PERSPECTIVE THERAPEUTICS

Analyst Day Presentation

18 March 2024

NYSE: CATX

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Forward-looking statements contained in this presentation are made as of this date, and the Company undertakes no duty to update such information whether as a result of new information, future events or otherwise, except as required under applicable law.

Analyst Day Agenda

NYSE, 18 March 2024

- Introductions
- Pipeline Update
- Clinical Update
- KOL Discussion
- Corporate / Manufacturing Update
- Questions

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Management Team

Deep Experience in Radiopharmaceuticals and Oncology Drug Development

Thijs Spoor

Chief Executive Officer

20+ years of expertise in biotechnology companies; public and private companies; oncology and nuclear pharmacy

Markus Puhlmann, MD MBA

Chief Medical Officer

20+ years of oncology drug development across all phases, experience coordinating multiple regulatory filings

Michael Schultz, PHD

Chief Science Officer

20+ years industry and research experience in radiopharmaceuticals; co-founder Viewpoint MT & inventor of Perspective products

Jonathan Hunt

Chief Financial Officer

20+ years of expertise in financial controls and public accounting for large and small companies across multiple industries

Frances Johnson, MD

Chief Innovation Officer

20+ years in clinical trials execution, managing academic research programs, founder and start-up of CareDx, Inc and Viewpoint MT

Amos Hedt

Chief Business Strategy Officer

20+ years of expertise in early-stage pharmaceutical and biotech drug development; 10+ years in radiopharmaceuticals

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Investment Highlights

Platform radiopharmaceutical company targeting **pan-cancer opportunities** utilizing 2nd generation α-emitter

Proprietary chelator-based peptide targeting platform provides engine for pipeline expansion

Robust clinical pipeline with focused three clinical-stage programs. VMT-α-NET for neuroendocrine tumors; VMT01 for melanoma; PSV359 for multiple solid tumors

Theranostic ^{203}Pb – ^{212}Pb dual isotope enables imaging and therapy, improving patient selection and outcomes

Multiple expected **near-term readouts and milestones** through to 2025

Vertically integrated in-house manufacturing of ^{212}Pb isotope simplifies manufacturing and can leverage existing radiopharmacy logistics for broad distribution

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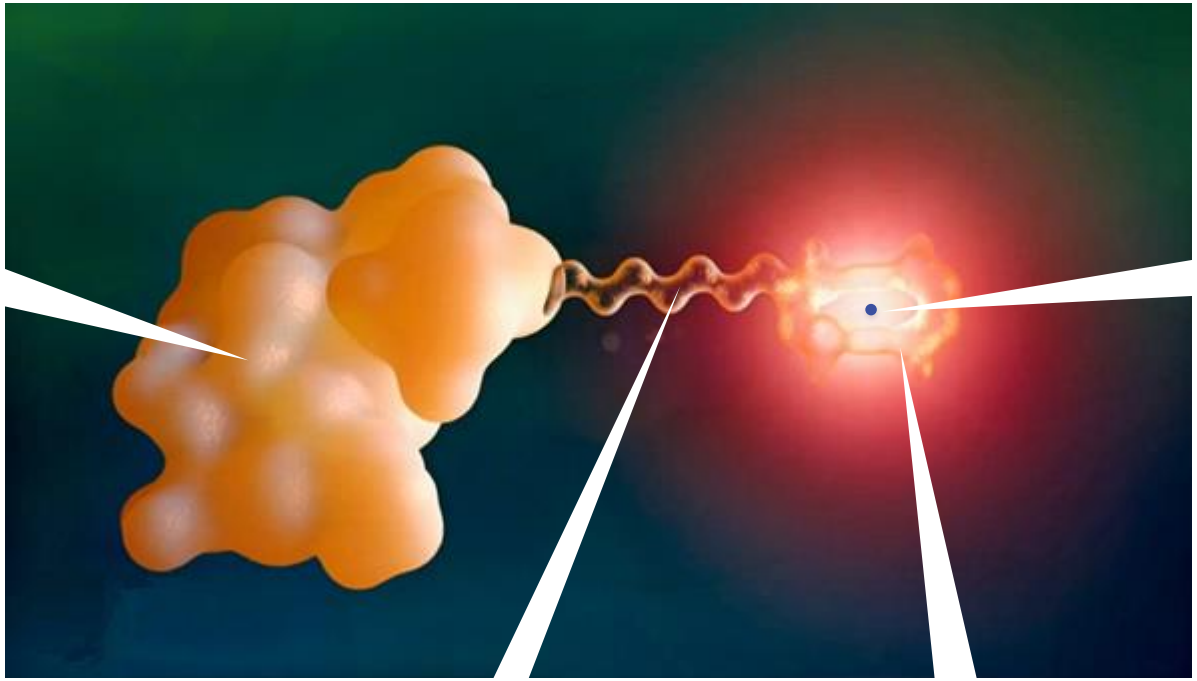
Perspective's Radiopharmaceutical Optimization Process

Unique Mechanism of Action Offers Pan-Cancer Opportunities

Targeting Peptide

Engineered for cancer-specific receptors to ensure highly directed uptake



Isotope

^{203}Pb for SPECT imaging

or

^{212}Pb for alpha particle therapy

Linker

Selected to assist peptide binding and optimize clearance from blood and healthy tissues

Chelator

Perspective's proprietary platform technology enabling stable radiolabeling with Pb isotopes

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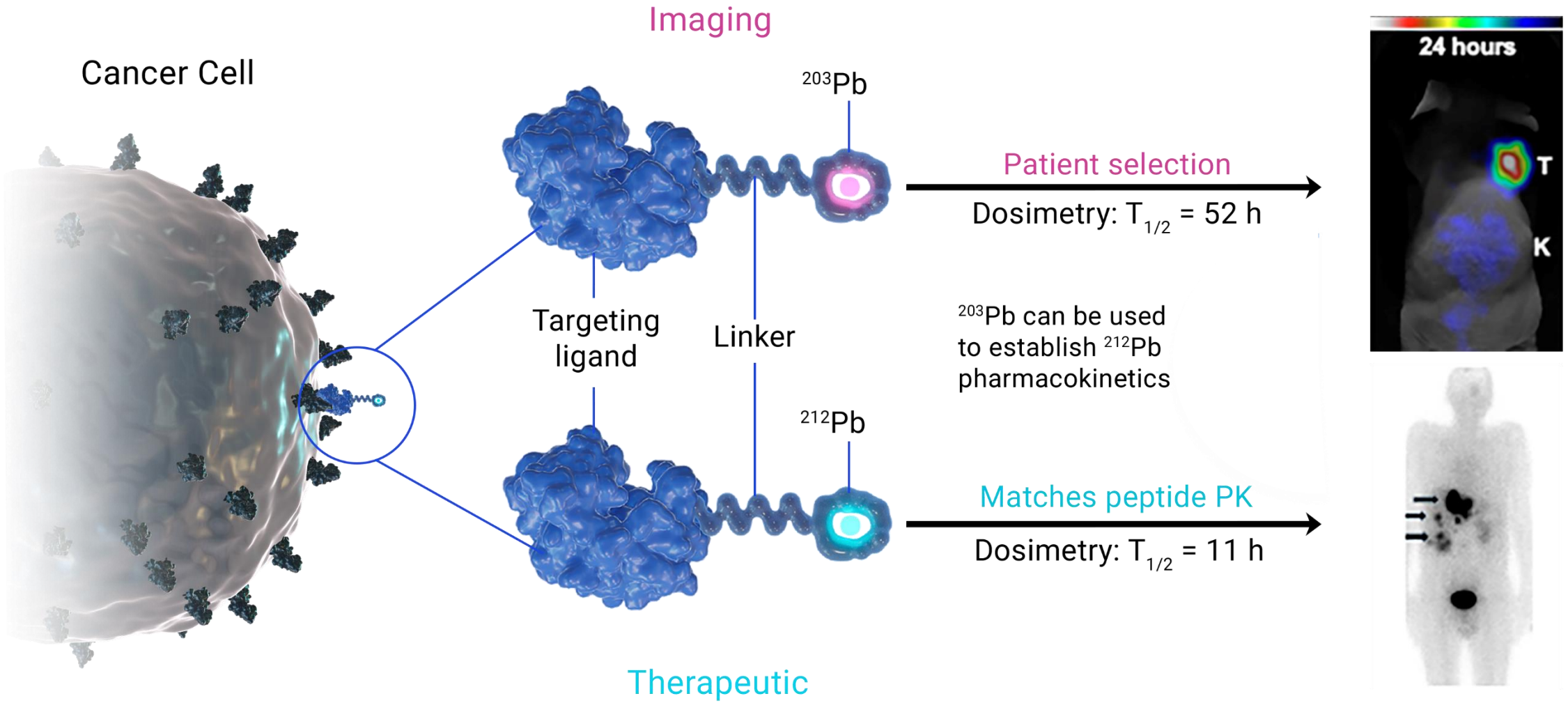
Pb-based Theranostics Enable Both Diagnosis and Targeted Treatment of Cancer

Identical Distribution of ^{203}Pb and ^{212}Pb for Imaging and Treatment, Respectively



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Platform Expansion Engine

Three Lead Programs in Clinic and Broad Proprietary Pipeline

Program	Indication	Discovery	Human Clinical Imaging	First in Human Therapy	Phase 1/2	Phase 3
VMT-α-NET	Neuroendocrine cancers				Safety Update	
	Pheochromocytomas, paragangliomas					
	Small cell lung cancer					
VMT01	Melanoma (MC1R)				Safety Update	
VMT02 *(PET agent)*	Melanoma (imaging of MC1R)					
PSV359 *(Novel peptide)*	Multiple solid tumors			First in Human Images of Clinical Candidate		
PSV40X *(Radio-hybrid)*	Prostate (PSMA imaging & therapy)			Technology Background		
Program 5 *(Novel peptide)*	Prostate, Breast					
Pre-targeting Platform *(mAbs)*	Solid and hematological tumors		Scientific Rationale and Technology Background			
Other Programs *(Novel peptides)*	Solid and hematological tumors					

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Pipeline Update

Clinical and Preclinical Programs

Pan Cancer Target: PSV359

Preclinical Efficacy and First in Human Images of Novel Peptide Targeting Fibroblast Activation Protein alpha (FAP-α)

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Fibroblast Activation Protein α is a Pan Cancer Target

Tumor stroma cells do not typically express cancer-specific markers like SSTR2 or MC1R

FAP is primarily expressed on tumor stroma cells, but also on some cancer cells

JNM
The Journal of Nuclear Medicine

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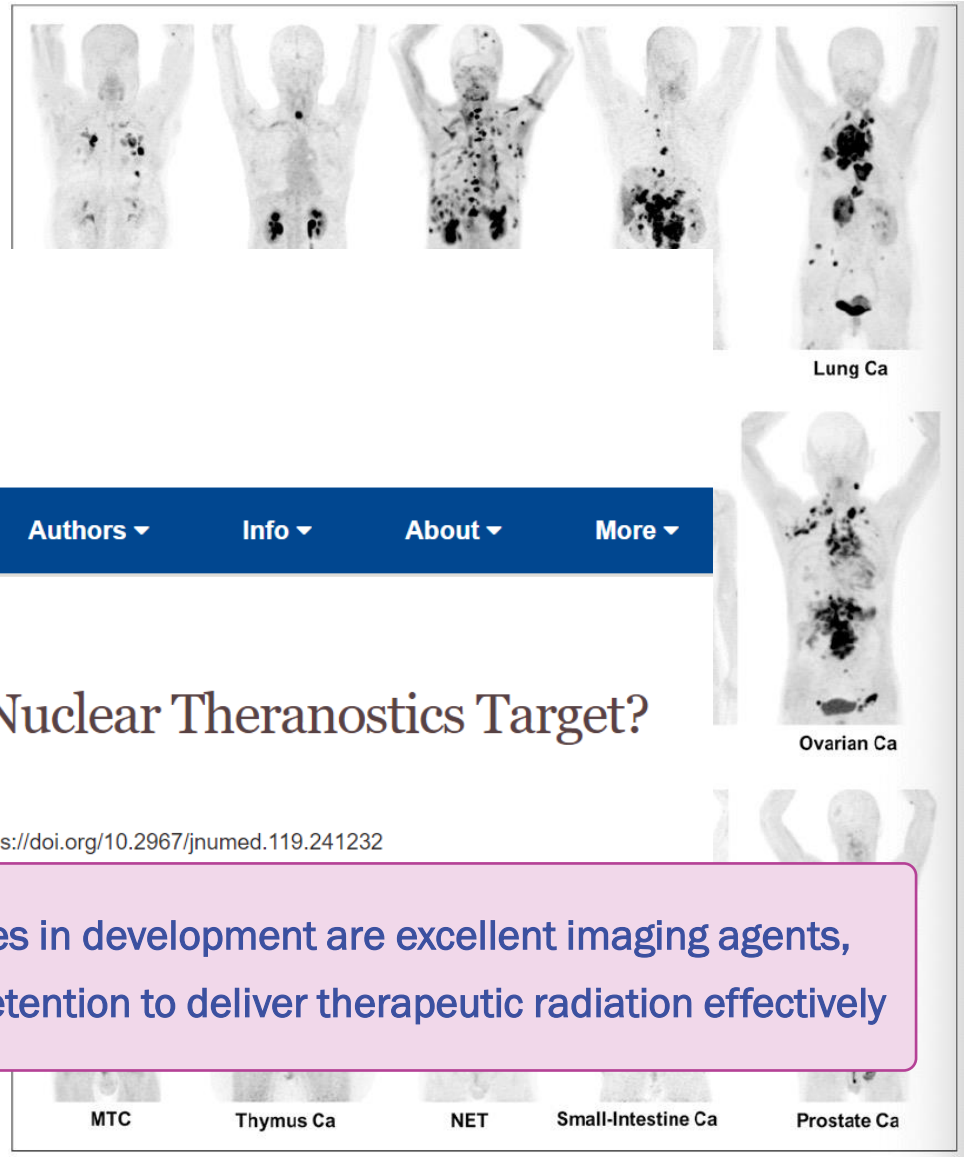
FAP: The Next Billion Dollar Nuclear Theranostics Target?

Jeremie Calais

Journal of Nuclear Medicine February 2020, 61 (2) 163-165; DOI: https://doi.org/10.2967/jnumed.119.241232



Small molecules in development are excellent imaging agents, but lack tumor retention to deliver therapeutic radiation effectively

Kratochwil et al., JNM, 2019

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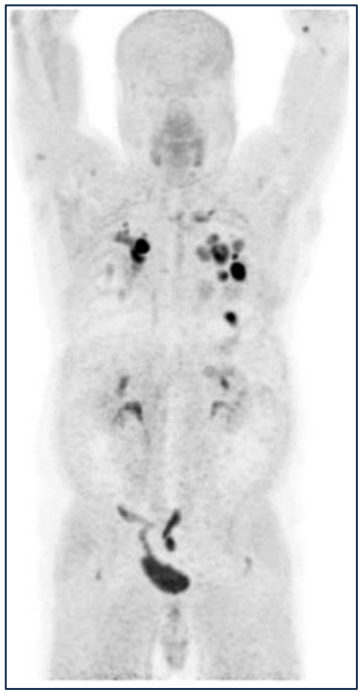
Fibroblast Activation Protein α is a Pan Cancer Target[1]

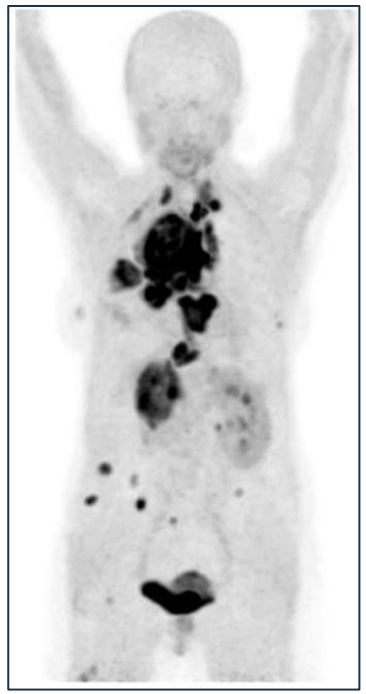
Multiple imaging products in development such as ^{68}Ga-FAPi, but significant therapeutic opportunity remains

Expression of FAP-α on Tumor Cells

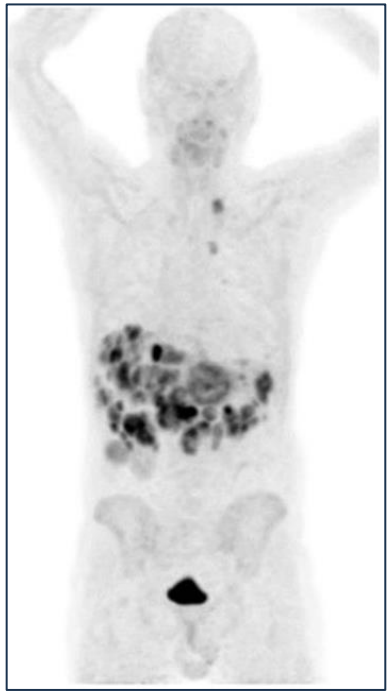


Sarcoma

Expression of FAP-α on Tumor Stroma Cells

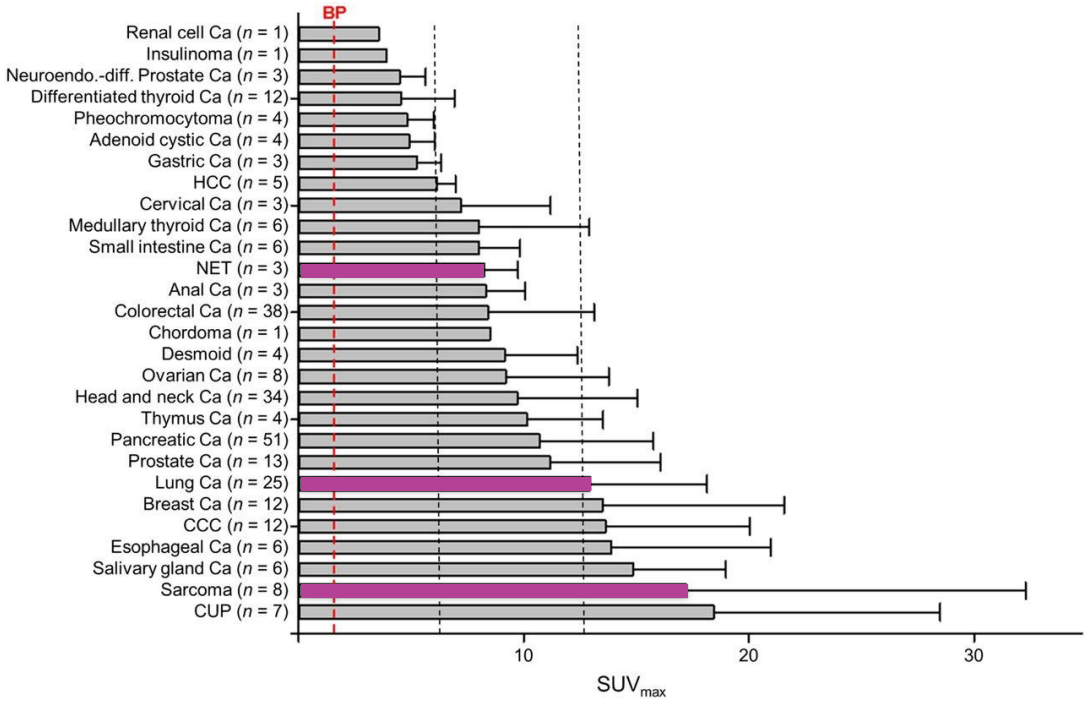


Lung Cancer



NETs

Average SUV_{max} of ^{68}Ga-FAPI PET/CT Across 28 Different Cancer Types



[1]Kratochwil et al., JNM, 2019

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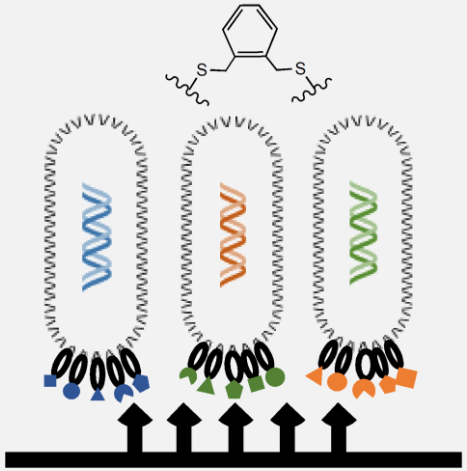
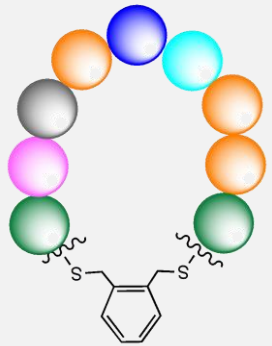
Development of PSV359 (Discovery Phase – Optimization Phase over 12 months)

In-house peptide synthesis and in vivo capability allows rapid iteration and optimization of novel compounds

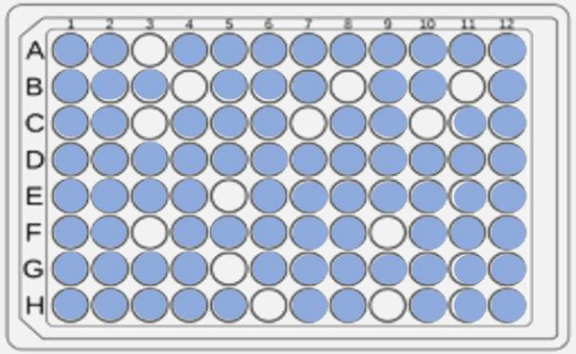
Phage display screening



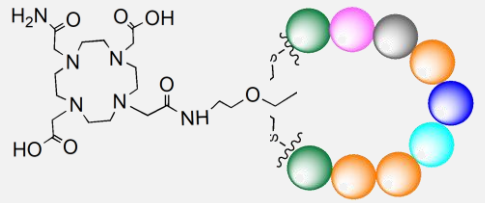
Initial hits



Affinity maturation



Chelator/linker optimization



Hit to lead

- Discovered through cyclic peptide phage-display (900 million AA sequences, 2.7 billion structural variants)
- Affinity matured through full-position scanning
- FAP-targeted peptide conjugated to PSC chelator for Pb-203/Pb-212 theranostics
- Bioconjugate chemistry and further optimization
- In vitro and in vivo binding assays identified lead candidates

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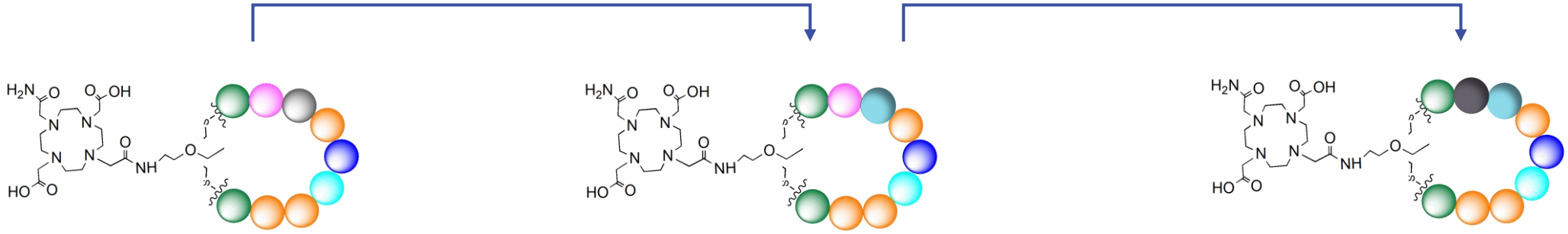
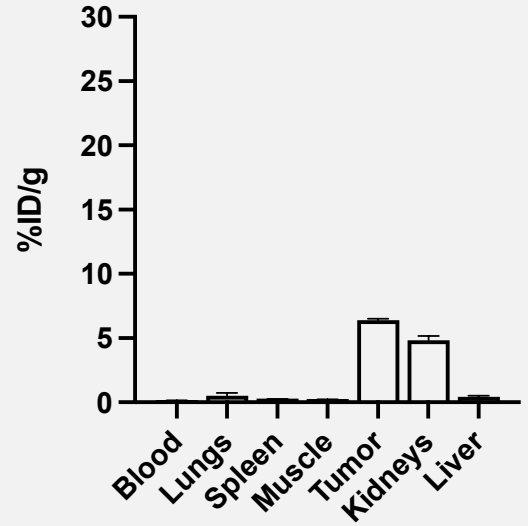
Hit-to-lead Structure Changes that Led to Optimized Compound

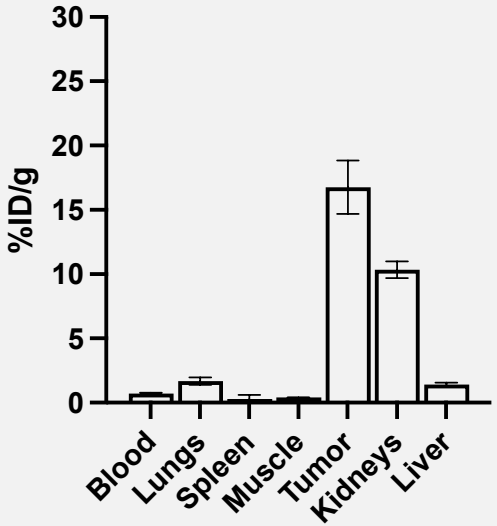
In-house peptide synthesis and in vivo capability allows rapid iteration and optimization of novel compounds



