Evaluation of Anti-uPAR Antibody as a Radiopharmaceutical for Imaging and Treatment of Solid Tumors

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Raji Nair/Program Management Lead, Andrew Cittadine/COO, Eric Kawamoto/Senior Scientist, Aidan Kelly/Program Management Associate, Chandler Robinson/CEO – Monopar Therapeutics/Preclinical Evaluation of Anti-uPAR Antibody as a Radiolabeled PET Imaging Candidate in Solid Tumors/ The Journal of Nuclear Medicine June 2024, 65 (supplement 2) 241463;
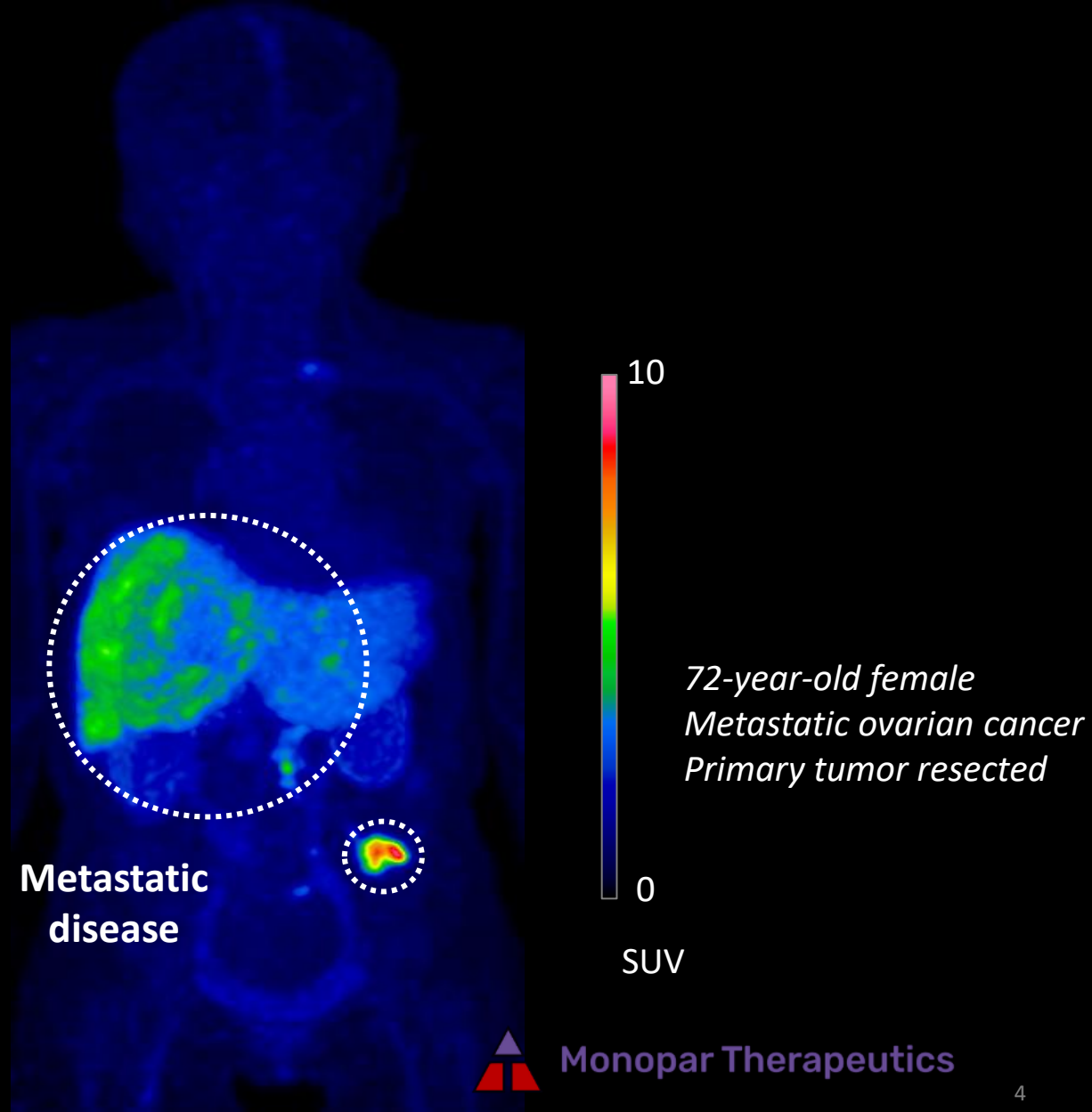
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uPAR - A Promising New Radiopharma Target
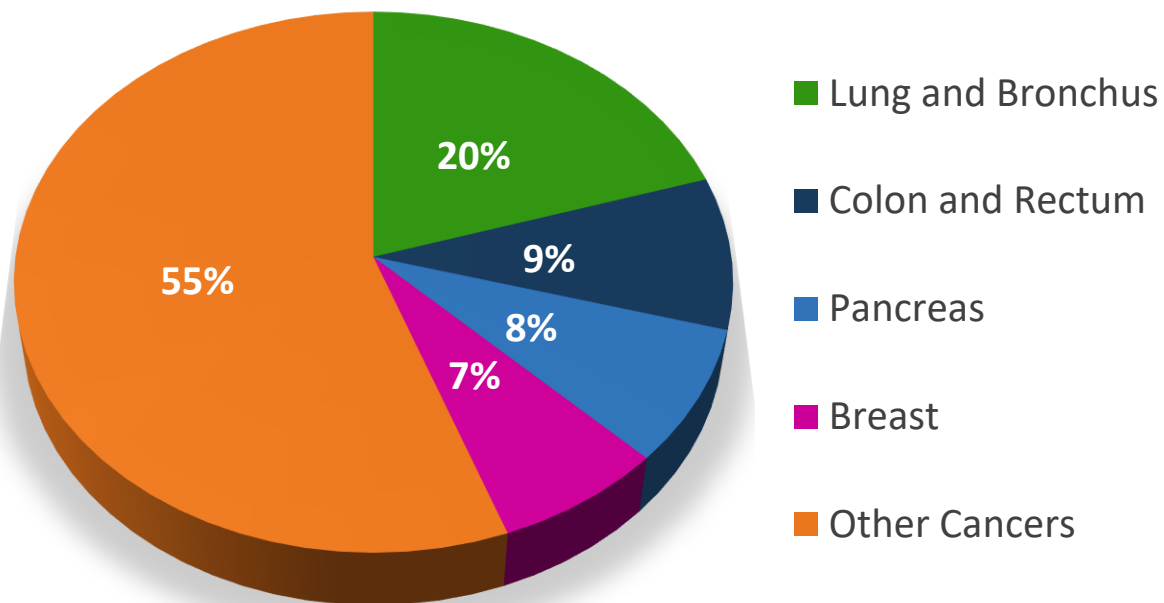
Pan-tumor target

