team

Mike Sathekge
Joseph Kabunda
Honest Ndlovu

Patients and their Families

MOLECULAR partners

Thank you for your interest!

Molecular Partners AG
Wagistrasse 14
8952 Zürich-Schlieren
Switzerland
www.molecularpartners.com
T +41 44 755 77 00
info@molecularpartners.com