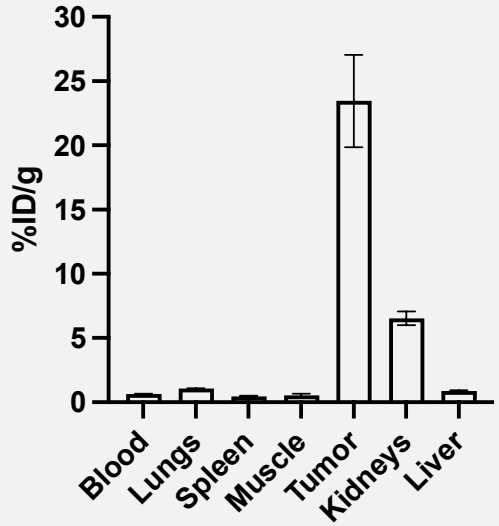
Compound 3-30



Compound 3-42



Compound 3-59



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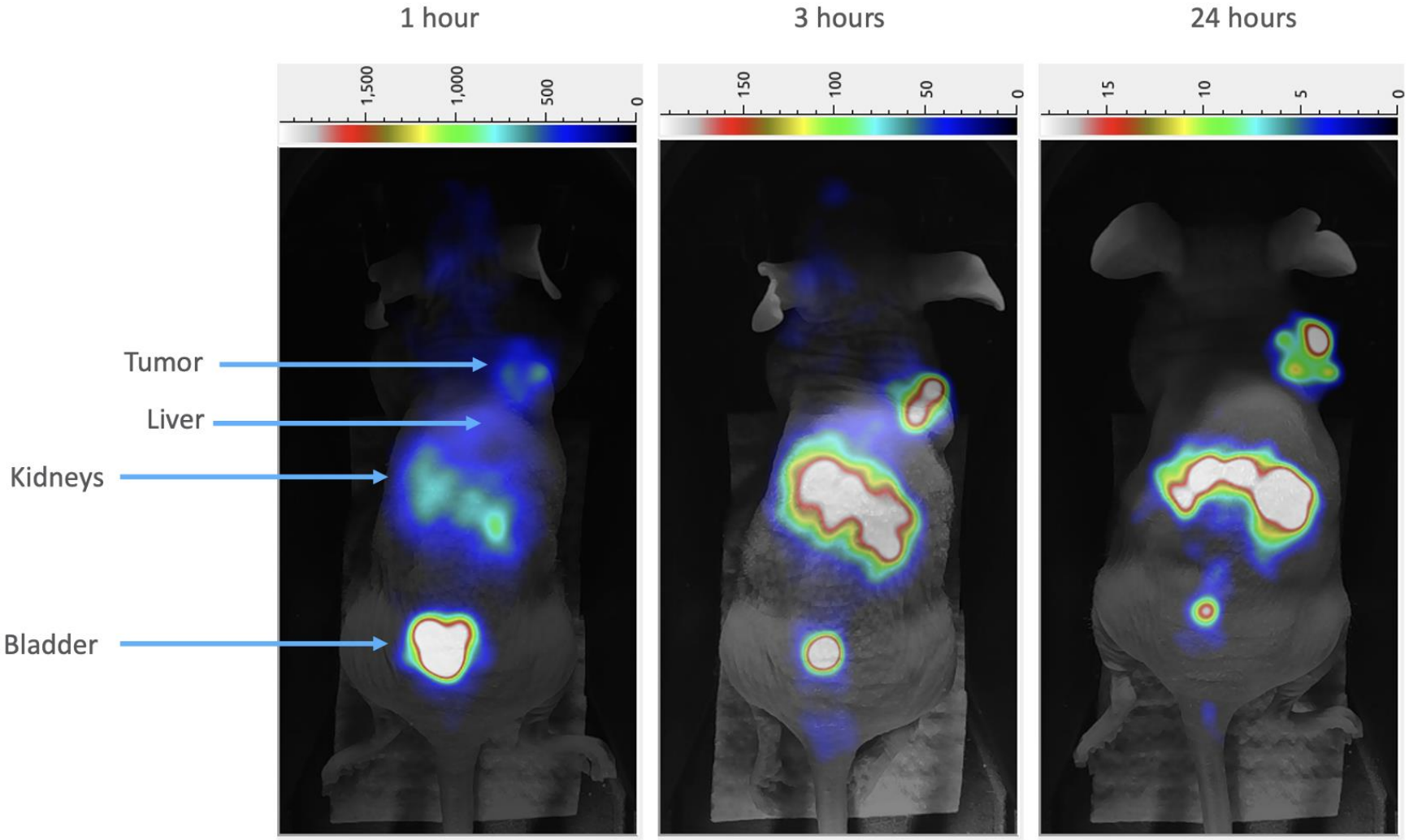
Initial [^{203}Pb] Candidate via Micro SPECT/CT Imaging



In vivo Evaluation

- Good tumor uptake but could be faster
- Some liver uptake
- Slight kidney retention
- Decision made to optimize further

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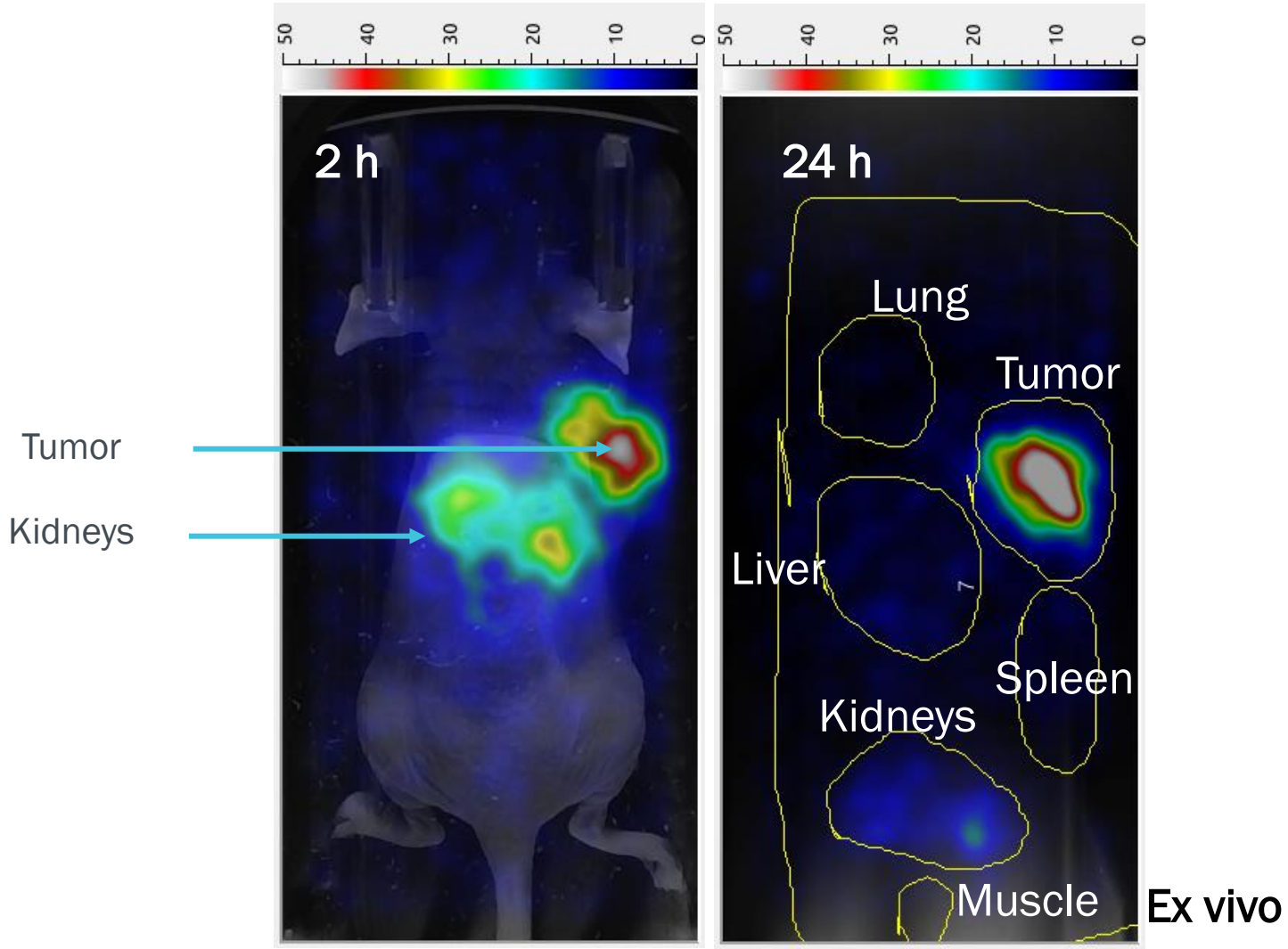
Optimization: Second [^{203}Pb] Candidate via Micro SPECT/CT Imaging



In vivo Evaluation

- Better tumor uptake
- Little liver retention
- Better kidney clearance
- Decision made to optimize further to decrease kidney uptake

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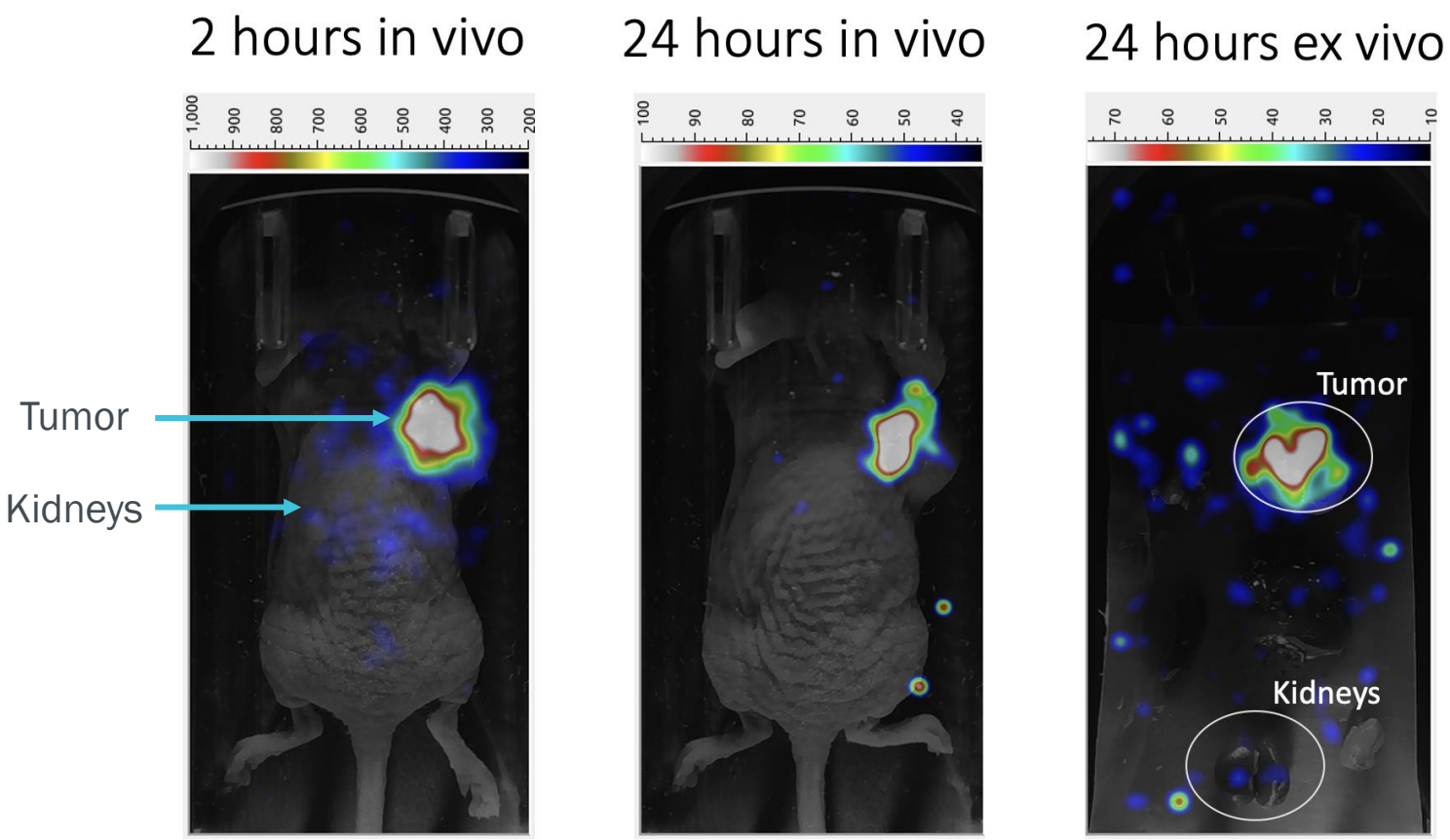
Clinical Candidate Selection: [^{212}Pb]PSV359 via Micro SPECT/CT Imaging



FAP Project Ready for Clinical Development Phase

- ~18 months development time
- Over 900 million amino acid sequences initially scanned
- Identified ~400 sequences for secondary evaluation
- Narrowed to approximately 30 sequences
- Optimized stability, tumor targeting, and clearance properties
- **Compared to competing leads**
- Identified final candidate

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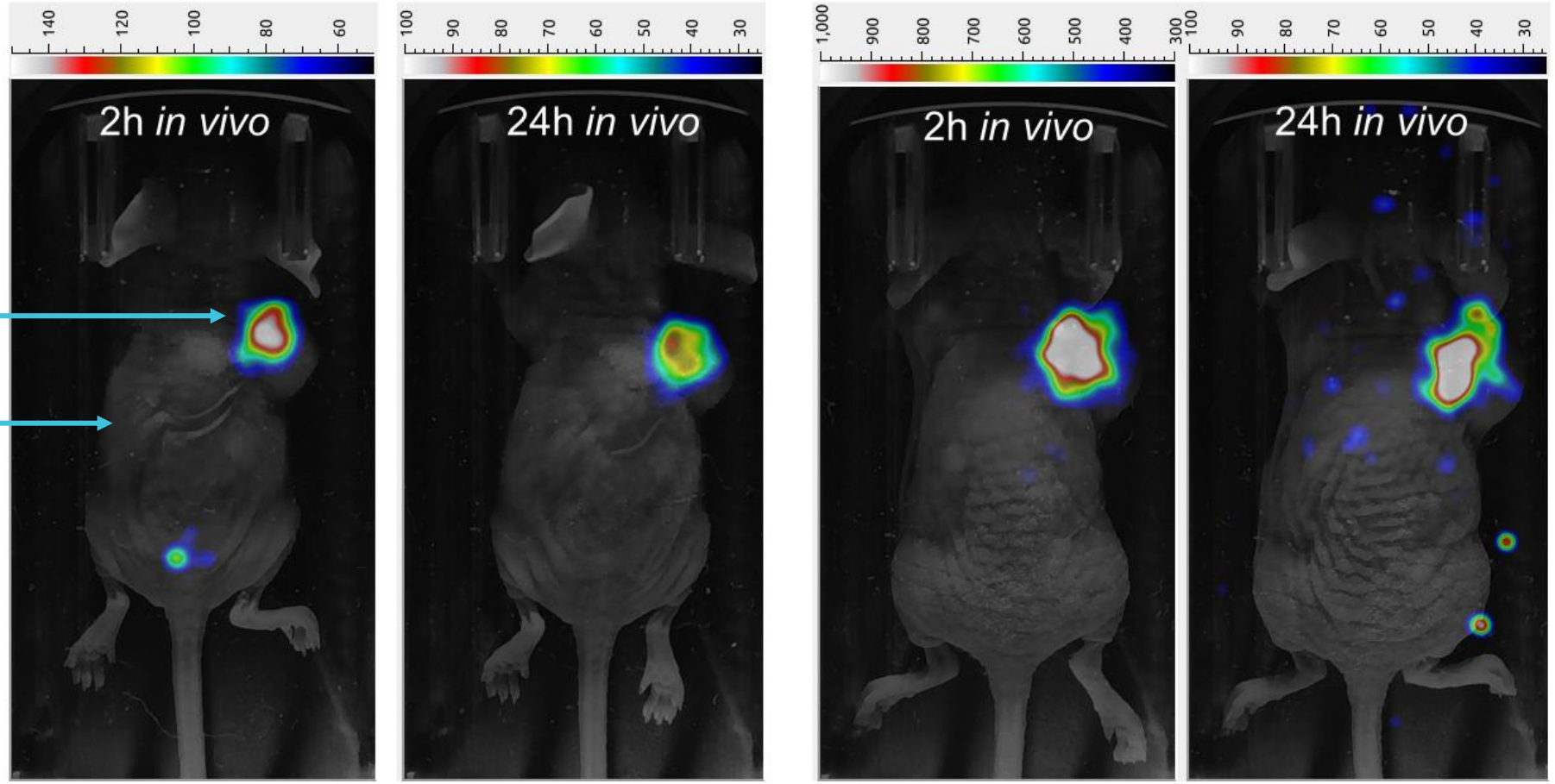
[^{212}Pb]PSV359 via Micro SPECT/CT Imaging

Confirms identical biodistribution of imaging and therapeutic isotopes

[^{203}Pb]Pb-PSV-359

[^{212}Pb]Pb-PSV-359



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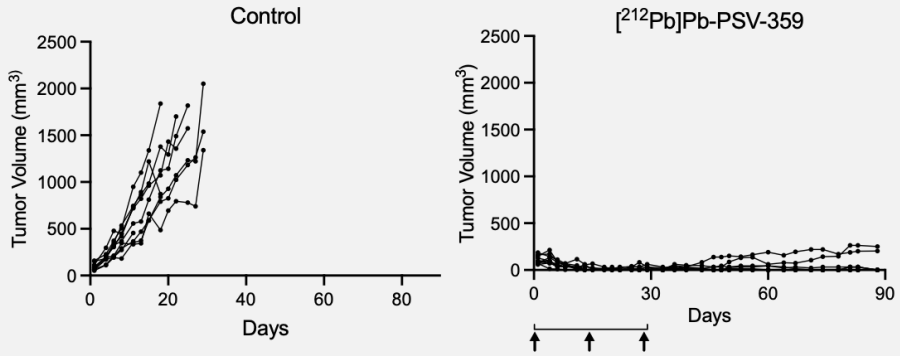
[^{212}Pb]PSV359 Demonstrates Preclinical Efficacy in Human Fibrosarcoma Model

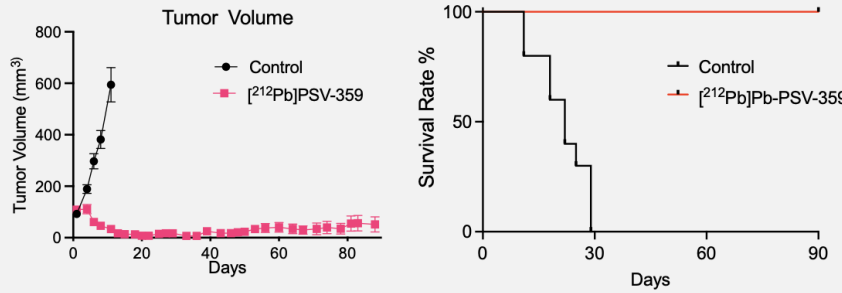
Compares favorably against other therapeutic products in development[2]

Preclinical [^{212}Pb]PSV359 Targeted Alpha Therapy[1]

hFAP-HT1080 Fibrosarcoma Model – Expressing hFAP-α



U87MG Human Glioma Model – Stromal Model (mFAP-α)



90-day results

European Journal of Nuclear Medicine and Molecular Imaging (2022) 49:3651–3667
https://doi.org/10.1007/s00259-022-05842-5

ORIGINAL ARTICLE

Check for updates

Preclinical evaluation of FAP-2286 for fibroblast activation protein targeted radionuclide imaging and therapy

Dirk Zboralski[1] · Aileen Hoehne[1] · Anne Bredenbeck[1] · Anne Schumann[1] · Minh Nguyen[2] · Eberhard Schneider[1] ·

Summary Table

Treatment	*MTV, Day 0 (mm³, mean ± SD)*	*MTV, Day 9 (mm³, mean ± SEM)*	*MTV, Day 23 (mm³, mean ± SEM)*	*TGI, Day 9 (%)*	*MST (Day)*	*Tumor Free Mice (N, %)*
Vehicle	169 ± 21	952 ± 195	NA	NA	16.5	0/10 (0)
^{177}Lu-FAP-2286 (30 MBq)	169 ± 23	107 ± 15	12 ± 4	108% (*P*<0.0001)*	NR	4/10 (40)
^{177}Lu-FAPI-46 (30 MBq)	168 ± 22	245 ± 76	1210 ± 185 (*P*<0.0001)*	90 (*P*=0.0006)*	27.5	0/10 (0)

BWL, body weight loss; MTV, mean tumor volume; SEM, standard error of the mean; TGI, tumor growth inhibition; MST, median survival time; *P-value was determined for day 9 comparisons to the vehicle group, while for day 23 comparison was between ^{177}Lu-FAP-2286 and ^{177}Lu-FAPI-46

40-day results

[1]Perspective unpublished data; [2]Zboralski et al., EJNMMI, 2022

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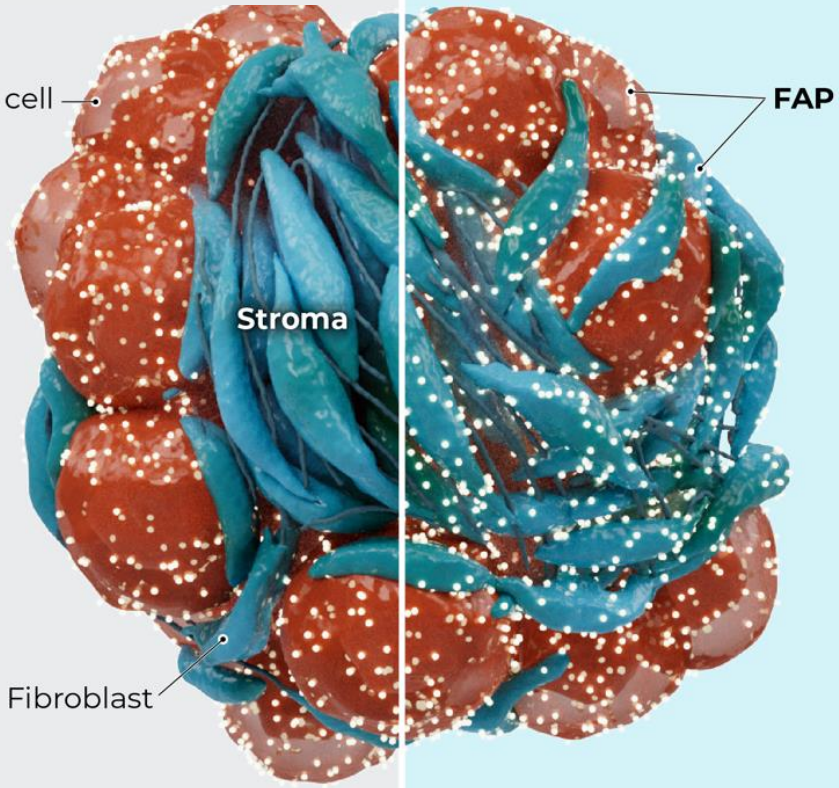
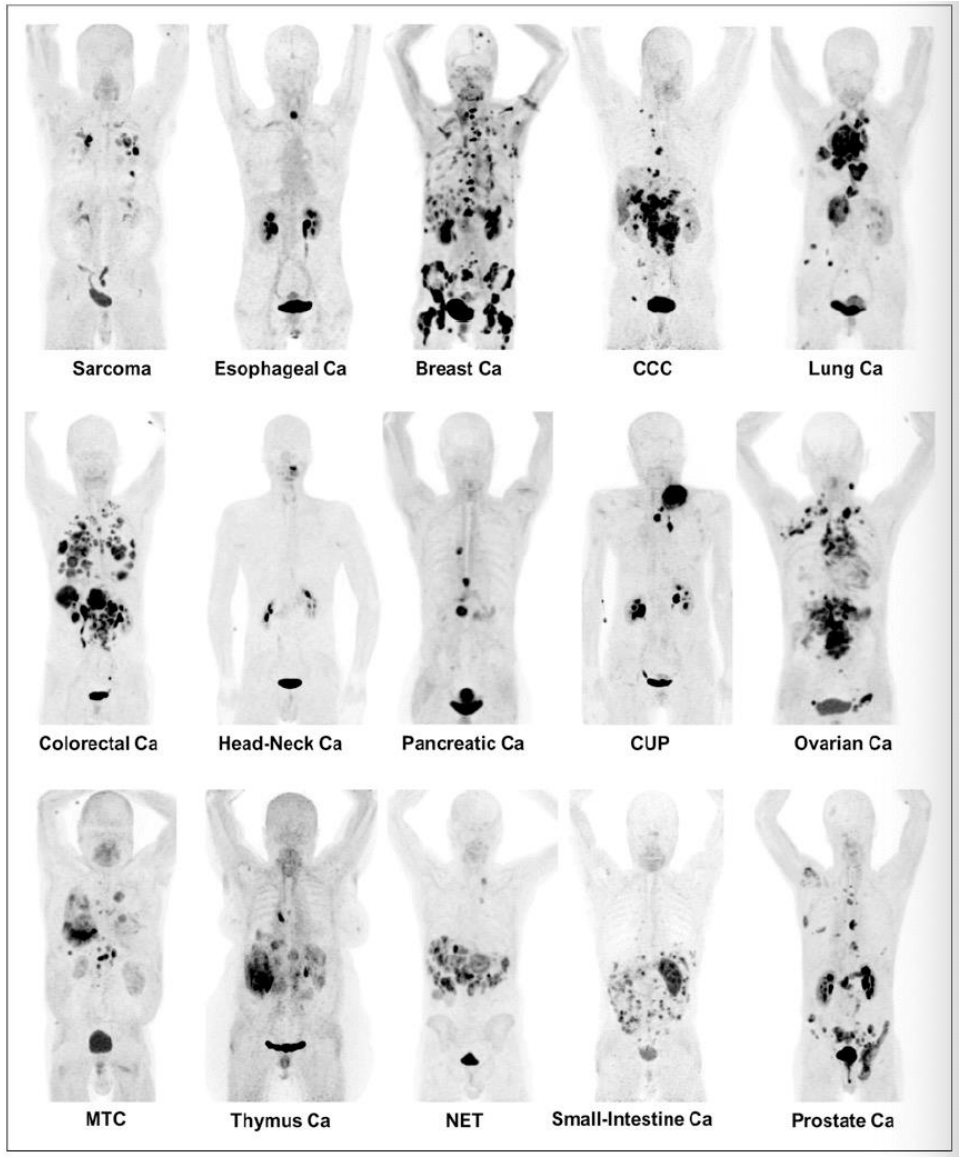
Fibroblast Activation Protein α is a Pan Cancer Target