Involved in tumor growth & metastasis

Expressed in aggressive cancers

Rarely present in healthy tissue

Metastatic disease

10

0

SUV

72-year-old female
Metastatic ovarian cancer
Primary tumor resected

Urokinase-Plasminogen Activator Receptor (uPAR)

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Aggressive Cancers Express uPAR

Leading Cancer Deaths 2024

- **Lung and Bronchus** — 20%
- **Colon and Rectum** — 9%
- **Pancreas** — 8%
- **Breast** — 7%
- **Other Cancers** — 55%

Data from NCI SEER

Cancer Type	% Patients with uPAR Expression
Breast[1]	97%
Bladder[2]	89%
Ovarian[3]	88%
Pancreatic[4]	87%
Colorectal[5]	85%
Lung[6]	50%

[1]*Dublin et al., Am J Pathol. (2000)*
[2]*Dohn et al., Urol. Oncol, (2015)*
[3]*Wang et al. , Gynecol Oncol (2009)*
[4]*de Geus et al., Cancer (2017)*
[5]*Boonstra et al., BMC Cancer (2014)*
[6]*Salden et al., Annals of Oncology, (2000)*

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MNPR-101: First-in-class uPAR-targeting agent

Humanized monoclonal antibody

Strong binding affinity, << nM

Not blocked by uPA - uPAR binding

MNPR-101
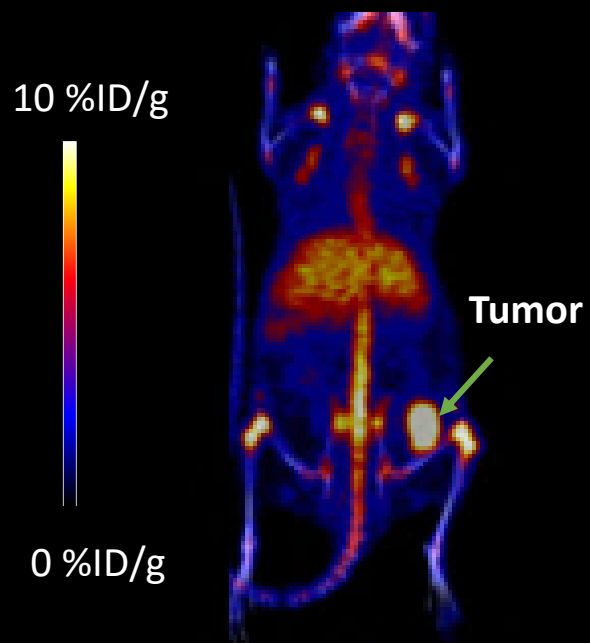*Fab region*

uPA

uPAR

Cell Surface
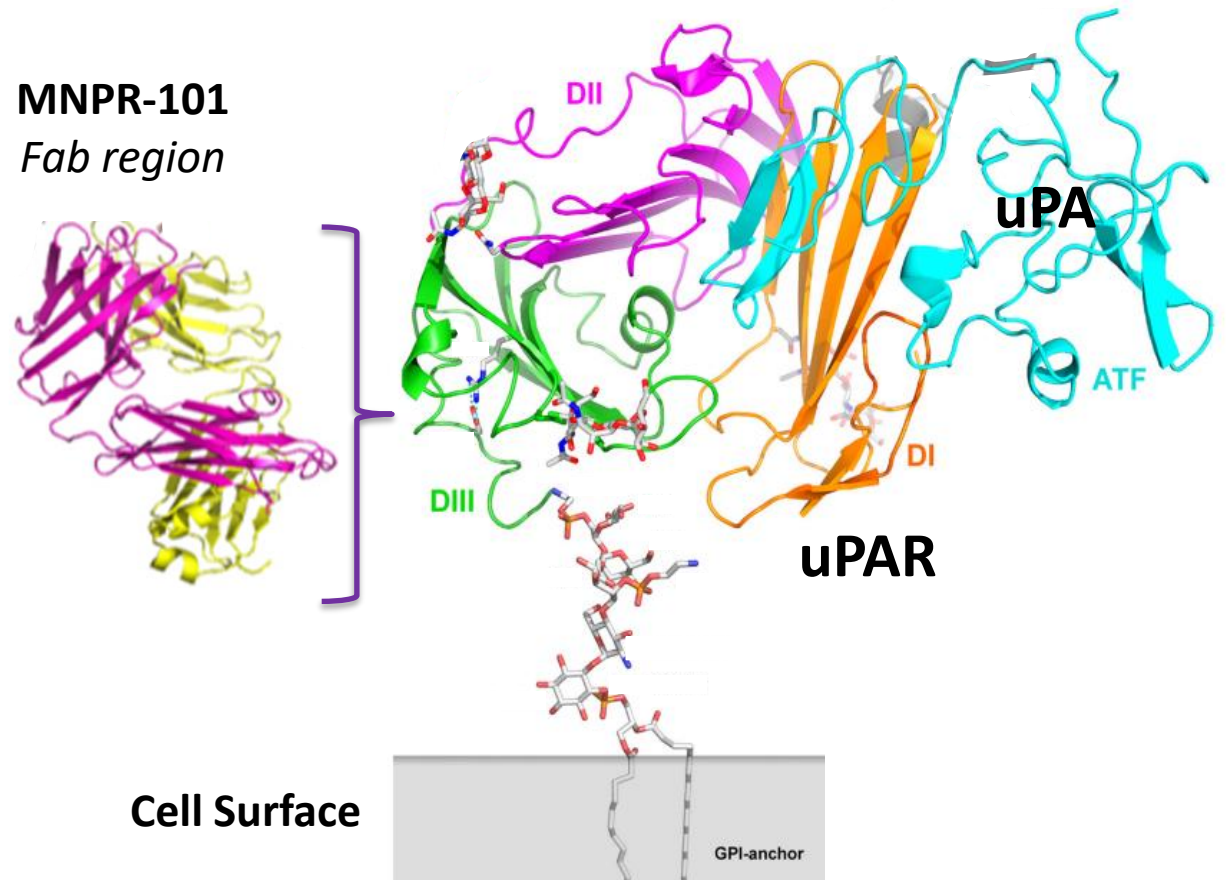
Molecular model of uPAR in complex with uPA showing uPA and MNPR-101 binding sites. Adapted from Xu 2012 JMB and Xu 2014 Plos One
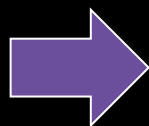
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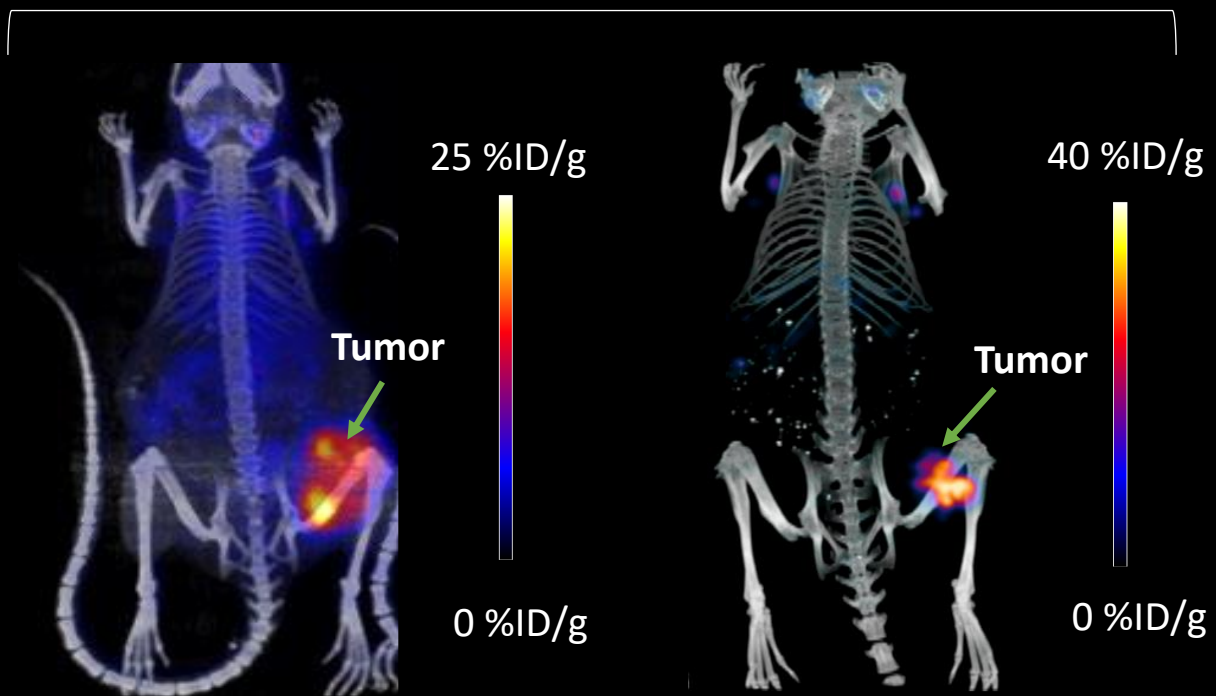# Optimizing MNPR-101 Radiopharmaceuticals for the Clinic