Tumor stroma cells do not typically express cancer-specific markers like SSTR2 or MC1R

FAP is primarily expressed on tumor stroma cells, but also on some cancer cells





Kratochwil et al., JNM, 2019

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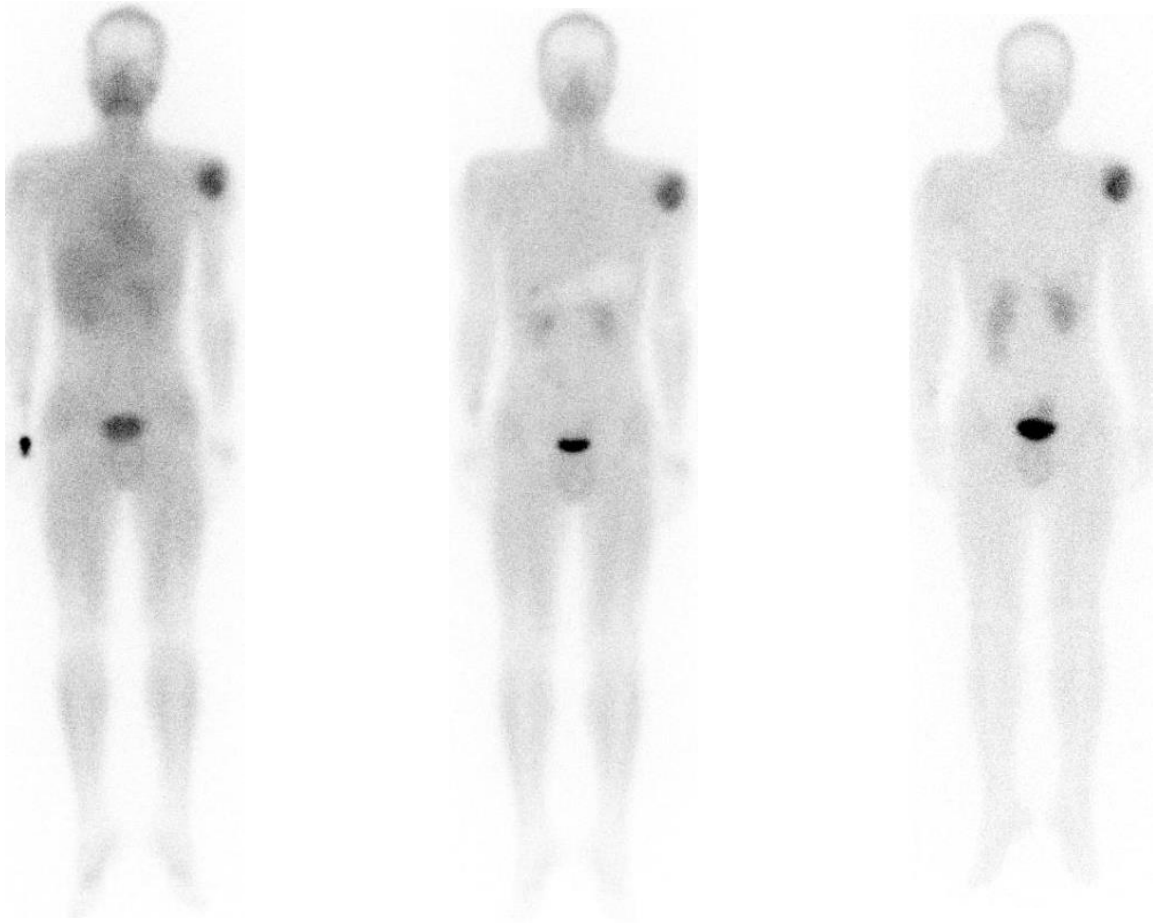
First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 1 Chondroblastic Osteosarcoma

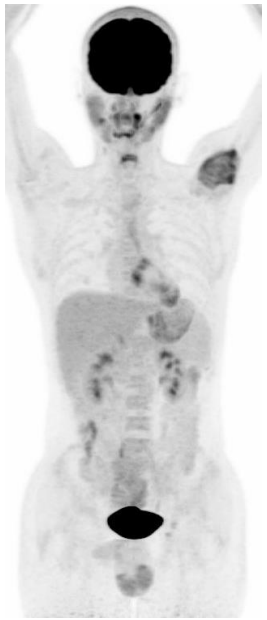
Treating Physician:
Dr. Ishita B Sen
Director & Head
Dept. of Nuclear Med.
& Molecular Imaging
Fortis Memorial Research
Institute, Gurgaon, India

[^{203}Pb]PSV359



1 hr | 4 hr | 18 hr

[^{18}F]FDG



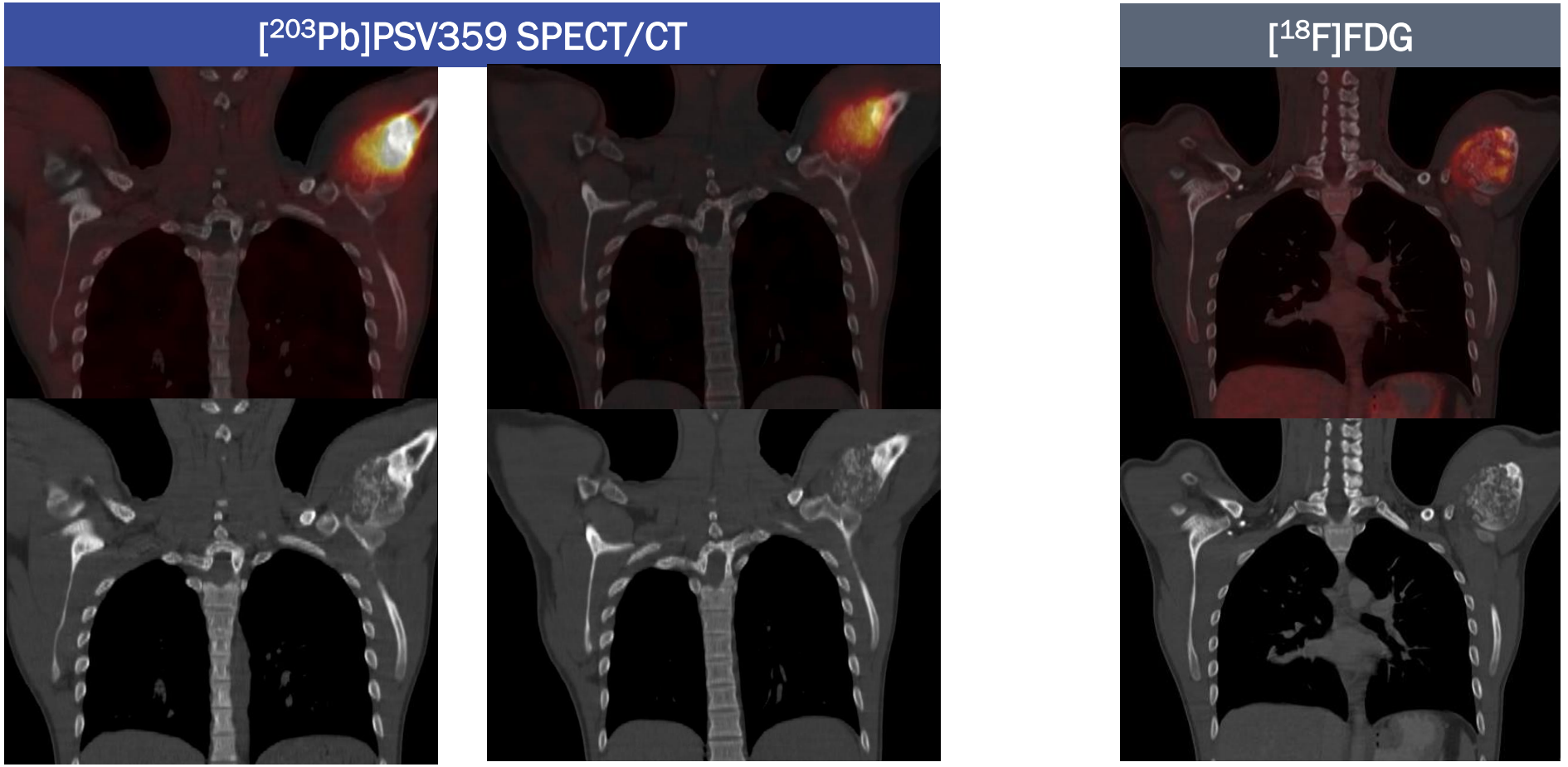
Case 3: 16 yrs/Male, Chondroblastic Osteosarcoma
Injected Dose 7.2 mCi (266.4 MBq)
(anterior views)

published data

PERSPECTIVE THERAPEUTICS

First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 1 Chondroblastic Osteosarcoma

Lesion in head of left humerus

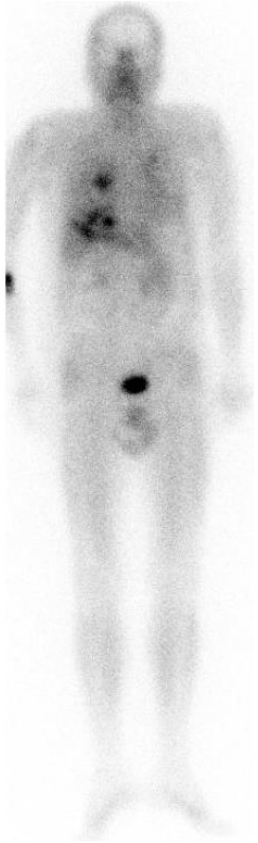


Fortis Hospital, Ishita Sen MBBS, unpublished data

PERSPECTIVE THERAPEUTICS

First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 2 Neuroendocrine Tumor

[^{203}Pb]PSV359



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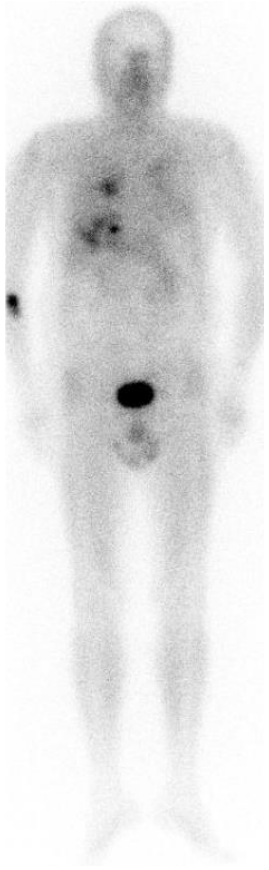

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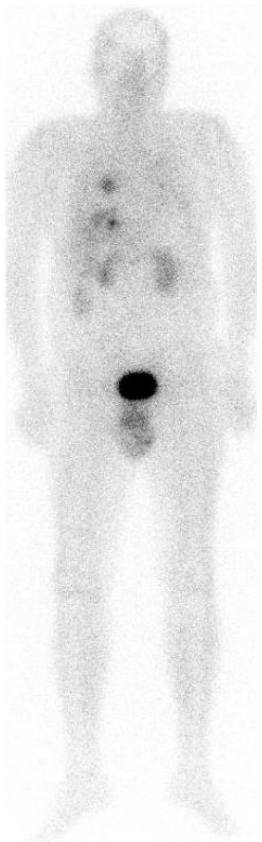

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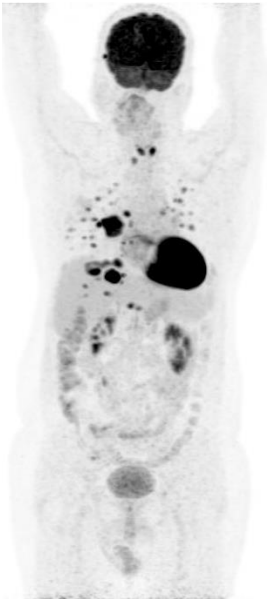
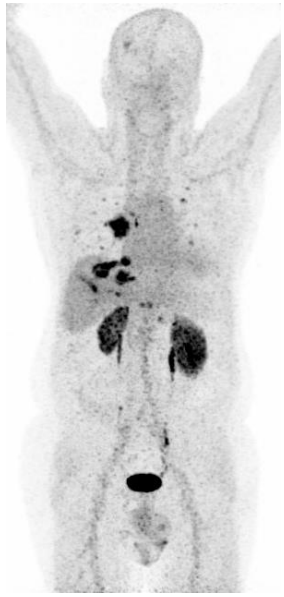
[^{18}F]FDG



[^{68}Ga]FAPI-2286



Case 2: 71yrs/Male, Metastatic GEP Neuroendocrine Tumor
Injected Dose: 7.0 mCi (259 MBq)
(anterior views)

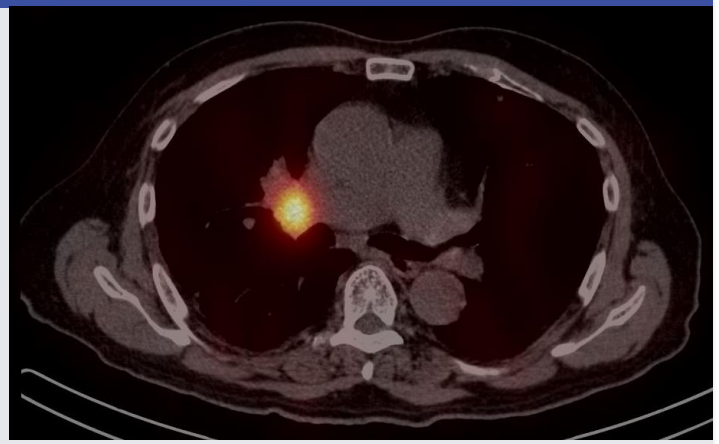
Fortis Hospital, Ishita Sen MBBS, unpublished data

PERSPECTIVE THERAPEUTICS

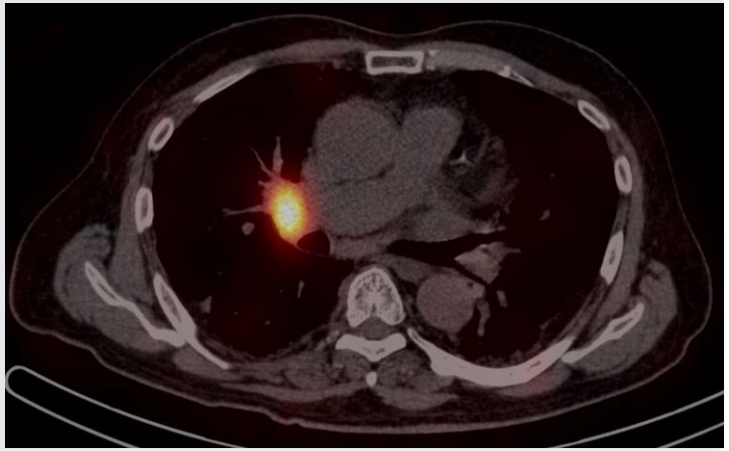
First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 2 Neuroendocrine Tumor

[^{203}Pb]PSV359 SPECT/CT

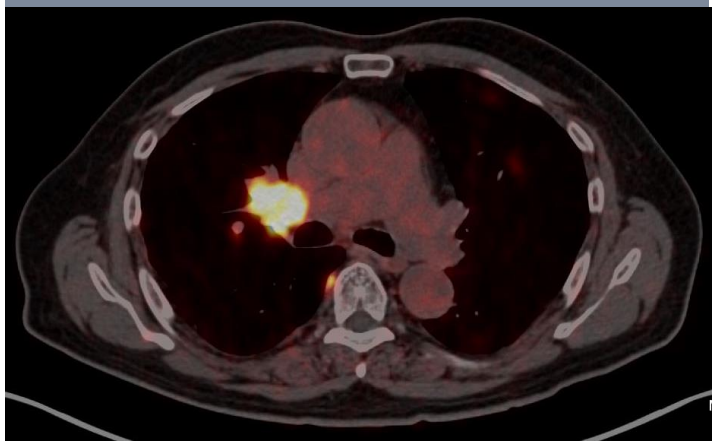
4 hr



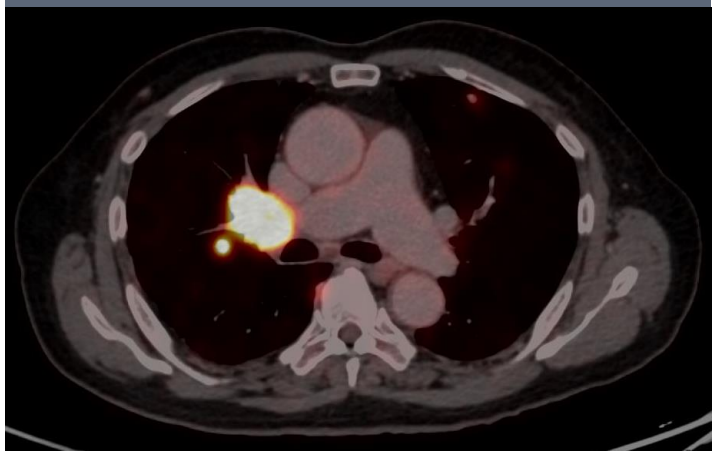
18 hr



[^{68}Ga]FAPI-2286 PET/CT



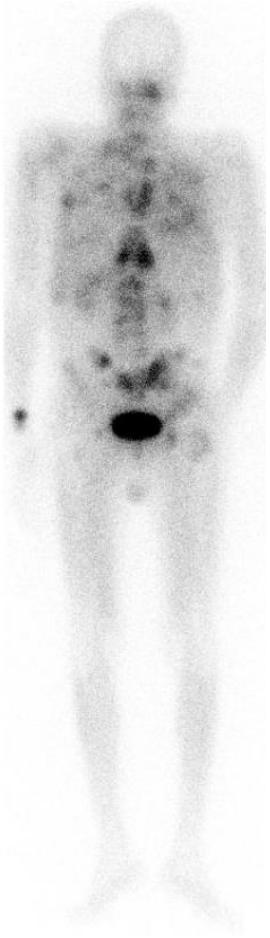
[^{18}F]FDG



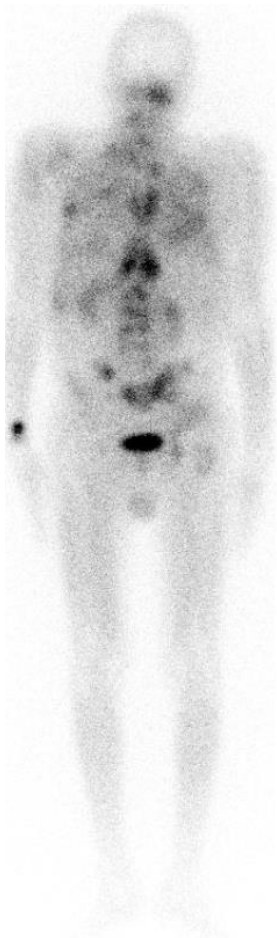
Fortis Hospital, Ishita Sen MBBS, unpublished data

First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 3 Lung Adenocarcinoma

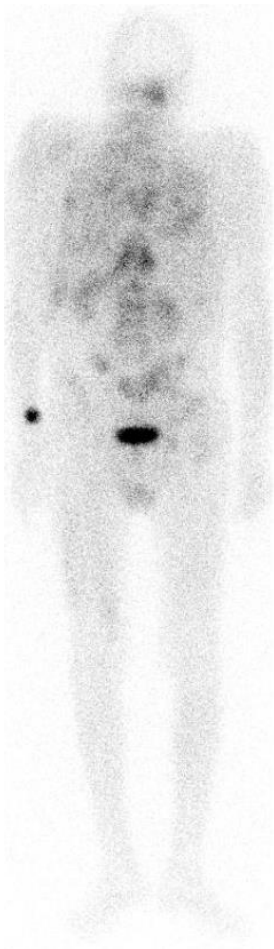
[^{203}Pb]PSV359



1 hr

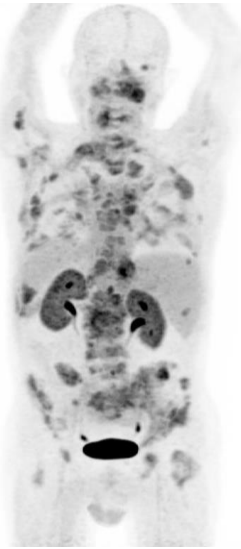


4 hr



18 hr

[^{68}Ga]FAPI-2286 PET



Case 3: 51 yrs/Male, Metastatic adenocarcinoma lung
Injected dose:
7.0 mCi (259 MBq)
(posterior views)

Fortis Hospital, Ishita Sen MBBS, unpublished data

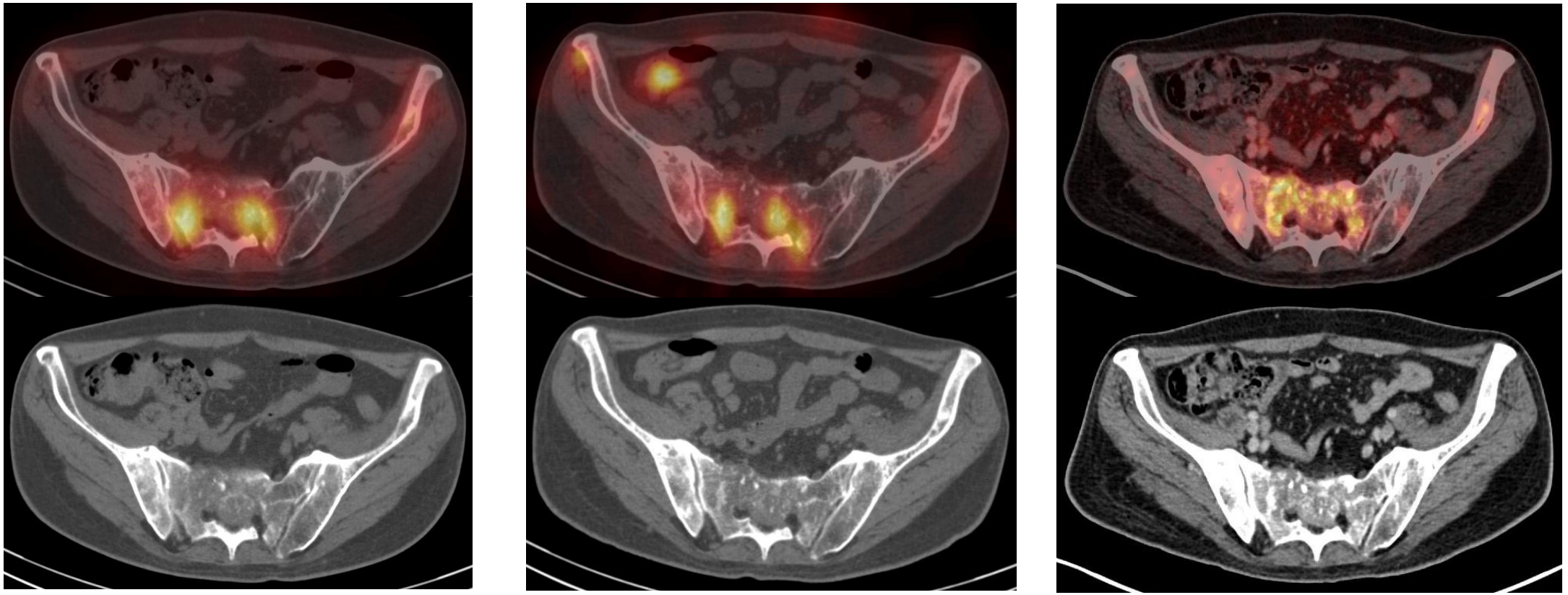
PERSPECTIVE THERAPEUTICS

First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 3 Lung Adenocarcinoma

Lytic lesion in sacrum

[^{203}Pb]PSV359 SPECT/CT

[^{68}Ga]FAPI-2286 PET/CT



4 hr

18 hr

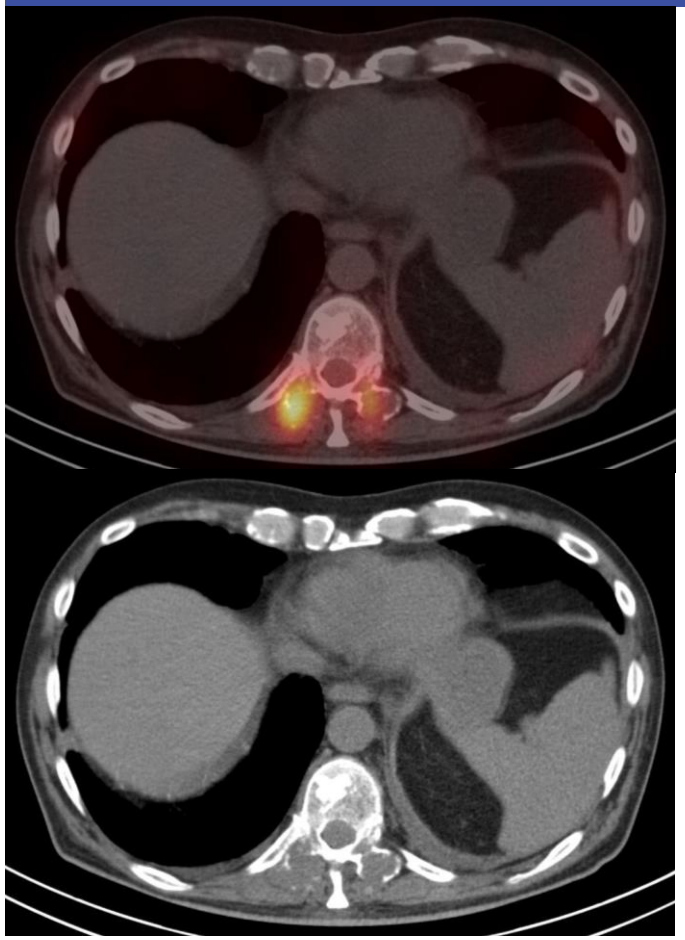
Fortis Hospital, Ishita Sen MBBS, unpublished data

PERSPECTIVE THERAPEUTICS

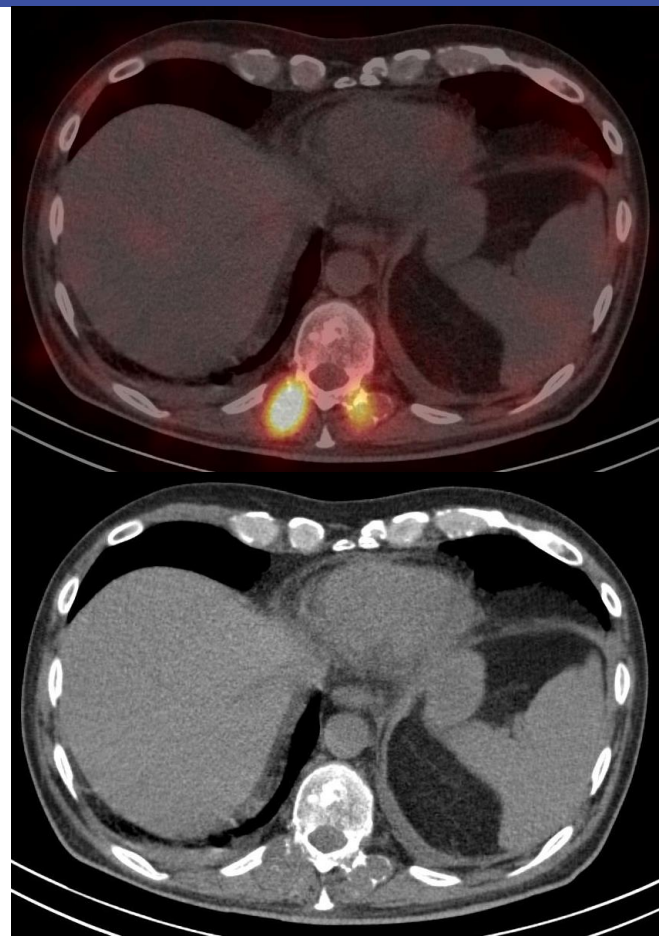
First in Human [^{203}Pb]PSV359 SPECT Imaging – Patient 3 Lung Adenocarcinoma

Lytic lesion in thoracic vertebra

[^{203}Pb]PSV359 SPECT/CT

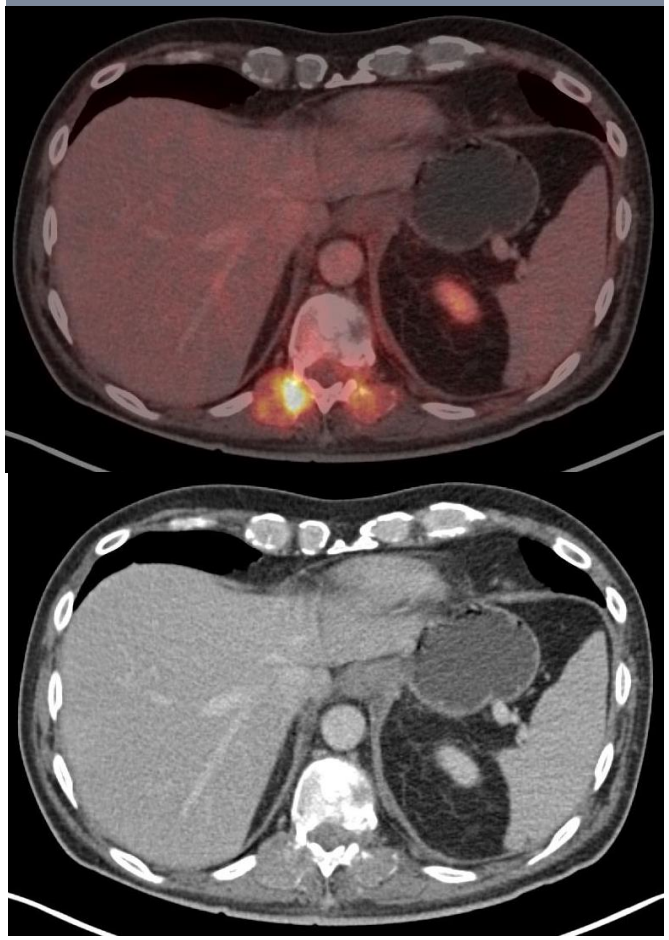


4 hr



18 hr

[^{68}Ga]FAPI-2286 PET/CT



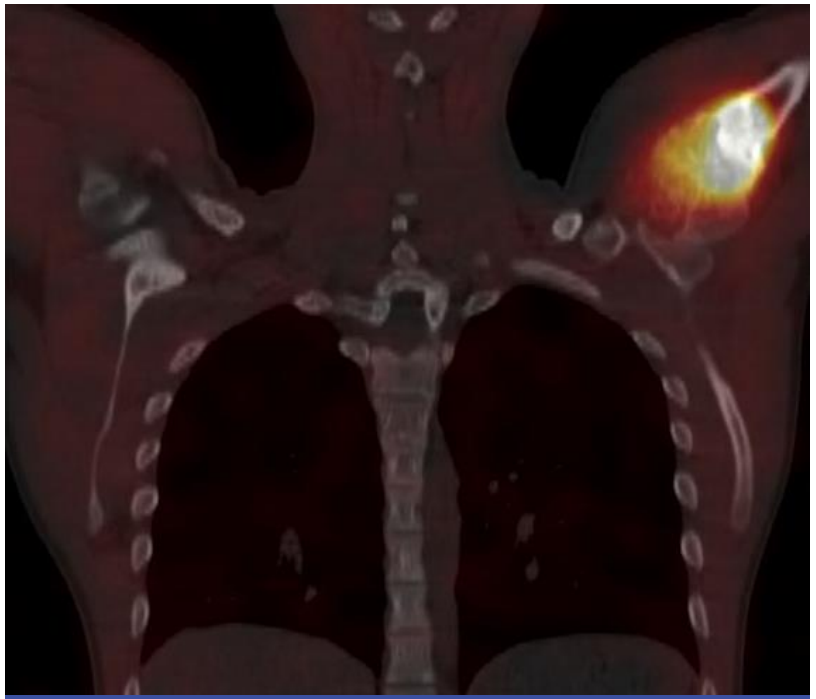
Fortis Hospital, Ishita Sen MBBS, unpublished data

PERSPECTiVE THERAPEUTICS

Summary – PSV359 FAP-α Program

Potential to be a best-in-class pan-cancer targeted alpha particle therapeutic

- FAP-α is a pan-cancer target that is highly expressed many cancers
- Perspective's in-house discovery team has developed an optimized peptide with potential best-in-class characteristics as demonstrated in preclinical models
- First in human clinical SPECT/CT imaging suggests the tumor targeting and retention of the PSV359 compound is excellent, while clearing from normal organs rapidly and completely
- The FAP-α PSV359 program is a significant addition to Perspective's clinical pipeline of targeted alpha therapeutic assets



[^{203}Pb]PSV359 SPECT/CT[1]

Fortis Hospital, Ishita Sen MBBS, unpublished data (Patient 1, osteosarcoma)

PERSPECTIVE THERAPEUTICS

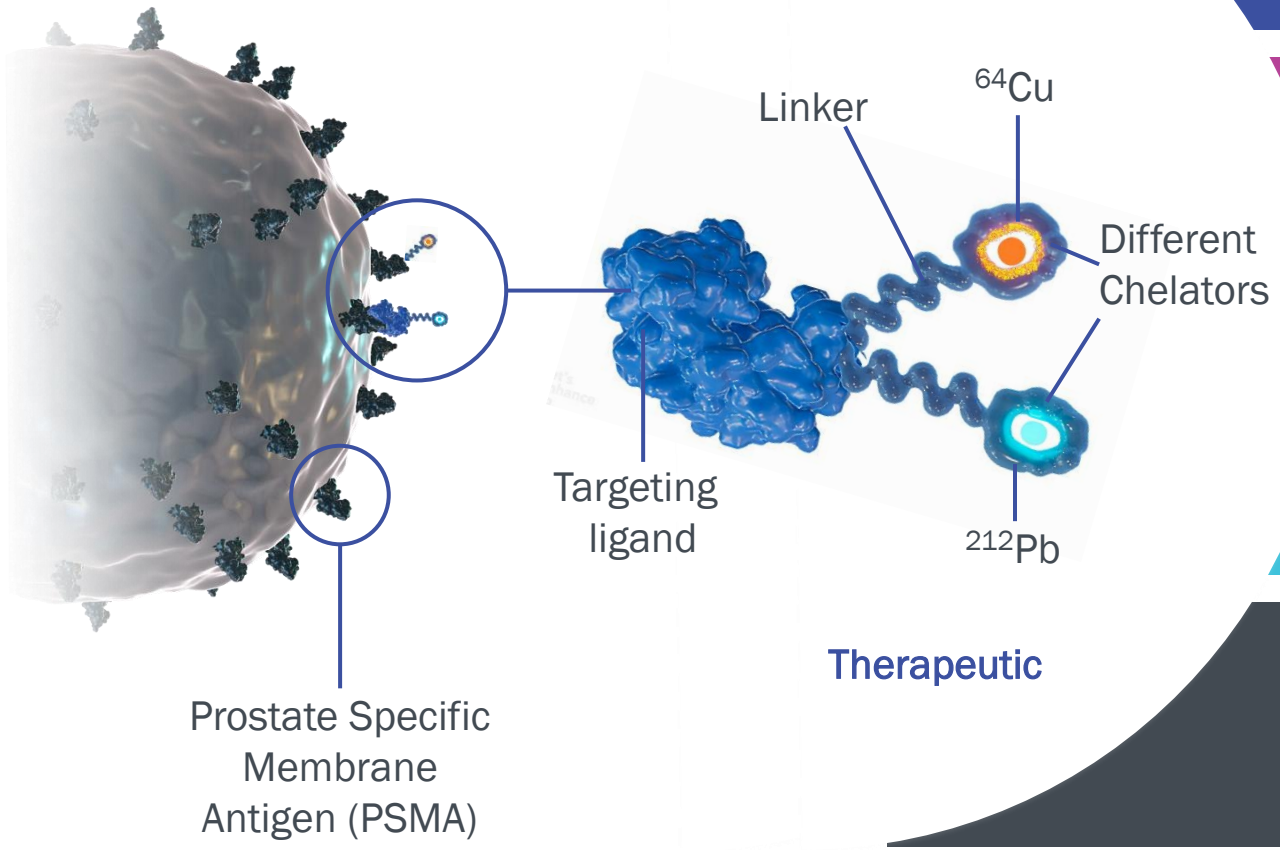
Preclinical Programs: Prostate Cancer

A differentiated PSMA-targeted radiohybrid molecule for dual PET imaging and targeted alpha therapy

PERSPECTIVE THERAPEUTICS

Prostate Cancer Program: PSV40X

A differentiated PSMA-targeted radiohybrid molecule for dual PET imaging and targeted alpha therapy



PSMA is a clinically and commercially validated target for radioligand therapy

Combines two chelators with single targeting ligand to provide identical distribution of imaging and therapeutic agents

Has shown promise in reduction of salivary gland uptake in preclinical models of prostate cancer[1]

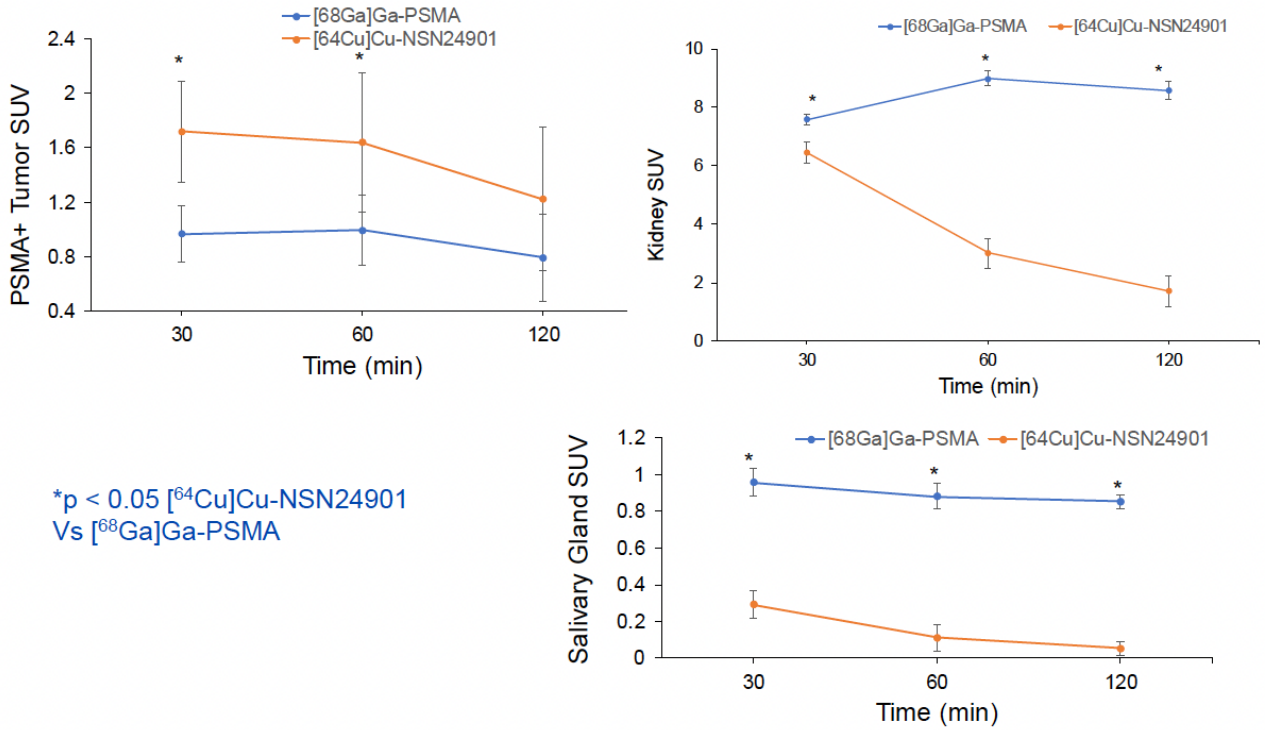
Technology licensed from Mayo Clinic January 2024
IND-enabling studies underway
First in human data expected in 2024

[1]Johnson et al., RPT Interest Group June 7 2023 https://rrp.cancer.gov/working_groups/AlphaPET-RPT_Int_group_lecture.pdf

PSV40X: Improved Preclinical Metrics for a Superior Therapeutic Window in Prostate Cancer

PSV404 (designated NSN24901 by Mayo Clinic) shows promise in preclinical setting

Comparison of Uptake of [^{68}Ga]PSMA-11 and [^{64}Cu]PSV404 ("NSN24901") in Tumor, Kidney and Salivary Gland of LNCaP Tumor Athymic Nude Mice



- Higher tumor accumulation/retention
- Significantly lower salivary gland uptake and retention
- Significantly lower kidney accumulation and retention
- Higher therapeutic window and reducing the potential for xerostomia that limits current PSMA-targeted prostate cancer radiopharmaceutical therapies

Multiple International Patents : Pending

25th June 2023
SNMMI-CE14, Chicago IL, USA

PERSPECTIVE THERAPEUTICS

Preclinical Programs: Pre-targeting Platform

The Next Generation of Targeted Alpha Particle Radiopharmaceuticals

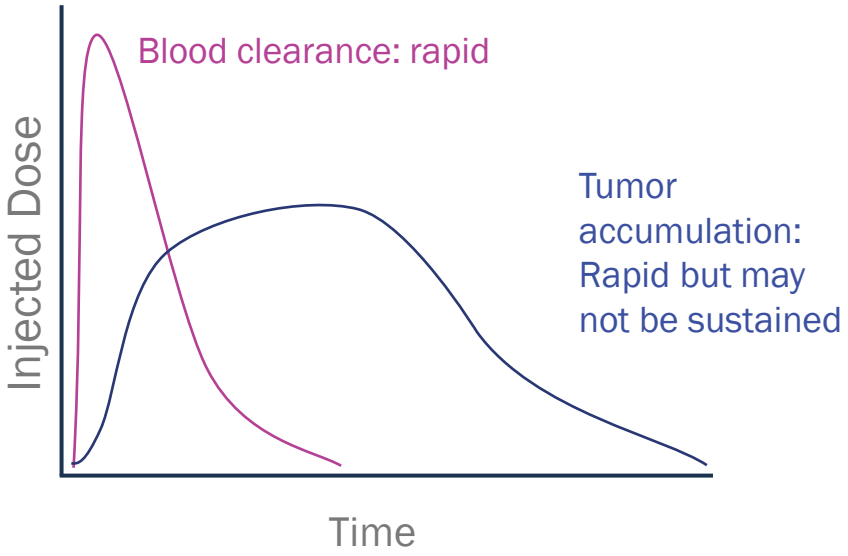
PERSPECTIVE THERAPEUTICS

Pre-targeting Rationale: Current Radiopharmaceutical State of the Art

Peptide-based radiopharmaceuticals are the most successful commercial radioligand products

- Peptide and peptide-like small molecules
- Rely on fast clearance from the body to reduce radiation dose to non-target tissues
- Typically clear through the kidneys
- Sometimes tumor retention is an issue
- Less suitable for long-lived isotopes
- Examples: LUTATHERA®, PLUVICTO®, VMT01, VMT-α-NET etc

Peptide & Small Molecule Kinetics



Peptides are the perfect targeting vectors for high dose-rate isotopes such as ^{212}Pb, as the biological and radiation half-lives are matched

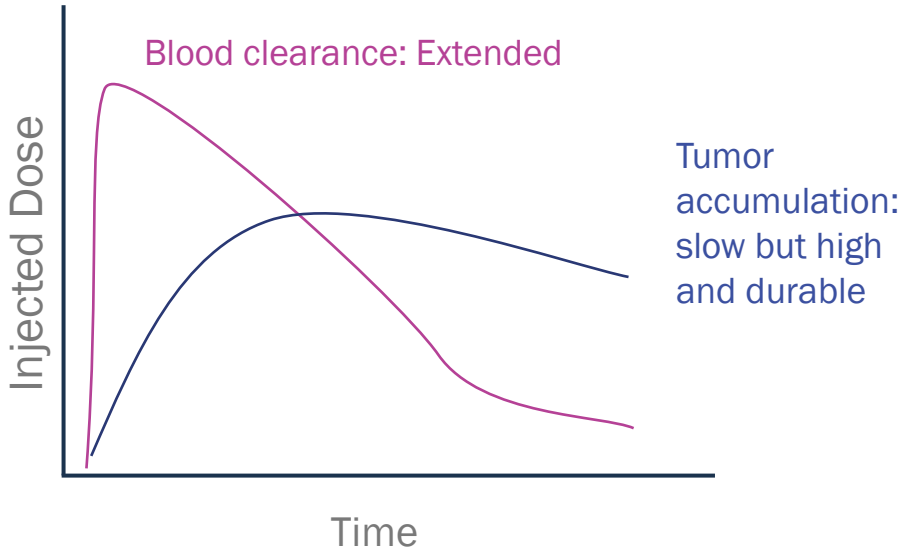
PERSPECTIVE THERAPEUTICS

Pre-targeting Rationale: mAbs Have Significant Role in Cancer Therapy

Antibody Drug Conjugates (ADCs) are a successful high-growth product class but mAbs are not ideal radiopharmaceuticals

- FDA has approved over 100 mAbs: 9 of the top 20 therapeutic products worldwide with more than $75 billion in sales (2021)[1]
- ADCs are commercially successful (current market size approx $10 billion[2]) but some safety issues with Blackbox warnings[3]
- Success of mAbs as vectors to target radiation has been limited (BEXXAR®, Zevalin®)[4]
- Long circulation times increase off-target radiation toxicity to marrow and healthy organs compared to peptides or small molecules[5]
- Tumor accumulation can be very high and retention long
- Very long list of targets for mAbs available

mAb Kinetics



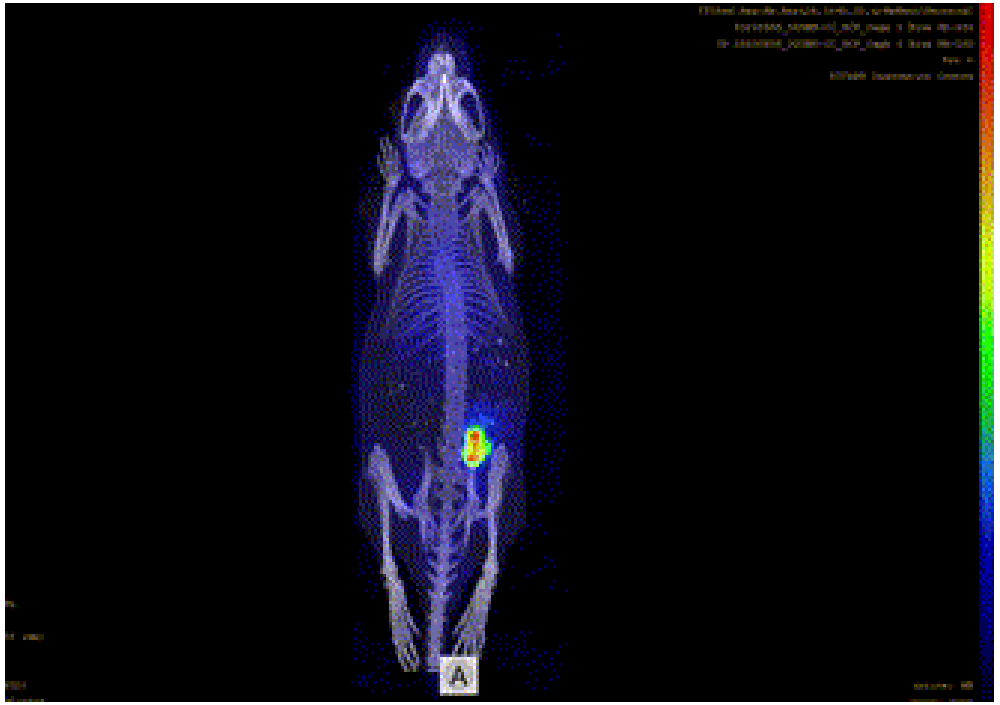
Antibodies and antibody fragments have high and specific tumor uptake but clear slowly so are not ideal radiopharmaceuticals

[1]Mullard, Nat Rev Drug Discovery 2021; [2]www.marketsandmarkets.com/Market-Reports/antibody-drug-conjugates-market-122857391.html; [3]Nguyen et al, Cancers, 2023; [4]www.nytimes.com/2007/07/14/health/14lymphoma.html; [5]Rondon et al, Cancers, 2021

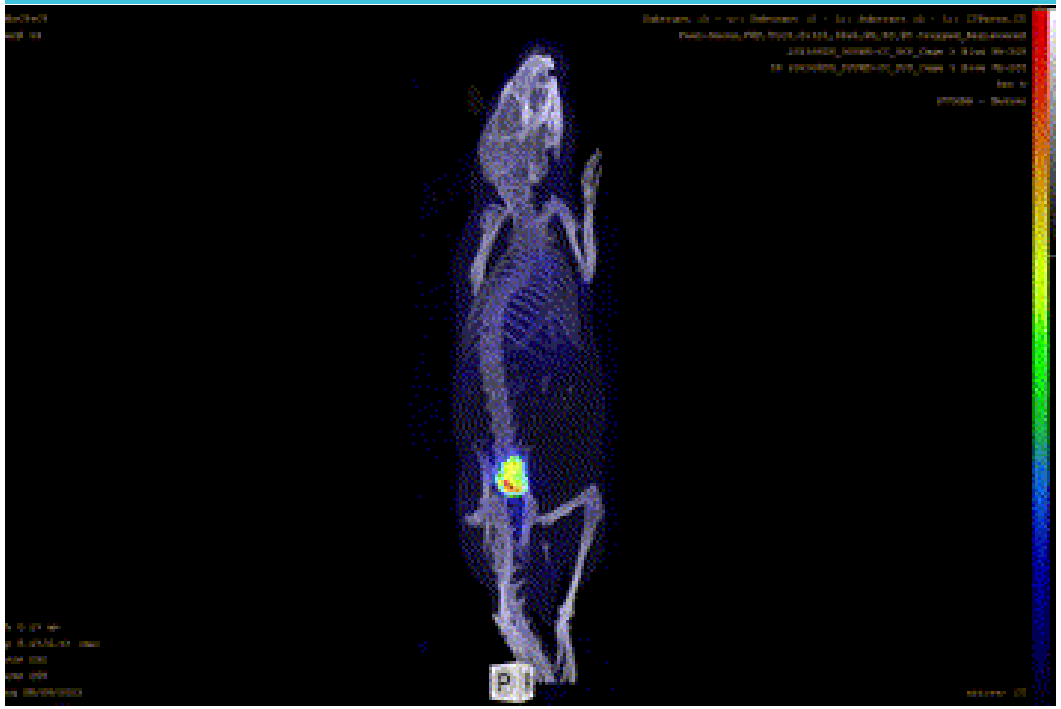
PERSPECTIVE THERAPEUTICS

Specificity of mAbs: [^{203}Pb]mAb SPECT Imaging Preclinical Example

48 hours post- injection



120 hours post- injection



Observations

- Precise tumor targeting
- Accumulation over days
- Residual radiation clears
- High-resolution image

Question?