Pancreatic Cancer (MIA PaCa-2) Images @ 6-7 days post injection

Biodistribution supports strong pre-clinical efficacy

Pancreatic Cancer
MIA-PaCa2 xenograft mouse model

Legend:
- Control Group (No treatment)
- 100 μCi MNPR-101-Lu Group

Y-axis: % of Initial Tumor Volume (0, 100, 500, 1000, 1500, 2000, 2500)
X-axis: Days Post-Injection (0, 10, 20, 30, 40, 50, 60, 70, 80, 90)

single injection
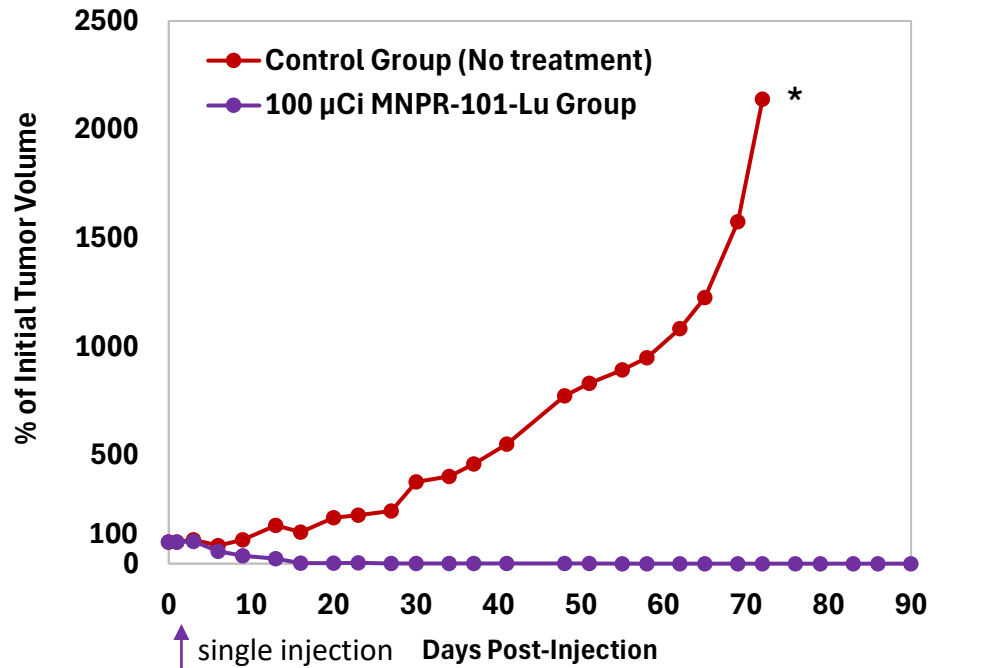
*Stopped due to tumor volume limit