Is it possible to exploit the tumor targeting and uptake of mAbs, but retain the rapid clearance properties of peptides and small molecules?

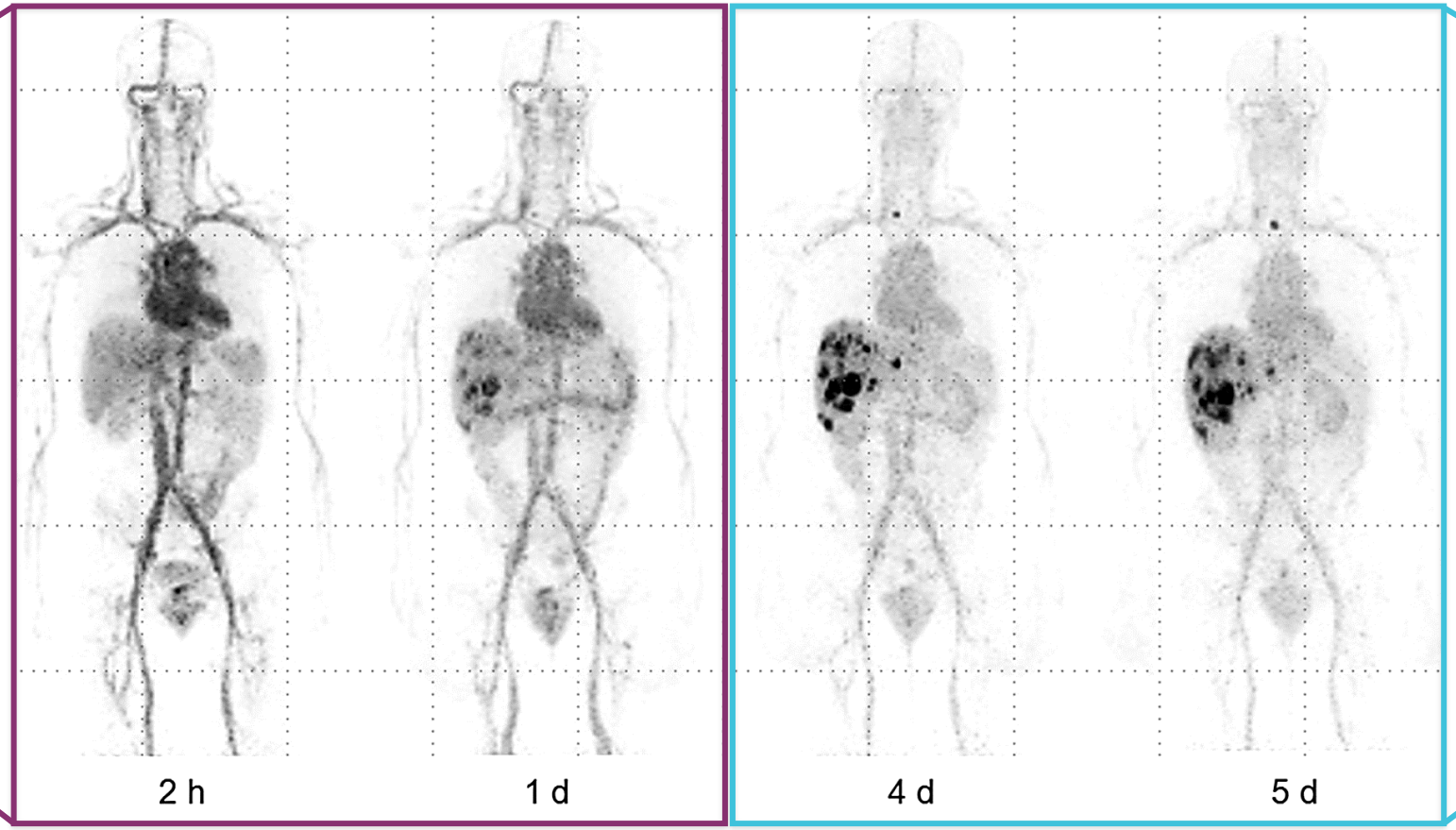
PERSPECTIVE THERAPEUTICS

Tumor Targeting Properties of mAbs are Ideal for Accumulation on Target (but slow)

Representative imaging across longer time frame demonstrates clearance and uptake kinetics

Patient with HER2 positive esophagogastric adenocarcinoma metastatic to liver, imaged with [^{89}Zr]trastuzumab[1]

Long circulation time with little tumor uptake for the first 24 h



High accumulation of mAb onto tumor with clearance from blood pool

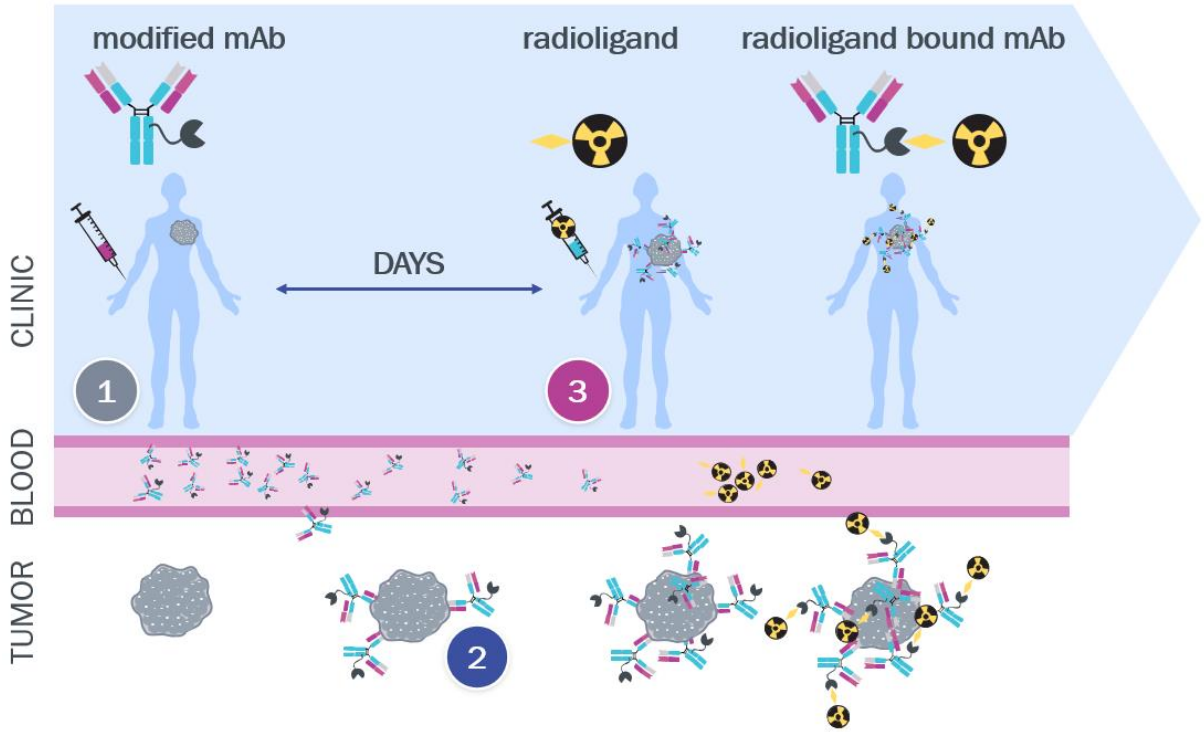
[1]O'Donoghue et al. J Nucl Med 2018

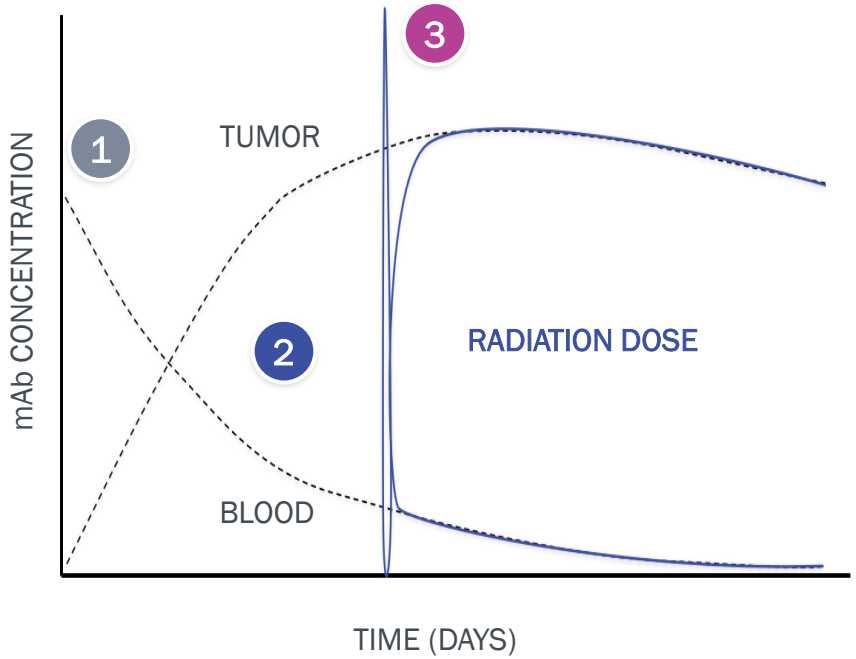
PERSPECTIVE THERAPEUTICS

Pre-targeting Platform: Combining the Best of mAbs and Small Molecules/Peptides

Relies on the different kinetics of large proteins and small molecules *or peptides* and a multi-step process

1. Administer cold modified monoclonal antibody or targeting protein
2. After several days, mAb will have accumulated on tumor and cleared from blood
3. Administer radiolabeled ligand, which binds specifically to mAb and clears rapidly from circulation



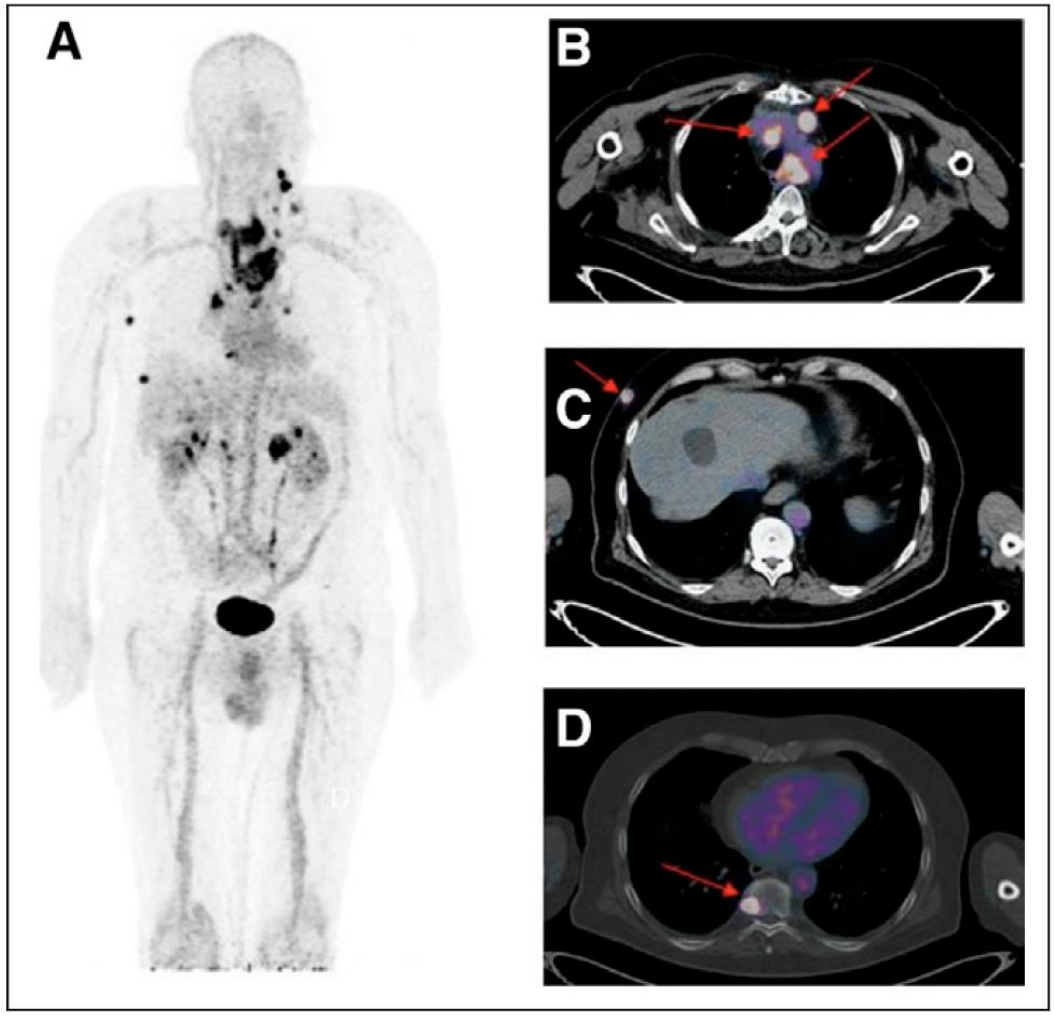


Figures adapted from Jallinoja et al., J. Nuc. Med., 2023 and Liu, Front. Pharmacol., 2018

PERSPECTIVE THERAPEUTICS

Promise of Pre-Targeted Approach – Clinical Data

^{68}Ga-IMP288 – Images ≥ 24 hours following Anti-CEA Bispecific mAb[1]



Immuno-PET/CT with anti-CEA BsmAb and ^{68}Ga-IMP288 peptide showing pathological lesions with heterogeneous SUV_{max} ranging from 3.0 to 20.1

Maximum-intensity-projection (MIP) image (A) showed several pathological lesions

On the fusion axial images, arrows located mediastinal nodes (B), subcutaneous lesions (C), and bone metastasis (D)

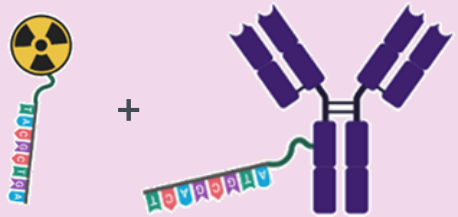
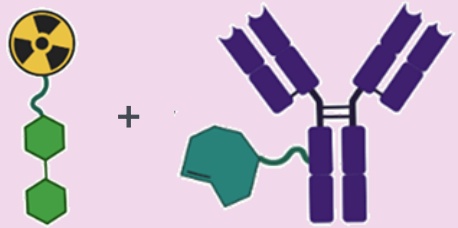
Compelling Proof of Concept for pretargeting, but this system lacks broad "modularity"

[1]Bodet-Milin et al., JNM 2021

PERSPECTIVE THERAPEUTICS

State of the Art in Pre-Targeting for Radiopharmaceuticals

Review of current state of the art technology platforms

	Clinically Evaluated (Phase I / II)	Preclinically Evaluated only
Not Modular	**A. Bispecific Antibody – Hapten (eg SADA)** 	**C. Oligonucleotide Hybridization** 
	B. Streptavidin - Biotin 	**D. Click Chemistry** 
	Immunogenic	Unstable

Current state of the art

- Four platforms reported prior to 2021
- 3 of 4 have been promising preclinically
- All face specific hurdles for widespread clinical use:
  - A. Lack of "modularity“
  - B. Immunogenicity
  - C. Poor tumor uptake
  - D. Stability
- Common hurdle = use of clearing agents

Renaissance School of Medicine
Stony Brook University

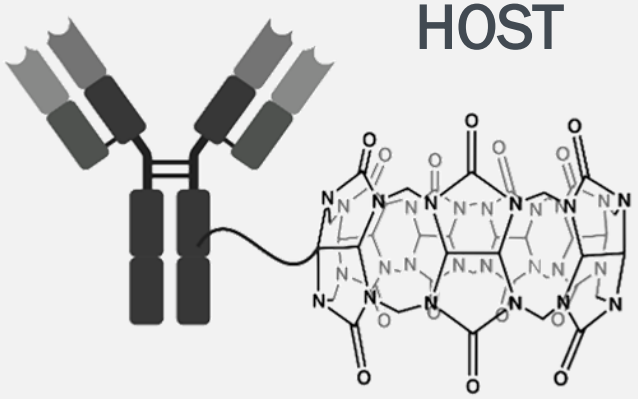
PERSPECTIVE THERAPEUTICS

Jallinoja *et al. J Nucl Med.* 2021.

Perspective Pre-Targeting Platform: Host - Guest Chemistry

After exhaustive review of State of the Art, Perspective chose CB7 (Host) - Adamantane (Guest) System

HOST



Cucurbit[7]uril (CB7) modified antibody (mAb)

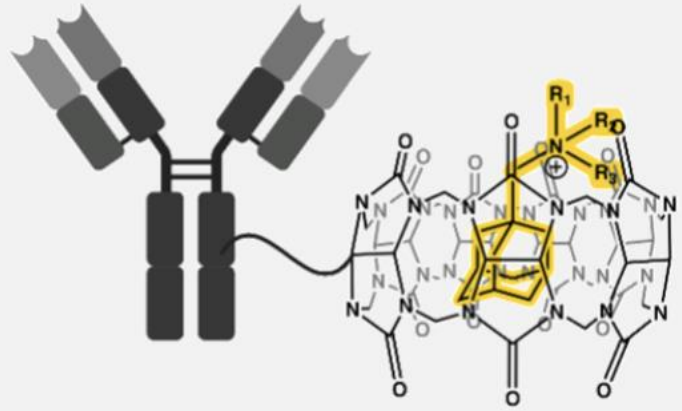
GUEST

Adamantane Radioligand

An ideal pretargeting agent:

- High *in vivo* stability
- Modular
- Non-toxic
- Non-immunogenic
- No need for a clearing agent

GUEST-HOST In vivo engagement on tumors

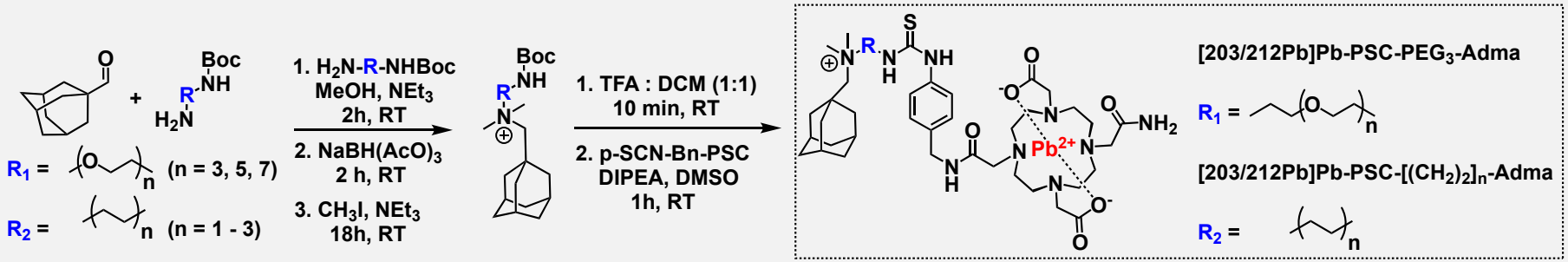


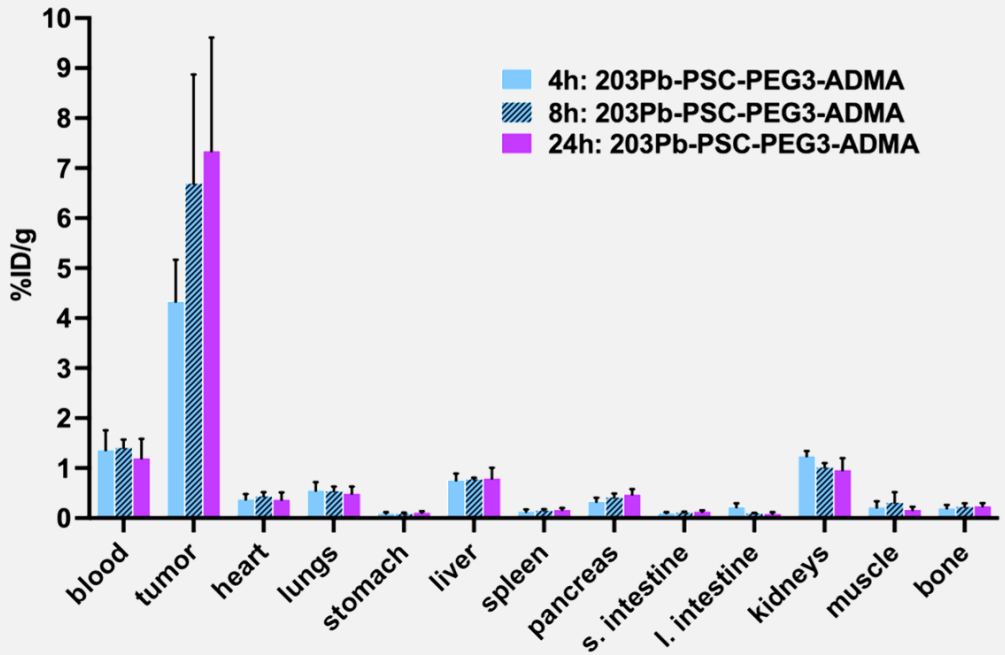
Cucurbituril history
First synthesized 1905 (Behrend, Germany)
Structure described analytically 1981
Named after the pumpkin family Cucurbitacea

PERSPECTIVE THERAPEUTICS

Perspective Pre-Targeting Platform: Host - Guest Chemistry and in vivo Experiment

Synthesized the Guest as an adamantane-PEG3-PSC (Perspective's proprietary chelator)





First in vivo Experiment: Observations

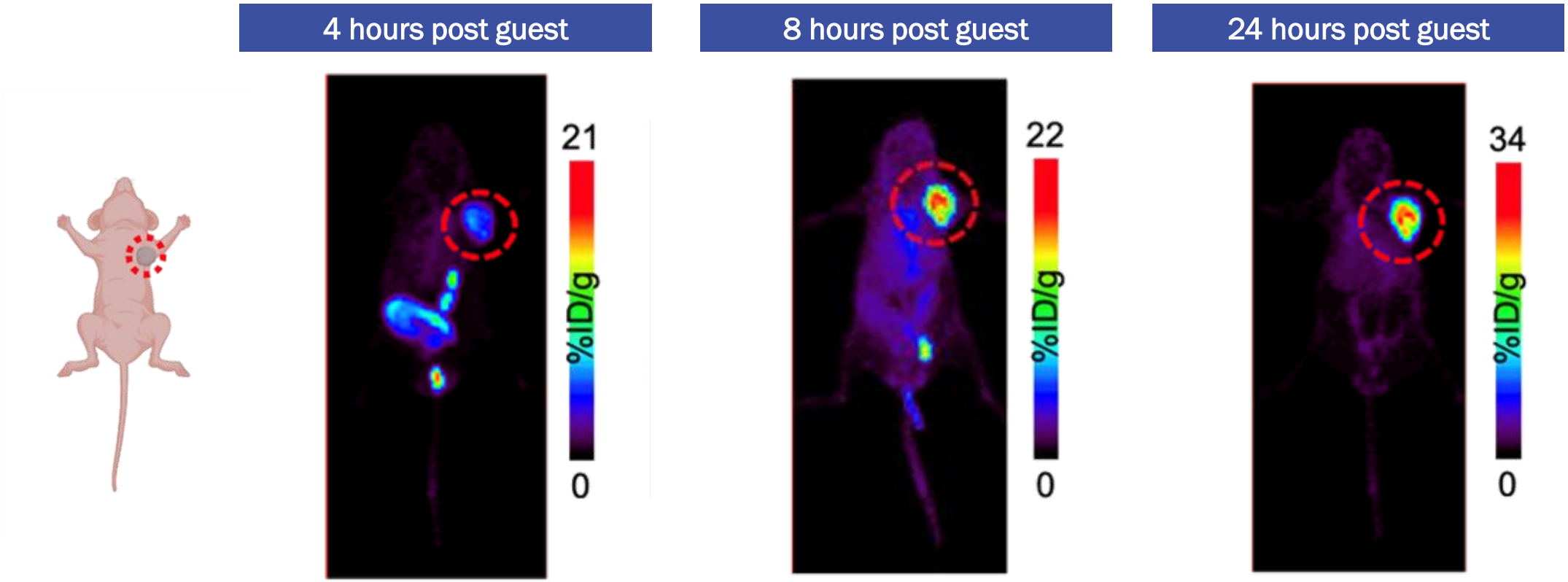
- 6-day lag time demonstrates stability of the CB7
- Terrific Tumor:Normal ratios
- Very low kidney/liver retention
- High tumor targeting
- Blood clearance of the radioligand a little slow
- System optimization underway

PERSPECTIVE THERAPEUTICS

Perspective Pre-Targeting Platform: Host - Guest Chemistry in vivo Imaging Experiment

Representative maximum intensity projection images of ligand during optimization process

- Host is a mAb targeting Carcinoembryonic Antigen (CEA)
- Guest is an adamantane-PEG3-NOTA labeled with ^{64}Cu
- Guest injection 72 hours after Host administration



PERSPECTIVE THERAPEUTICS

Perspective Pre-Targeting Platform: Significant Opportunity to Expand into "ADC" space

Vast number of mAb targets and ligands available to exploit

Expansive Range of Targets Available

- **Bosi et al., EJ Cancer 2023**
  - 54 distinct cell surface targets
- **Li et al., Cancers, 2022**
  - 371 target membrane protein-coding genes
- **Subbiah, Curr. Probl. Cancer, 2021**
  - 13 ADC targets – compared to radiopharmaceuticals

Many mAbs with Clinical Data

- Vast number of mAbs that are humanized and have been in human clinical trials
- Many have failed as Antibody Drug Conjugates and unmodified ligand may be available for licensing
- These mAbs bind in general with high affinity and specificity to their tumor targets
- Opportunity to significantly increase potency of these molecules

Perspective's Best in Class pre-targeting platform has the potential to transform a large range of existing molecules and targets into "radio-ADCs" with superior efficacy and reduced toxicity

PERSPECTIVE THERAPEUTICS

Clinical Programs: VMT-α-NET and VMT01

Safety Update from Dose Escalation Studies

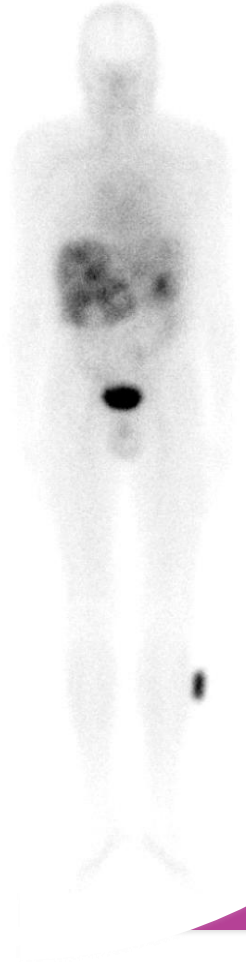
PERSPECTIVE THERAPEUTICS

Neuroendocrine and SSTR2+ Tumors: VMT-α-NET

Phase I Dose Escalation Recruitment and Safety Update

PERSPECTIVE THERAPEUTICS

VMT-α-NET Development Status



Targeting somatostatin receptor type 2 (SSTR2) for the imaging and treatment of neuroendocrine tumors with possible expansion into other SSTR2+ tumor types

Initiated therapy (2022) under compassionate use in India – complete data of 12 patients to be presented at SNMMI in June 2024

Fast Track Designation for first line therapy received October 2022

Therapeutic trial in radiotherapy naïve currently recruiting at 7 sites in the US

US Phase 1 study in PRRT refractory patients recruiting at the University of Iowa VMT-α-NET will potentially expand into this population as well as first line

Image Panel: SPECT scan of NETs patient imaged with [^{203}Pb]VMT-α-NET

Clinical Investigation of [^{212}Pb]VMT-α-NET in Metastatic SSTR2 Positive Patients

Interim Results in 10 of 12 patients as of September 28, 2023, for Ongoing Investigation in India

Treating Physician:
Dr. Ishita B Sen
Director & Head
Dept. of Nuclear Med.
& Molecular Imaging
Fortis Memorial Research
Institute, Gurgaon, India

Current Status

- Patients with prior lines of therapy, late-stage, anatomically different NETs (mean age: 48 years; 4 females)
- 10 patients administered [^{212}Pb]VMT-α-NET
- 7/10 patients continuing on therapy
- 1 patient completed 4x treatments
- 2 patients discontinued due to progressive disease
- 25 total [^{212}Pb] VMT-α-NET doses administered to date

Response

- Response (radiological or biochemical) is seen in 8/10 patients
- Death: 1/10 (not drug related)
- Awaiting Evaluation: 1
- Quality of Life (EORTC QLQ–GLNET21 Score) trending positively

Safety

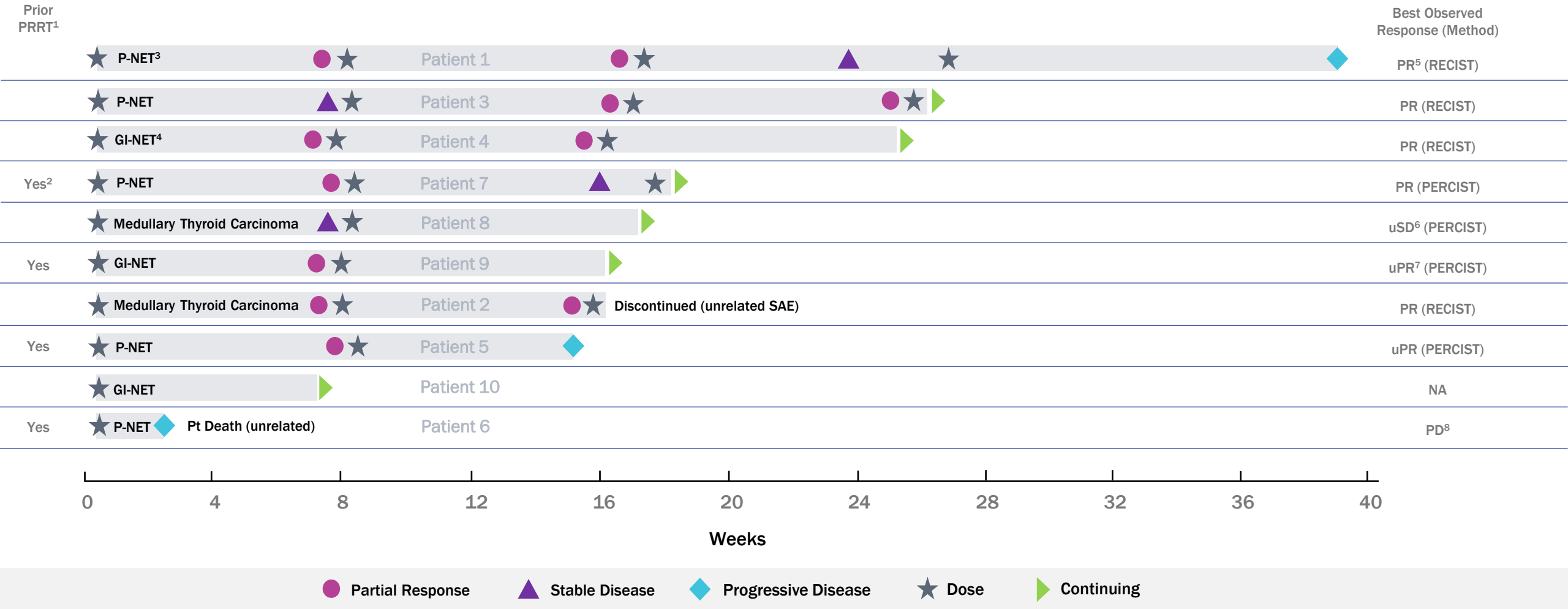
- No significant renal or hepatic function derangement to date
- Mild Adverse Effects:
  - Grade I Anemias
  - Alopecia
  - Fatigue – usually up to 1 week after administration
- 2 SAEs (unrelated to study drug):
  - Acute Cardiac Event in 25-year-old pNET patient (heavily pretreated)
  - Myelodysplastic Syndrome (MDS) in 79-year-old Medullary Thyroid Carcinoma patient (found positive for BCR-ABL gene)

Dr Dharmender Malik, Fortis Memorial research institute (FMRI), Gurugram, India. Presented at EANM 2023 - Interim Results

PERSPECTIVE THERAPEUTICS

High Partial Response Rate at Starting Dose in Patients with SSTR+, Late-Stage NETs

Interim Results as of September 28, 2023, for Ongoing Clinical Investigation Program in India



[1] 4 x [^{177}Lu]DOTATATE
[2] 4 x [^{177}Lu]DOTATATE plus 3 x [^{225}Ac]DOTATATE
[3] Pancreatic NET
[4] Gastro-intestinal NET
[5] Partial Response
[6] unconfirmed Stable Disease
[7] unconfirmed Partial Response
[8] Progressive Disease

PERSPECTIVE THERAPEUTICS

Trial Design: [^{212}Pb]VMT-α-NET mTPI-2[1] Phase 1/2a For Neuroendocrine Tumors

Primary Objective:	To determine the MTD/MFD of [^{212}Pb]VMT-α-NET (RP2D)	**Imaging:**	FDA approved SSTR2 PET/CT
Population:	Escalation n ≈ 10-32 Expansion n ≈ 20 – 100 Unresectable or metastatic SSTR2-positive NETs PRRT naïve	**Therapeutic Dose:**	2.5–10 mCi dose escalation with fixed dosing every 8 weeks for up to 4 cycles
		Estimated Time to Primary Completion:	~18 months
Design Methodology:	Bayesian mTPI2 based on iterative toxicity probability monitoring	**Dosimetry:**	To be assessed during screening for cohorts 1 & 2 using 5-7 mCi [^{203}Pb]VMT-α-NET

Note: average administered activity from Indian compassionate use study was 2.9 mCi per cycle

Escalation phase
n ≈ 10-32

Recruitment Complete
Cohort 1
[^{212}Pb]VMT-α-NET
n = 2 / 2.5 mCi x 4

Recruiting
Cohort 2
[^{212}Pb]VMT-α-NET
n = 2 – 8 / 5 mCi x 4

Cohort 3
[^{212}Pb]VMT-α-NET
n = 3 – 8 / 7.5 mCi x 4

Cohort 4
[^{212}Pb]VMT-α-NET
n = 3 – 8 / 10 mCi x 4

De-escalation possible for Cohort 2 – 4 including for intermediate doses

Recommended Phase 2 Dose

Expansion phase
n ≈ 20 - 100

Expansion Cohort
[^{212}Pb]VMT-α-NET
RP2D mCi x 4

Expansion into non-NET indications (eg SCLC) also possible

[1]mTPI-2: Modified toxicity probability index
https://clinicaltrials.gov/study/NCT05636618

PERSPECTIVE THERAPEUTICS

VMT-α-NET Treatment Emergent Adverse Events by CTCAE[1] Grade as of March 7, 2024

Preferred term	Cohort 1 and 2 N=3[2]			
	All CTCAE Grades	Grade 2	Grade 3	Grade Missing
Total number of TEAEs	24	3	1	3
Alopecia	3	-	-	1
Diarrhea	3	-	1	-
Nausea	3	-	-	1
Fatigue	2	1	-	-
Lethargy	2	-	-	-
Abdominal pain	1	-	-	-
Dry mouth	1	-	-	-
Dyspepsia	1	1	-	-
Edema limb/ pedal edema on the left foot	1	-	-	-
Elevated amylase	1	1		-
Elevated AST	1	-	-	-
Elevated bilirubin	1	-	-	-
Gastritis	1	-	-	
Headache	1	-	-	-
Metallic taste	1	-	-	1
Skin hyperpigmentation/ left dorsal focal discoloration	1	-	-	-

[1] Common Terminology Criteria for Adverse Events; [2]Data only available on first patient from Cohort 2

Summary VMT-α-NET Trial Status and Safety Update as of March 7, 2024

Study Status

- 7 sites active, additional sites in feasibility assessment
- High level of interest by clinicians and patients
- 6 patients in screening to complete Cohort 2
- Total Patients dosed = 4
  - 2 patients at 2.5 mCi
  - 2 patients at 5 mCi

Safety Update

- Safety Review Committee after Cohort 1 unanimous agreement to escalate dose
- Total Treatment Emergent Adverse Events (TEAEs): 24
- No Serious Adverse Events (SAEs)
- No Dose Limiting Toxicities (DLTs)
- No discontinuations due to drug related toxicity

At the time of data cut-off, VMT-α-NET was well tolerated with no unexpected AEs

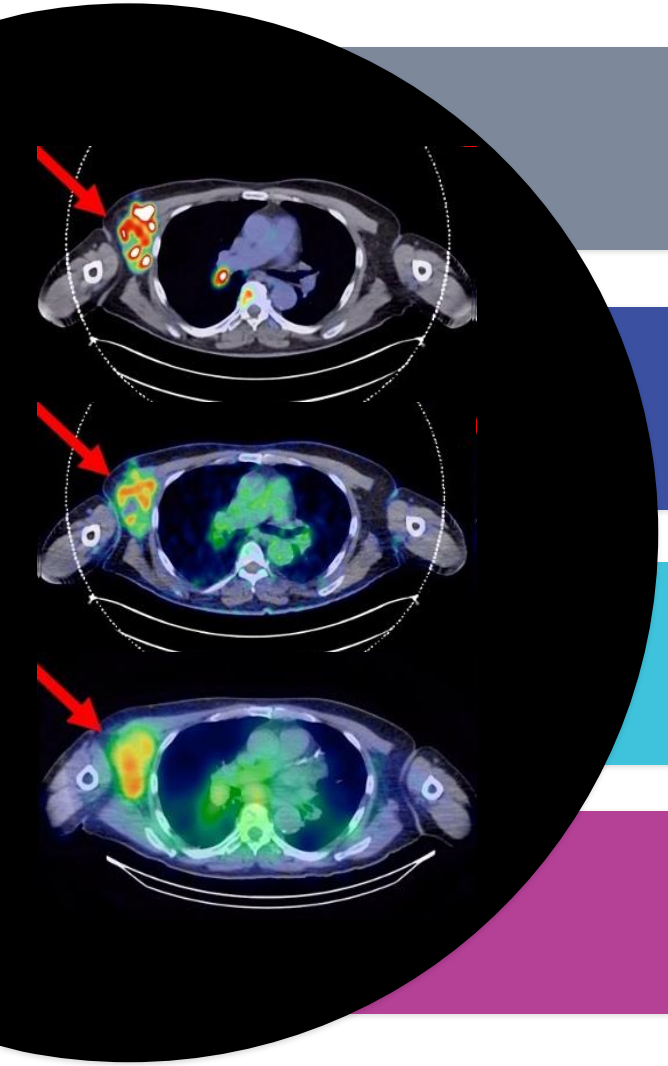
PERSPECTIVE THERAPEUTICS

Metastatic Melanoma: VMT01

Phase I Dose Escalation Recruitment and Safety Update

PERSPECTIVE THERAPEUTICS

VMT01 Development Status



Targeting melanocortin 1 receptor (MC1R) which is over-expressed in melanoma

US Therapeutic Dose Escalation Trial recruiting currently at 8 sites in US
Expected to Receive Orphan Drug Designation and Fast Track Application

Preclinical data shows synergistic effect with Immune Checkpoint Inhibitors
Planning underway for VMT-01 /ICI combination in second line setting

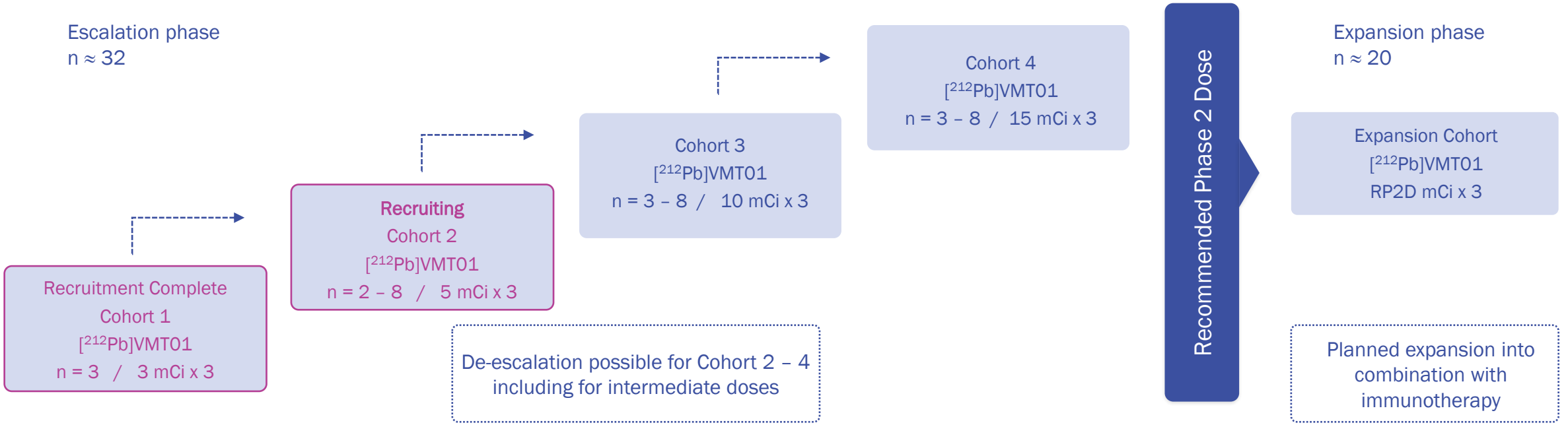
Phase 1 imaging study at Mayo Clinic Rochester indicates feasibility of patient selection using [^{203}Pb]VMT-01

Image: Top panel - PET/CT cross section of a metastatic melanoma patient using FDG;
middle panel - PET/CT of the same patient with VMT02; lower panel - SPECT/CT of same patient with VMT01

PERSPECTiVE THERAPEUTICS

Trial Design: [^{212}Pb]VMT01-T101 mTPI1 Phase 1/2a For Metastatic Melanoma

Primary Objective:	To determine the MTD/MFD of [^{212}Pb]VMT01 (RP2D)
Population:	Enroll ~52 subjects Unresectable or metastatic MC1R-positive melanoma After 1L SOC
Design Methodology:	Bayesian mTPI2 based on iterative toxicity probability monitoring
Imaging:	[^{203}Pb]VMT01 SPECT/CT or [^{68}Ga]VMT02 PET/CT
Therapeutic Dose:	3 – 15 mCi dose escalation of [^{212}Pb]VMT01 with fixed dosing every 8 weeks for up to 3 cycles
Estimated Time to Primary Completion:	~18 months
Dosimetry:	To be assessed using 15 - 25 mCi therapeutic surrogate [^{203}Pb]VMT01



[1]mTPI-2: Modified toxicity probability index
https://clinicaltrials.gov/study/NCT05655312

PERSPECTIVE THERAPEUTICS

VMT01 Treatment Emergent Adverse Events by CTCAE[1] Grade as of March 7, 2024

Preferred Term	Cohort 1 and 2 N = 5	
	All Grades	Grade 2
Total number of TEAEs	27	7
Nausea	4	2
Lymphocyte count decreased	3	1
Anaemia	2	-
Hyponatraemia	2	-
AST increased	1	-
Contusion	1	-
COVID-19	1	1
Dizziness	1	-
Dyspnoea	1	1
Hypoalbuminaemia	1	-
Hypokalaemia	1	-
Infusion site extravasation	1	-
INR (International normalized ratio) increased	1	-
Muscle spasms	1	-
Pain in extremity	1	-
Platelet count decreased	1	-
Pollakiuria	1	-
Sinusitis	1	1
Urinary tract infection	1	1
Wheezing	1	-

[1] Common Terminology Criteria for Adverse Events.

Summary VMT01 Trial Status and Safety Update as of March 7, 2024

Study Status

- 8 sites active, additional sites in feasibility assessment
- High level of interest by clinicians and patients
- 4 patients in screening for Cohort 2
- Total Patients dosed = 5
  - 3 patients at 3 mCi
  - 2 patients at 5 mCi

Safety Update

- Safety Review Committee after Cohort 1 unanimous agreement to escalate dose
- Total Treatment Emergent Adverse Events (TEAEs): 27
- No Serious Adverse Events (SAEs)
- No Dose Limiting Toxicities (DLTs)
- No discontinuations due to drug related toxicity

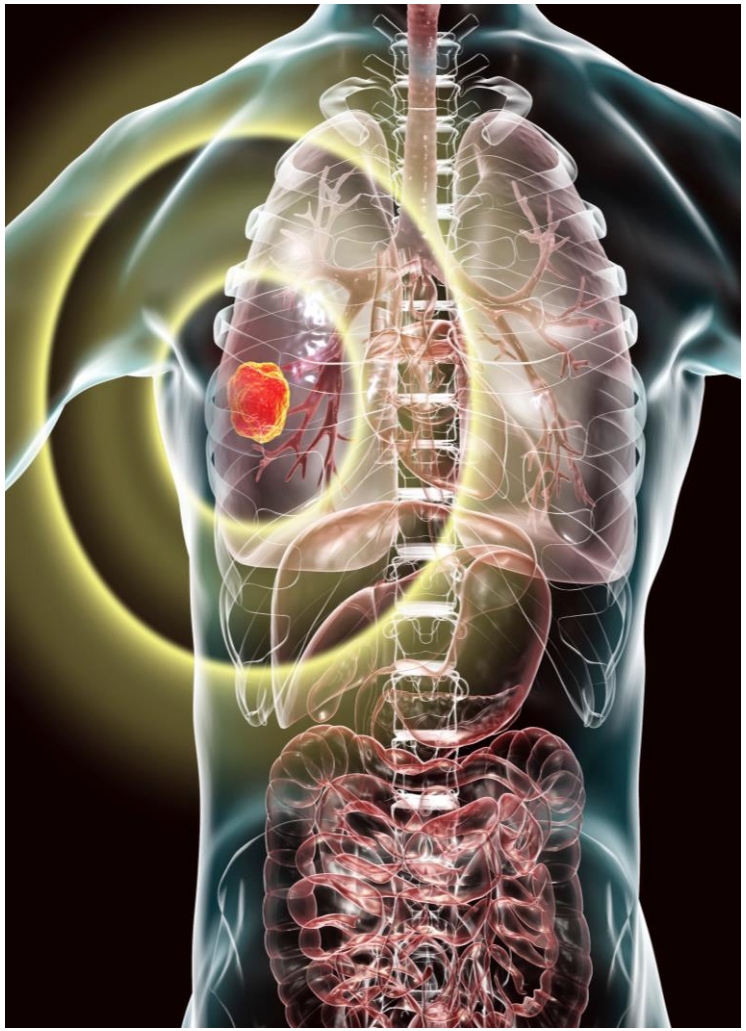
At the time of data cut-off, VMT01 was well tolerated with no unexpected AEs

PERSPECTIVE THERAPEUTICS

Summary of Current Safety Evaluation of VMT-α-NET and VMT01

- Both programs have completed Cohort 1 and continue to enroll in their respective Cohort 2
- No DLTs were observed across either program
- Except for G3 diarrhea, only G1 and G2 AEs have occurred
- Dose escalation is ongoing

- Preliminary safety and efficacy results from Phase I Cohort 1 and 2 from VMT-α-NET and VMT01 projected to be available in 3Q24



PERSPECTIVE THERAPEUTICS

Combination Targeted Alpha Particle Therapy & Immunotherapy

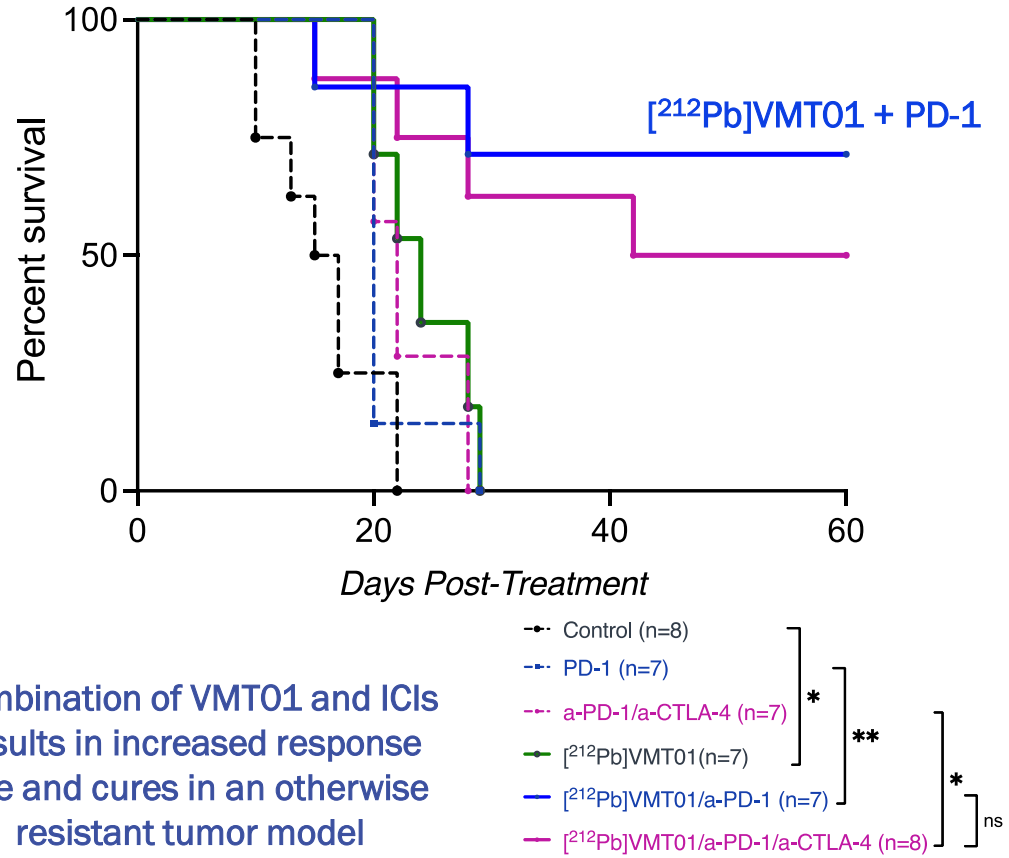
Clinical Collaboration Agreement with Bristol-Myers Squibb signed for OPDIVO® (nivolumab) supply March 2024