Triple Negative Breast Cancer
MDA-MB-231 xenograft mouse model

Legend:
- Control Group(No treatment)
- 100 nCi MNPR-101-Ac Group

Y-axis: % of Initial Tumor Volume (0, 100, 500, 1000, 1500, 2000, 2500, 3000)
X-axis: Days Post-Injection (0, 10, 20, 30, 40, 50, 60, 70, 80, 90)

single-injection

*Stopped due to tumor volume limit

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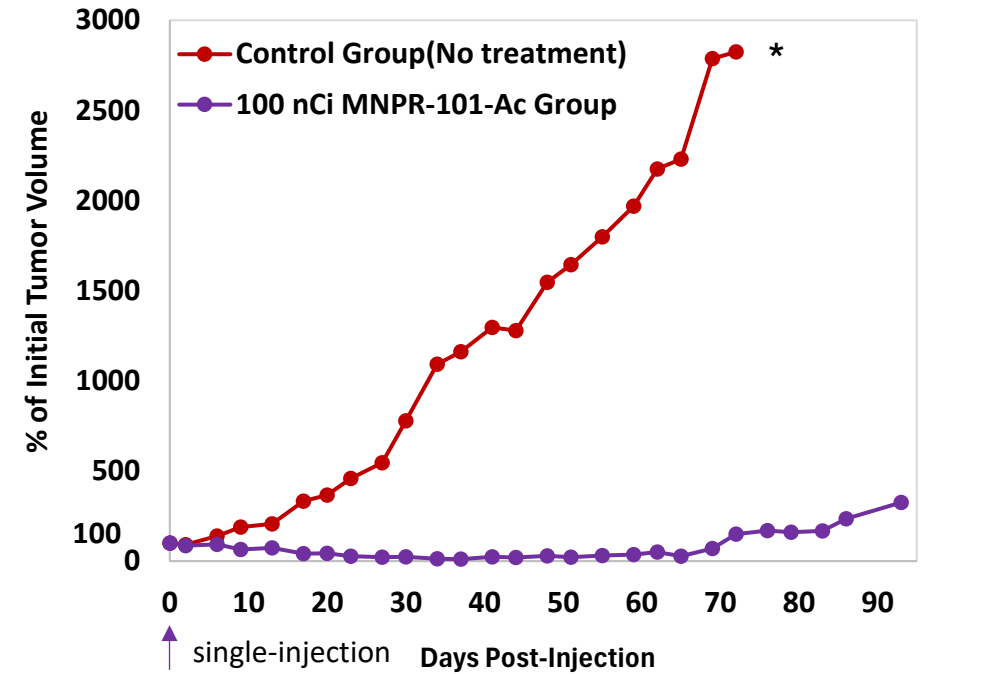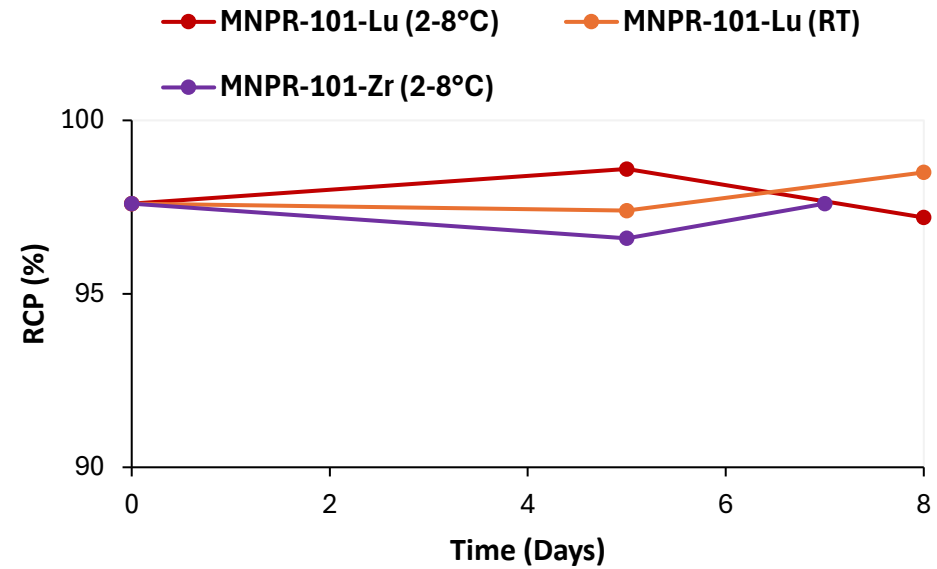
Appealing Stability and Shelf-life

Whole-Body Retention

MNPR-101-Zr and MNPR-101-Lu Shelf-life
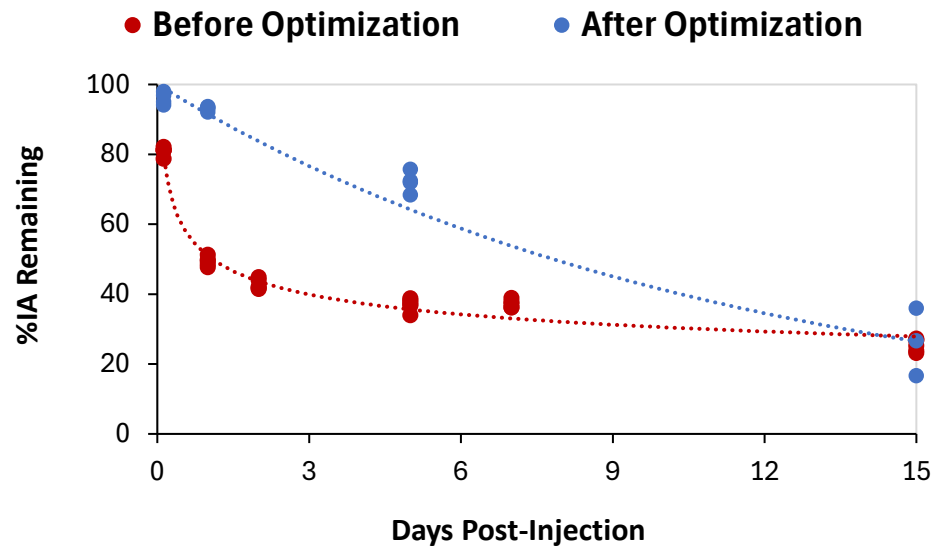
Highly stable in vivo

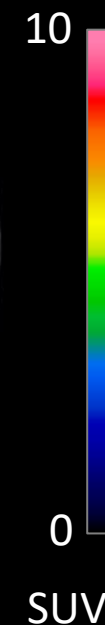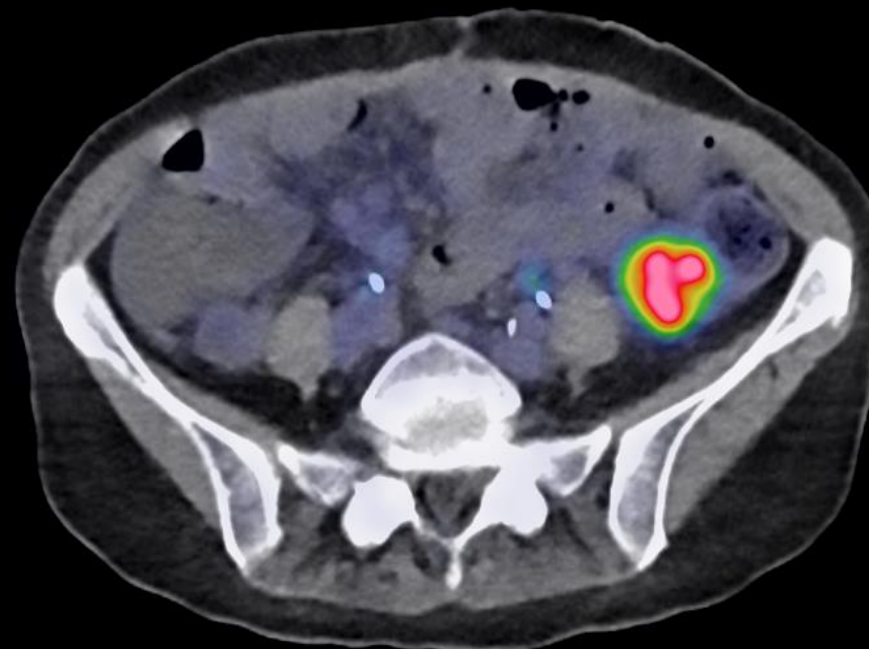**> 7 days shelf life**