Combination with Standard of Care Immunotherapy

- In melanoma, immune checkpoint inhibitors (ICIs) have revolutionized treatment, but the majority of patients are non-responsive[3]
- Ionizing radiation is an inducer of immunogenic cell death[1]
- Due to their destructive nature, alpha particles are particularly good at generating neoantigens for immuno-sensitization[2]
- MC1R-targeted alpha particles might synergize with existing SoC ICIs

Clinical Collaboration Agreement with Bristol-Myers Squibb signed for OPDIVO® (nivolumab) supply

ICI-resistant B16 F10 Murine Melanoma Model[4]



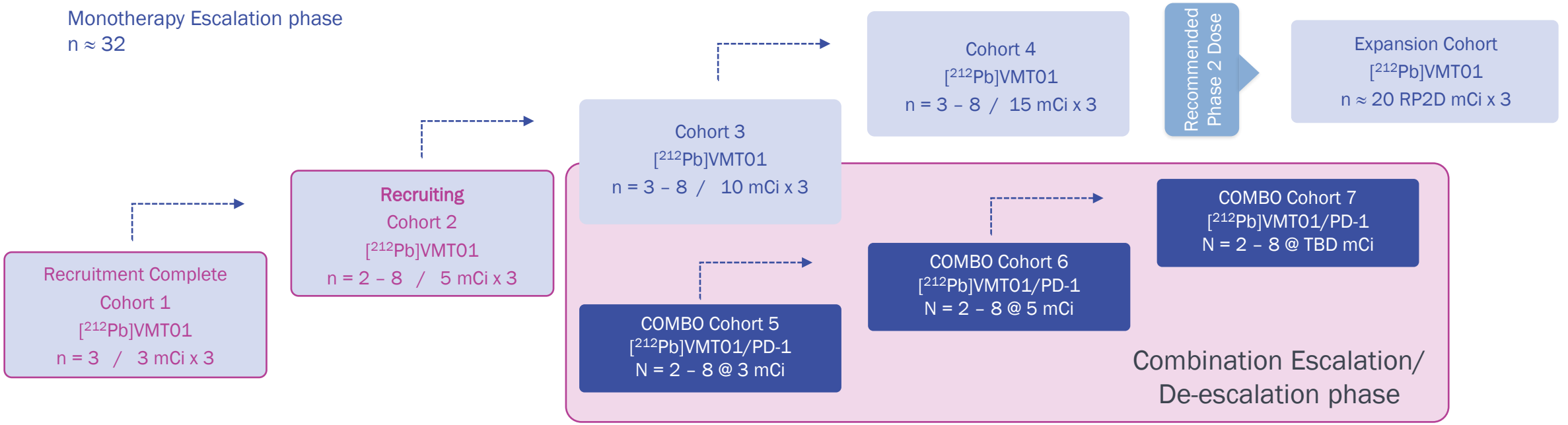
Combination of VMT01 and ICIs results in increased response rate and cures in an otherwise resistant tumor model

[1]Maier et al., Int. J. Mol. Sci. 2016; [2] Pouget et al., Front. Med. 2021; [3] Sharma et al., Cell, 2017, [4] Unpublished data - Statistical analysis was performed by Log-rank (Mantel-Cox): *p<0.05, **p<0.01, ns: non-significant

PERSPECTIVE THERAPEUTICS

Phase I Amendment: [^{212}Pb]VMT01 in Combination with Nivolumab – Sequential Design

Primary Objective:	To determine the MTD/MFD of [^{212}Pb]VMT01 (RP2D) in combination with PD-1 inhibitor (nivolumab)
Population:	Enroll ~52 subjects Unresectable or metastatic MC1R-positive melanoma After 1L SOC
Design Methodology:	Bayesian mTPI2 based on iterative toxicity probability monitoring
Imaging:	[^{203}Pb]VMT01 SPEC/CT
Therapeutic Dose:	3 – 15 mCi dose escalation of [^{212}Pb]VMT01 with fixed dosing every 8 weeks for up to 3 cycles **Combination: Nivolumab 480 mg Q4W for up to 2 yrs**
Estimated Time to Primary Completion:	~18 months
Dosimetry:	To be assessed using 15 - 25 mCi therapeutic surrogate [^{203}Pb]VMT01



[1]mTPI-2: Modified toxicity probability index
https://clinicaltrials.gov/study/NCT05655312

PERSPECTIVE THERAPEUTICS

KOL Discussion

Richard L. Wahl, MD

Professor of Radiology and Radiation Oncology

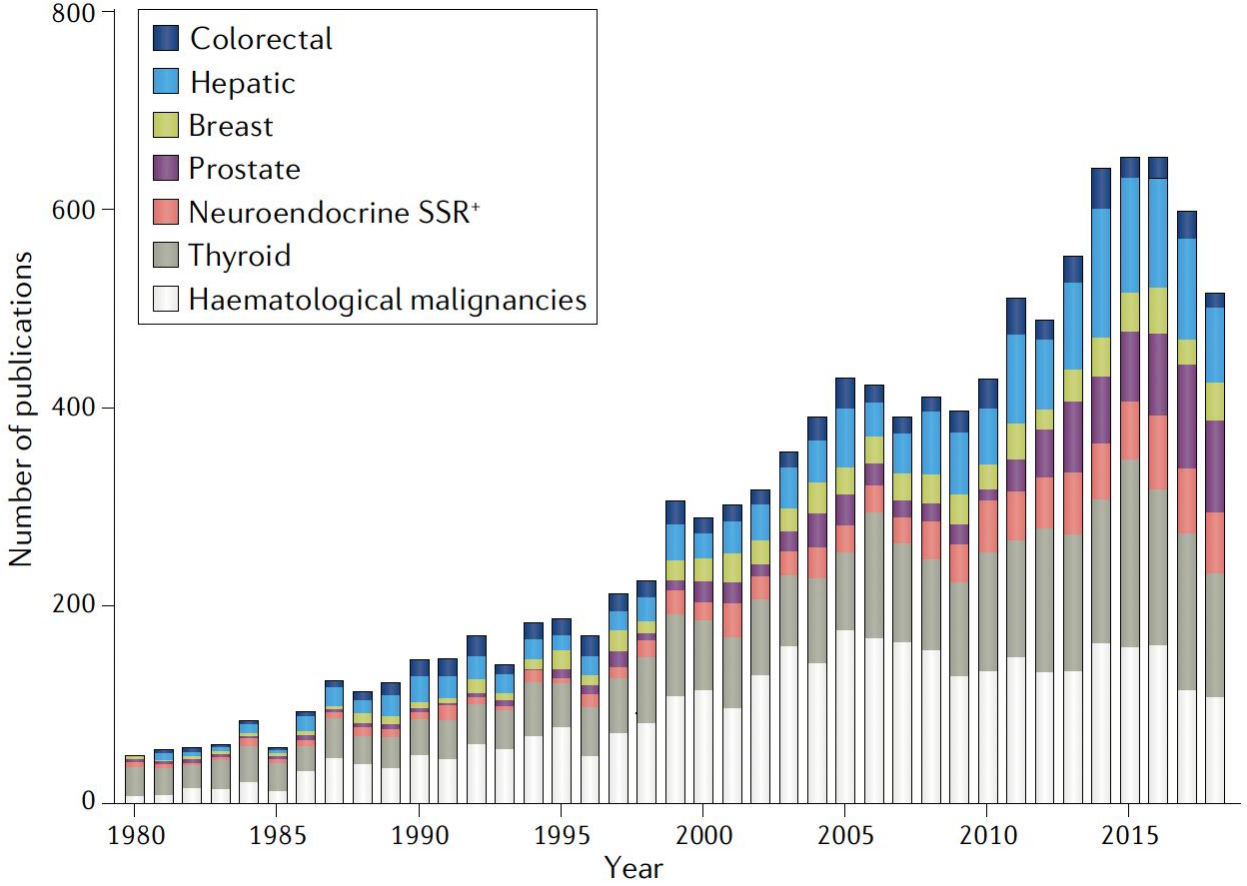
Washington University School of Medicine

Trends in Radiopharmaceutical Therapy (RPT)

What is most exciting to you?

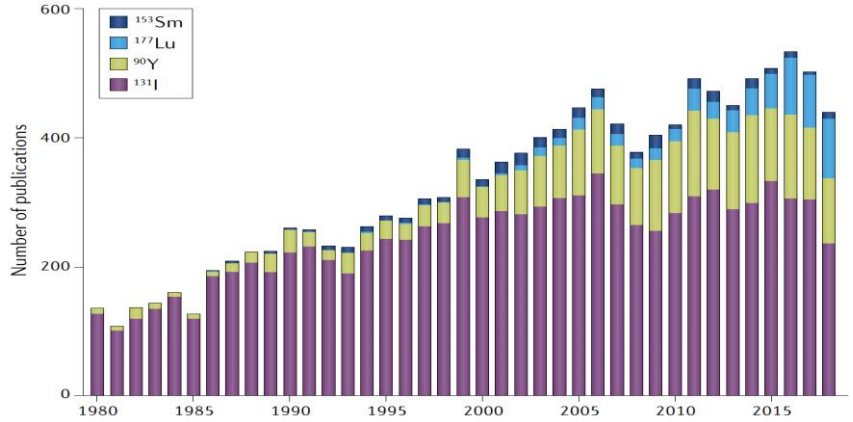
Growth in Radiopharmaceutical Therapy Published Research

Publications per year related to RPT by cancer type

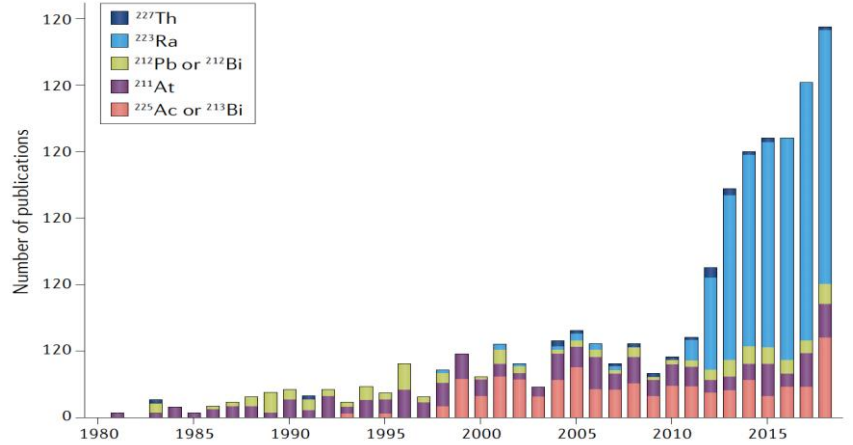


Publications per year by isotope emission profile

beta-emitters



alpha-emitters



G Sgouros, et.al. 2020. Nature Reviews Drug Discovery. Radiopharmaceutical therapy in cancer: clinical advances and challenges.19:589

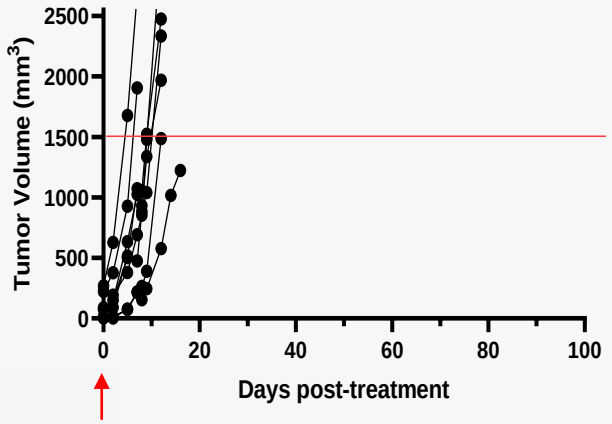
Alpha and Beta RPT

The differences, opportunities and challenges

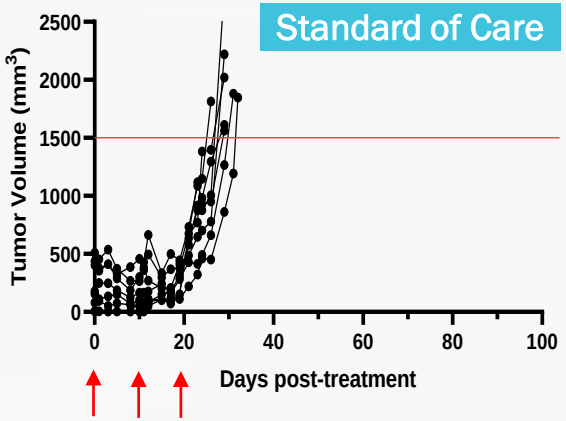
VMT-α-NET Shows Significant Improvement vs Standard of Care in Preclinical Models

Superior Efficacy with Single Dose or Multiple Administrations in AR42J SSTR2-Expressing Tumor

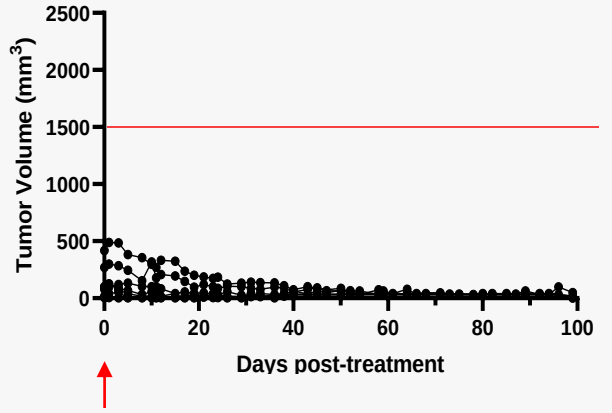
Vehicle



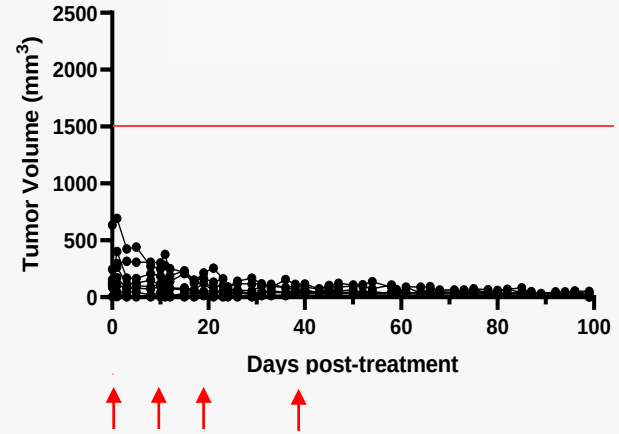
[^{177}Lu]DOTATATE (3 x 500 µCi)



[^{212}Pb]VMT-α-NET (1 x 120 µCi)



[^{212}Pb]VMT-α-NET (4 x 30 µCi)

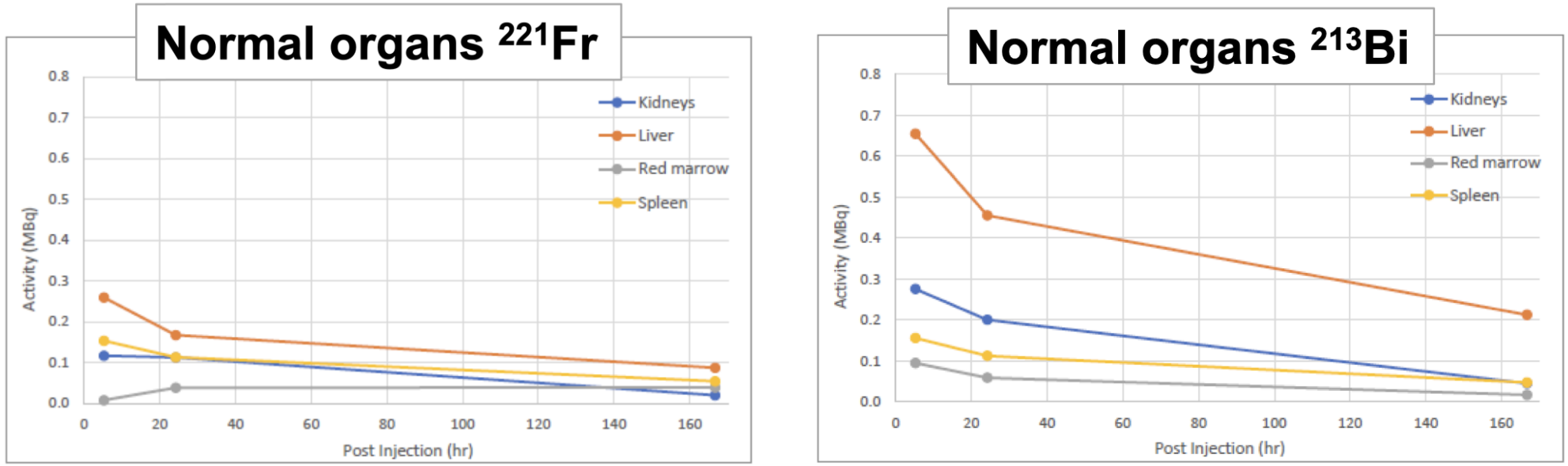


PERSPECTIVE THERAPEUTICS

Mythbusting: "Daughters from ^{225}Ac-225 don't redistribute"

^{225}Ac daughter redistribution – ACTION-1 trial measurement of early and late gamma emissions from healthy tissue

Early (^{221}Fr) and Late (^{213}Bi) Decay



- Extrapolations for radioactivity were seen based on the gamma emissions from the ^{221}Fr and ^{213}Bi daughters
- Higher values in organs were observed with ^{213}Bi than ^{221}Fr, particularly at early time points and in kidneys and liver

This provides evidence of a free isotope bolus with injection AND daughter redistribution during ongoing ^{225}Ac decay over the imaging interval

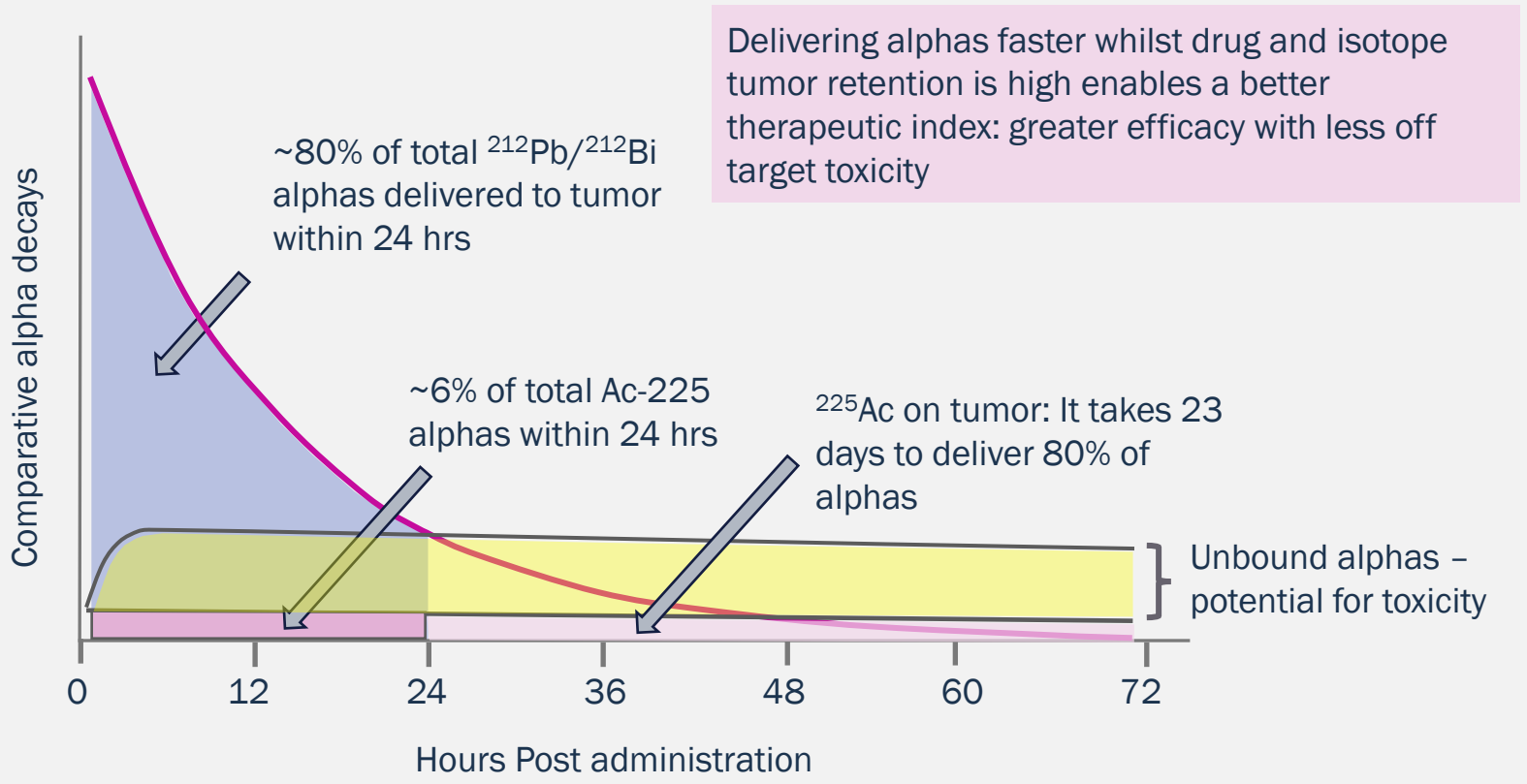
SNMMI 2023 Oral Presentation. RayzeBio website https://rayzebio.wpengine.com accessed March 11, 2024 (y axis scale matched)

PERSPECTIVE THERAPEUTICS

Mythbusting: "^{212}Pb Doesn't Get Enough Energy Into the Tumors"

^{212}Pb is a "high dose rate" alpha emitter with a short half life – energy is deposited rapidly to tumor and then gone

Comparative alpha Particle Decay Over Time[1]



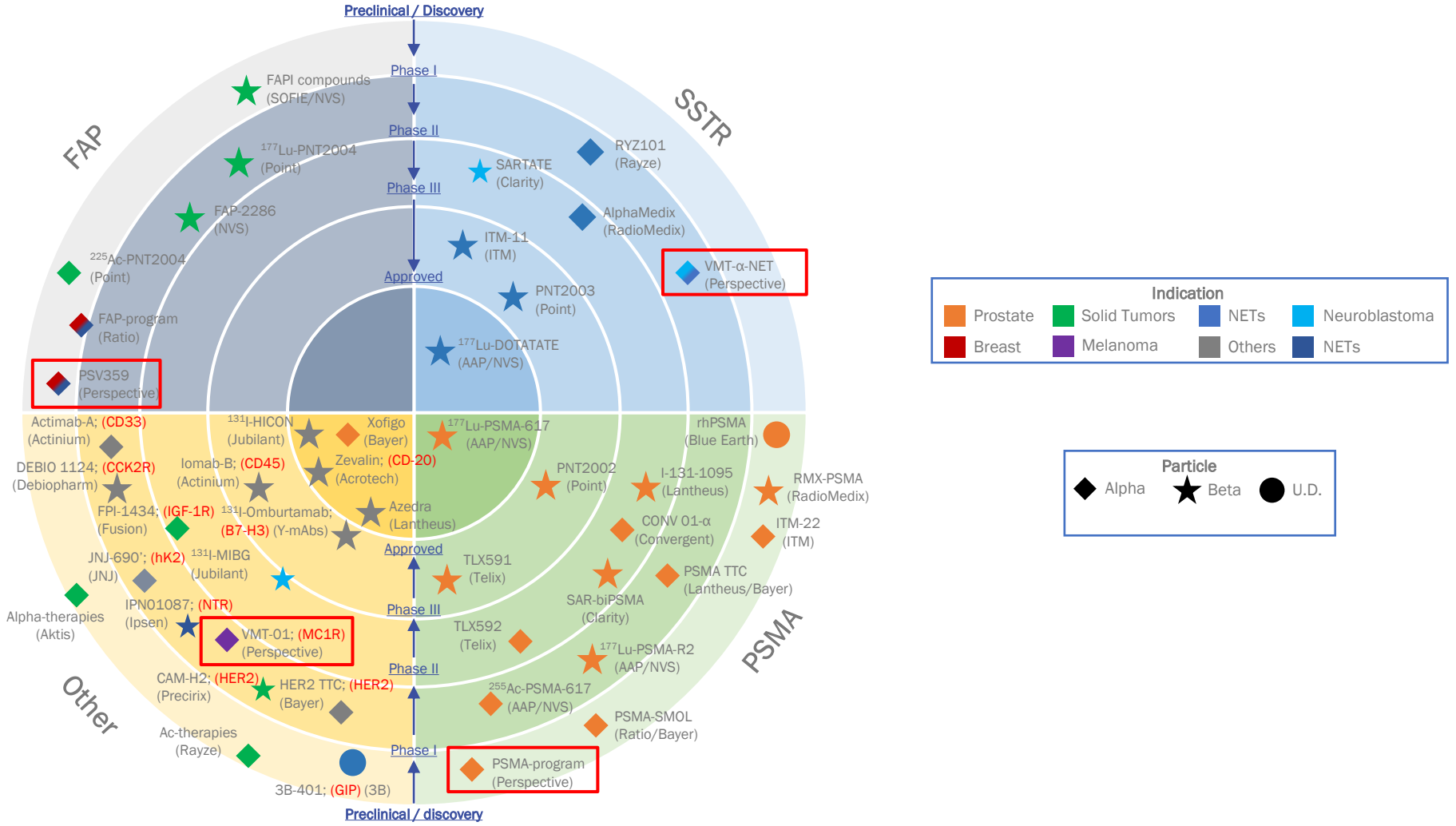
- "Activity" is measured in decays per second, so depends on isotope half-life
- Pb-212 will likely be administered at 20 times the Ac-225 activity
- Ac-225 is administered in smaller activities due to its 10 day half-life and the total alphas decays from its daughters
- Most drugs stay bound to tumor for only a limited time – this directly affects the amount of radiation that can be delivered
- The effectiveness of longer-lived isotopes therefore diminishes over time the alphas are also removed from the tumor

[1] Representative activity administrations only, based on clinical projections – company estimates

Why are NETs and prostate cancer the big winners in targeted RPT?