Human Clinical Data Confirms MNPR-101's Tumor Targeting Ability

¹⁸F-fluorodeoxyglucose (FDG)
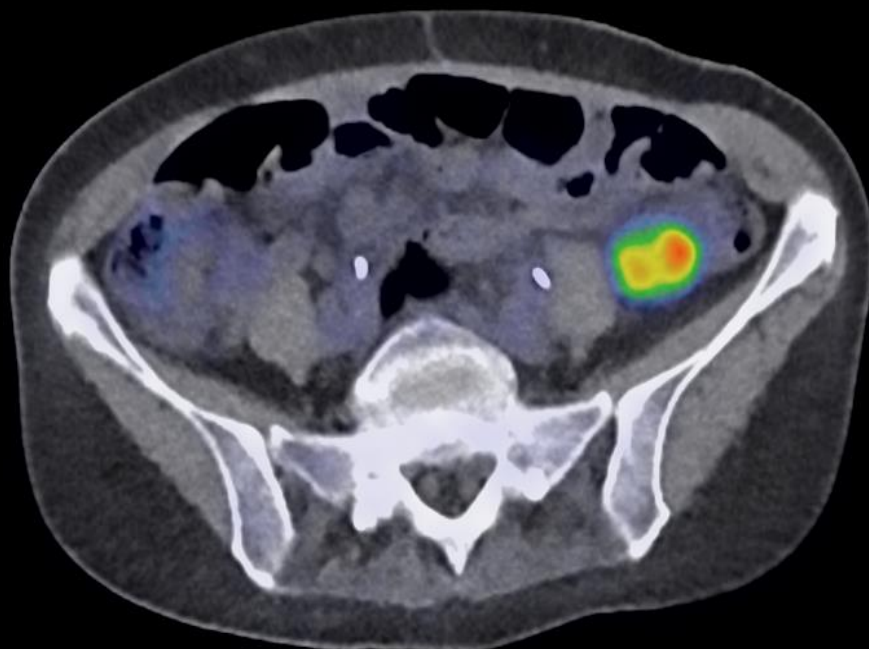
MNPR-101-Zr (72h)

FDG image acquired 14 days prior to MNPR-101-Zr administration on the same Siemens Biograph Vision Quadra™ PET/CT System.

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Favorable Human Radiation Dosimetry Profile

Target Organ	MNPR-101-Zr	Projected MNPR-101-Lu		Organ Safety threshold (Gy)
	Absorbed Dose @43 MBq (Gy)	Dose Coefficient (Gy/MBq)	Absorbed Dose @5624 MBq (Gy**)	
Liver	7.85×10^{-2}	1.63×10^{-3}	9.14	30
Kidneys	5.20×10^{-2}	1.12×10^{-3}	6.30	23
Lungs	3.54×10^{-2}	6.35×10^{-4}	3.57	20
Red marrow*	1.96×10^{-2}	2.73×10^{-4}	1.53	2-3

Actual MNPR-101-Zr and projected MNPR-101-Lu organ dosimetry (at the highest per cycle Lu-177 mAb therapeutic dose we are aware of in the clinic) suggest a favorable safety profile

* Blood-based analysis

** Lu-177 projected dosimetry uses the highest per cycle dose we are aware of – an ongoing Phase 3 trial of an Lu-177 radiolabeled antibody – 2 fractions @ 45 mCi/m^2 for a standard 1.7 m^2 patient equivalent to 5624 MBq

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# Conclusion: uPAR is a Promising Radiopharma Target

MNPR-101-Zr

Metastatic disease
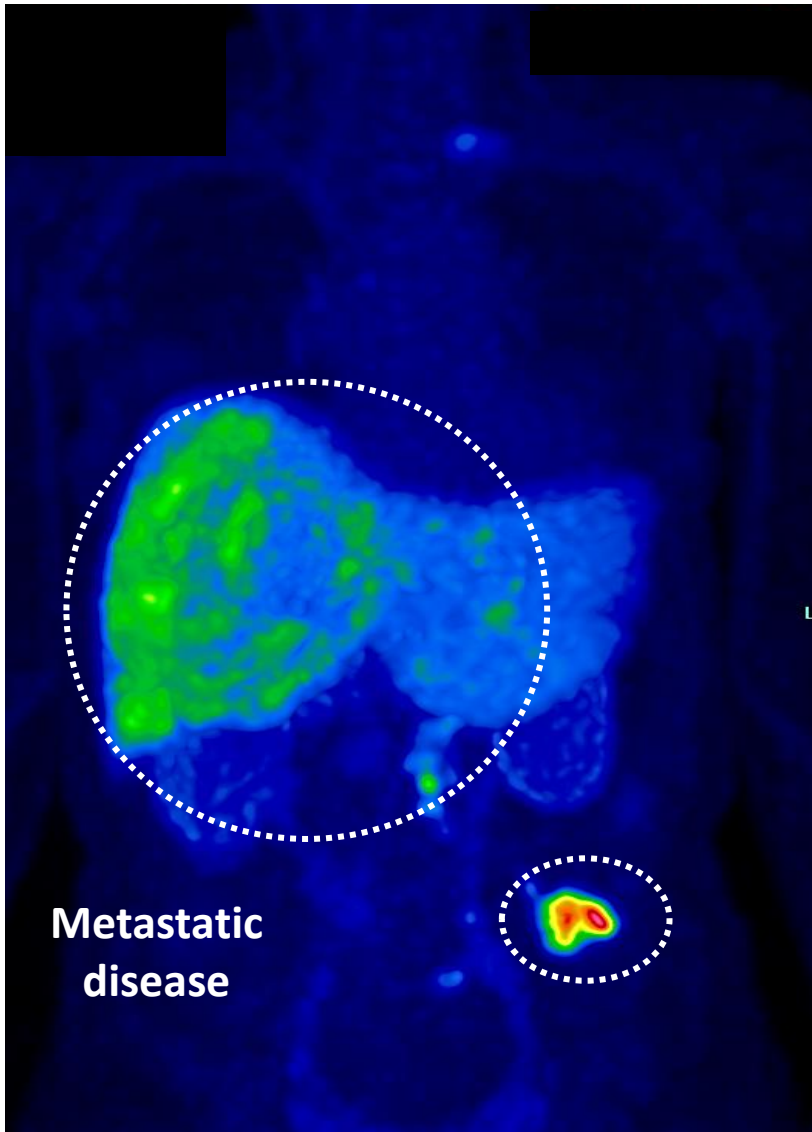
- Expressed in multiple aggressive cancers

- uPAR-targeted MNPR-101-Zr dosimetry analytics show favorable MNPR-101-Lu profile

- Radiopharma Imaging and Therapy studies **open and enrolling:**

  – MNPR-101-Zr ClinicalTrials.gov: NCT06337084

  – MNPR-101-Lu ClinicalTrials.gov: NCT06617169

Lead investigator is Prof. Rod Hicks MD (Melbourne Theranostic Innovation Centre)

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Thank you!
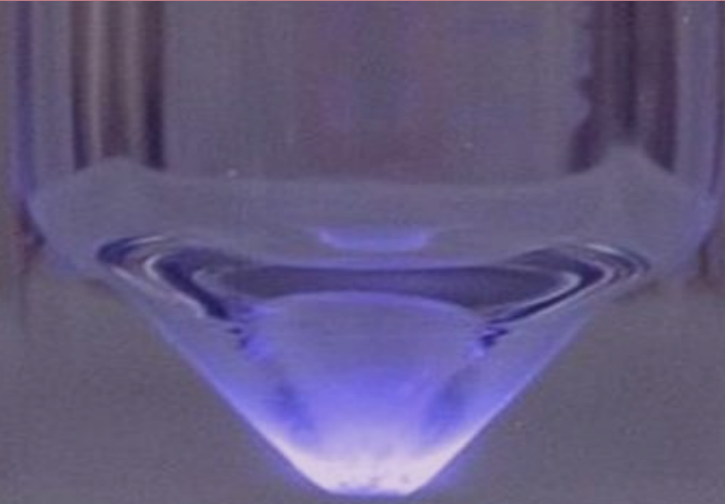
October 2024

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