Can we improve on currently approved products?

A few molecular targets have dominated radiopharmaceutical therapy

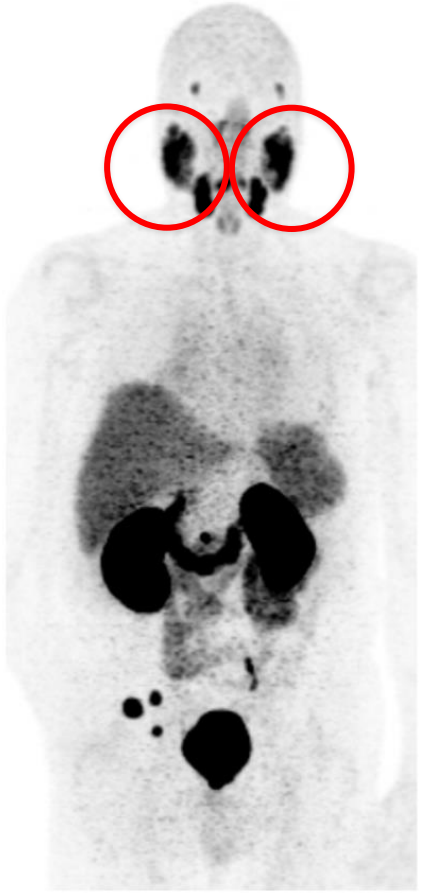


Source: Perspective market research

PERSPECTIVE THERAPEUTICS

PSMA-directed RPT today binds to lacrimal and salivary gland tissue

^{68}Ga-PSMA-11-PET[2]



Adverse side effects of salivary and lacrimal gland uptake of PSMA-RPT compounds

- Xerostomia (dry mouth)
- Difficulty swallowing
- Loss of taste
- Dental decay
- Keratoconjunctivitis sicca (dry eyes)

Source: 1. D Campana, et.al. 2010 J Nuc Med. 51 (3) 353-359. 2. www.snmmi.org accessed March 16, 2024

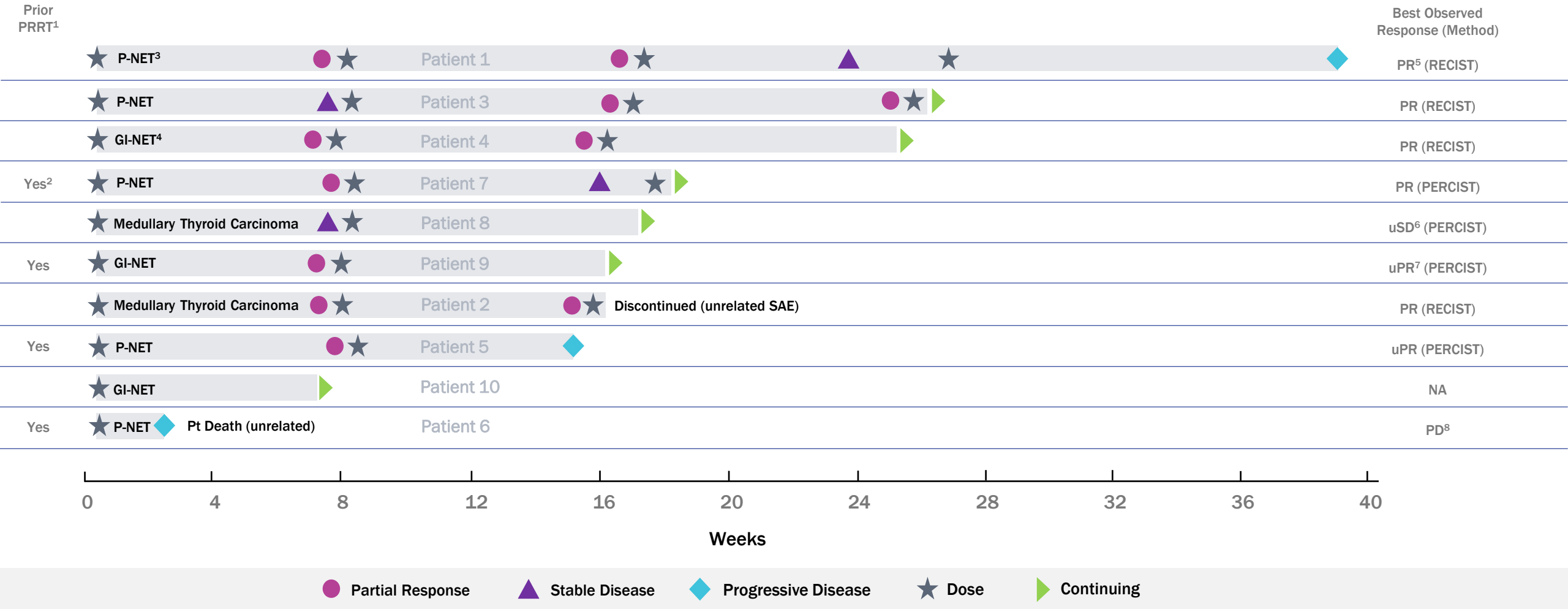
PERSPECTIVE THERAPEUTICS

What can be learned from compassionate use studies?

How do the results impact how patients and doctors view the field?

High Partial Response Rate at Starting Dose in Patients with SSTR+, Late-Stage NETs

Interim Results as of September 28, 2023, for Ongoing Clinical Investigation Program in India



[1] 4 x [^{177}Lu]DOTATATE
[2] 4 x [^{177}Lu]DOTATATE plus 3 x [^{225}Ac]DOTATATE
[3] Pancreatic NET
[4] Gastro-intestinal NET
[5] Partial Response
[6] unconfirmed Stable Disease
[7] unconfirmed Partial Response
[8] Progressive Disease

PERSPECTIVE THERAPEUTICS

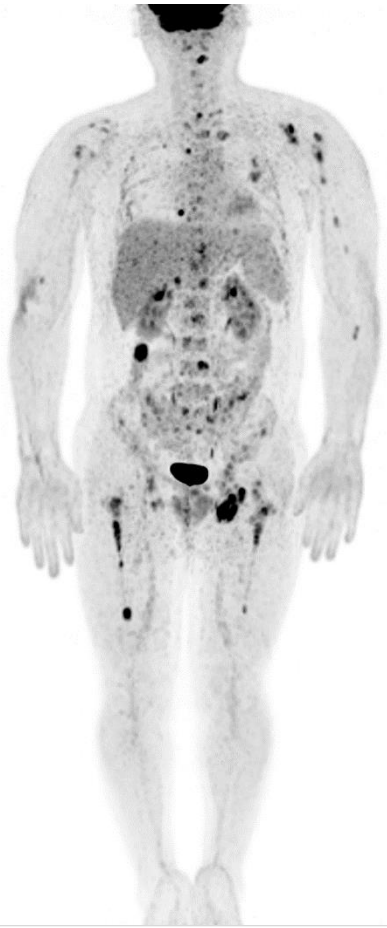
Do you see a future for RPT in combination with other oncology drugs?

Melanoma and beyond

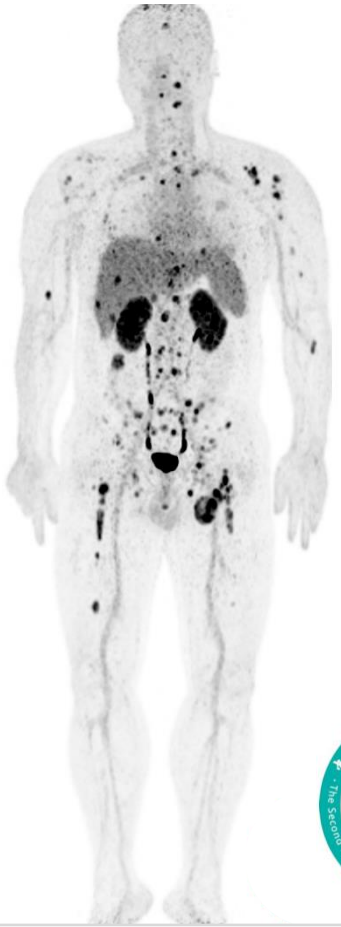
[^{68}Ga]VMT02 PET Imaging in Patient with MC1R Positive Metastatic Melanoma

Diagnostic Peptide Demonstrates Similar Uptake to FDG in Tumors

^{18}F-FDG (Standard of Care)



[^{68}Ga]VMT02



Patient information:

- Male, Asian, 33 years old
- [68Ga]VMT02: 7 mCi injection, 45 min post-injection imaging

Clinical Collaborator:

Xiaowei Ma, M.D., Ph.D.
Assoc. Prof. & Director
Department of Nuclear Med.
The Second Xiangya Hospital
Central South University
China

Combination Targeted Alpha Particle Therapy & Immunotherapy

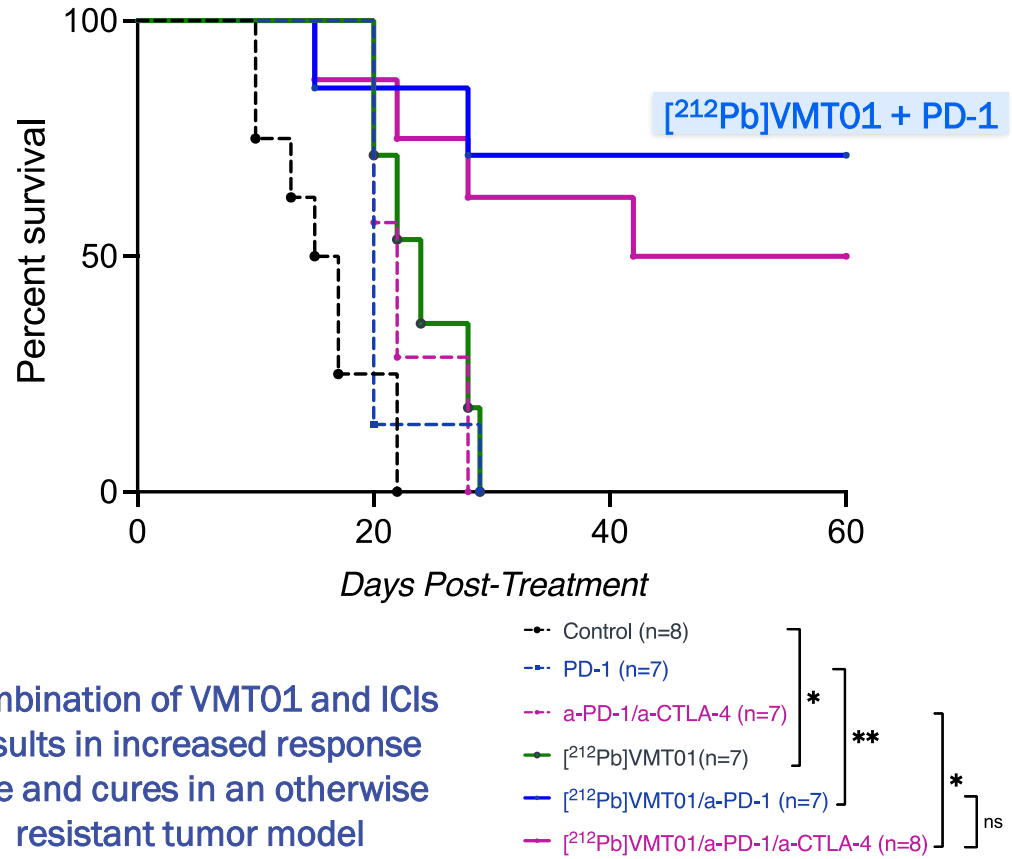
Clinical Collaboration Agreement with Bristol-Myers Squibb signed for OPDIVO® (nivolumab) supply March 2024

Combination with Standard of Care Immunotherapy

- In melanoma, immune checkpoint inhibitors (ICIs) have revolutionized treatment, but the majority of patients are non-responsive[3]
- Ionizing radiation is an inducer of immunogenic cell death[1]
- Due to their destructive nature, alpha particles are particularly good at generating neoantigens for immuno-sensitization[2]
- MC1R-targeted alpha particles might synergize with existing SoC ICIs

Clinical Collaboration Agreement with Bristol-Myers Squibb signed for OPDIVO® (nivolumab) supply

ICI-resistant B16 F10 Murine Melanoma Model[4]



Combination of VMT01 and ICIs results in increased response rate and cures in an otherwise resistant tumor model

[1]Maier et al., Int. J. Mol. Sci. 2016; [2] Pouget et al., Front. Med. 2021; [3] Sharma et al., Cell, 2017, [4] Unpublished data - Statistical analysis was performed by Log-rank (Mantel-Cox): *p<0.05, **p<0.01, ns: non-significant

PERSPECTIVE THERAPEUTICS

Mythbusting

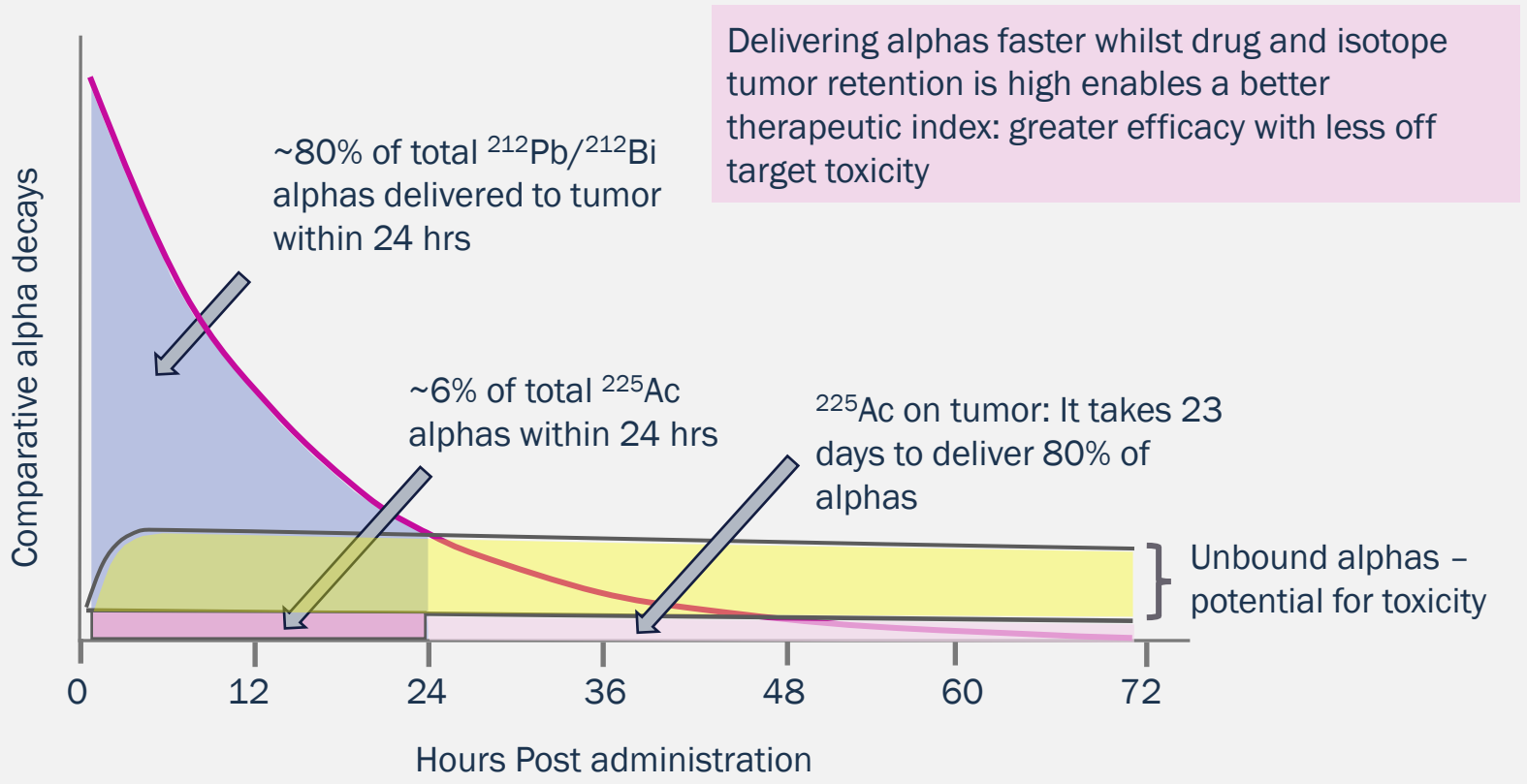
^{212}Pb and Other Alphas

PERSPECTIVE THERAPEUTICS

Mythbusting: "^{212}Pb Doesn't Get Enough Energy Into the Tumors"

^{212}Pb is a "high dose rate" alpha emitter with a short half life – energy is deposited rapidly to tumor and then gone

Comparative alpha Particle Decay Over Time[1]



- "Activity" is measured in decays per second, so cumulative dose depends on isotope half-life
- ^{212}Pb will likely be administered at 20 times the ^{225}Ac activity
- ^{225}Ac is administered in smaller activities due to its 10-day half-life and the total alphas decays from its daughters
- Most drugs stay bound to tumor for only a limited time – this directly affects the amount of radiation that can be delivered
- The effectiveness of longer-lived isotopes therefore diminishes over time the alphas are also removed from the tumor

[1] Representative activity administrations only, based on clinical projections – company estimates

PERSPECTIVE THERAPEUTICS

Manufacturing Update

Scaling Finished Radiopharmaceutical Production

PERSPECTIVE THERAPEUTICS

Mythbusting: "Regulatory environment doesn't suit ^{212}Pb"

Manufacturing regulations are clear and practical for production of ^{212}Pb radiopharmaceuticals

Nuclear Pharmacy	PET Manufacturing	Radiotherapeutic Manufacturing
• Licensed at the state level under the Board of Pharmacy adhering to USP 797 & 825 • Traditionally diagnostics (e.g. ^{99m}Tc) with some legacy therapeutics (e.g. ^{131}I) • Low energy (140 KeV) shielding ¼ inch (primarily lead) • 5,000 sq ft	• Licensed at the Federal level under 21 CFR Part 212 (currently migrating to 21 CFR Part 211) • Traditionally diagnostics (e.g. ^{18}F-FDG) with no therapeutics • High energy (511 KeV) shielding 2 – 3 inches (primarily lead, tungsten & concrete) • 10,000 sq ft	• Licensed cGMP under 21 CFR Part 211 • Annex 1 a developing Global Sterile Products standard • Therapeutics (^{177}Lu, ^{225}Ac, ^{212}Pb) • High energy gamma-ray (2.6 MeV) shielding 4 – 6 inches (primarily lead, tungsten & concrete) • 15,000 to 20,000+ sq ft

Reminder: No capital equipment (reactor/cyclotron/accelerator) required for ^{212}Pb production

PERSPECTIVE THERAPEUTICS

Accelerated Expansion of Manufacturing Capabilities: Build *and* Partner

Owned
Vertical Integration

- Purpose-built factory equipped to process high energy, high activity production
- Leverage an extensive portfolio against large scale production within a single facility
- Utilize internal expertise for ^{212}Pb to design batched production close to the patient
- Maintain flexible production schedules
- Available for clinical work, especially Phase 3, using a near-commercial facility

CDMOs
Outsourced Model

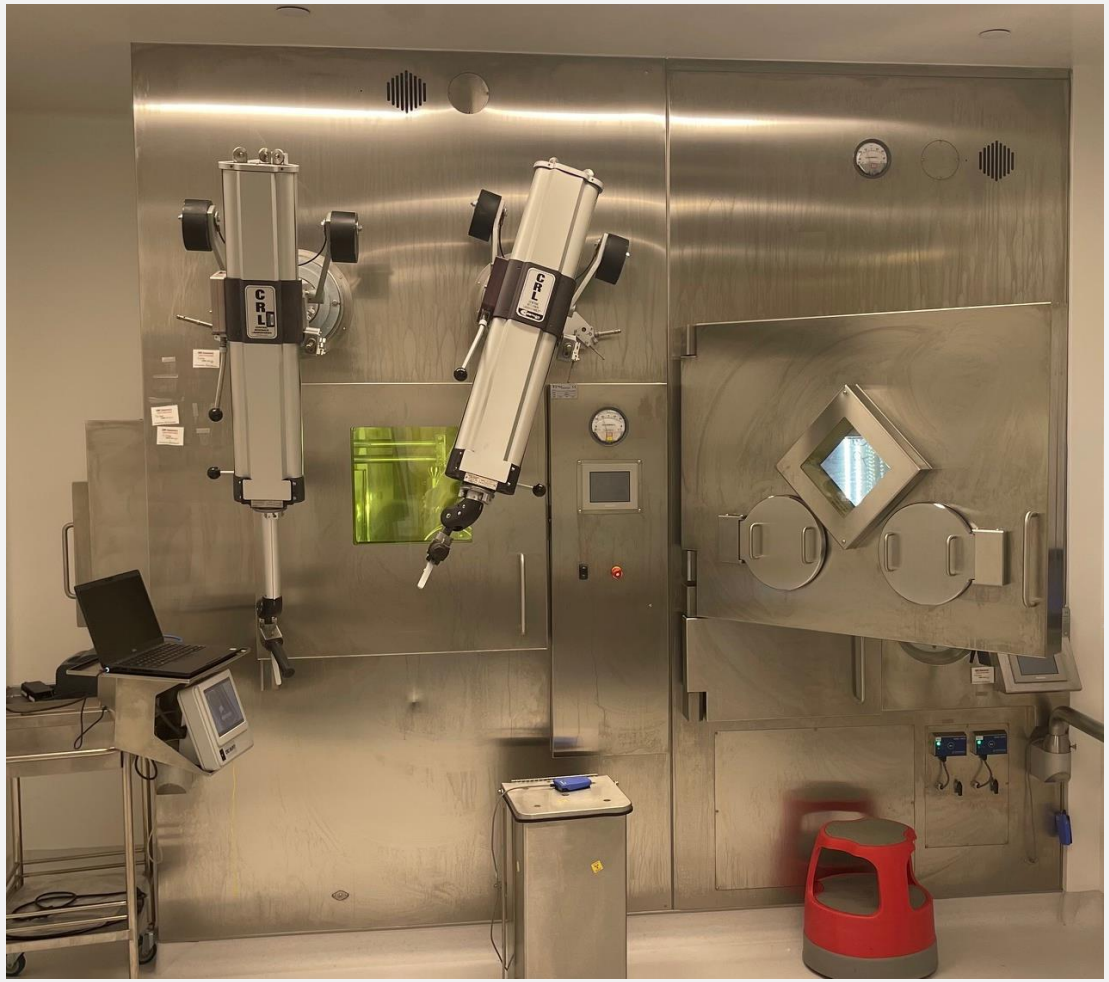
- Existing infrastructure built around 511 KeV / cyclotron products with focus on diagnostics
- Primary business expertise in High Volume / Large Batch Production and End Customer Service
- Emerging knowledge and expertise in therapeutics, especially alpha emitters (e.g., ^{212}Pb)
- Some CDMOs focus on tailored clinical work specifically suitable for CATX
- Facilities can be upgraded for ^{212}Pb commercial production

With a pipeline of multiple ^{212}Pb products, building dedicated manufacturing facilities in partnership with outsourced CDMOs is an efficient, scalable, and flexible approach

PERSPECTIVE THERAPEUTICS

Expansion of Manufacturing Capabilities: Acquisition of GMP Facility in Somerset, NJ

Former AZEDRA® facility acquired from Lantheus March 2024



Jump-starts east coast production for clinical trials and early commercial scale up

- Acquisition of 3 Part 211 compliant manufacturing suites with additional clinical suite
- On-boarding of 24 talented engineering, manufacturing and quality assurance employees
- Experienced team with cGMP compliance and FDA audits
- 2+ years savings in equipment and construction
- Immediate production and delivery of clinical doses and commercialization capability
- Room for expansion with additional suites

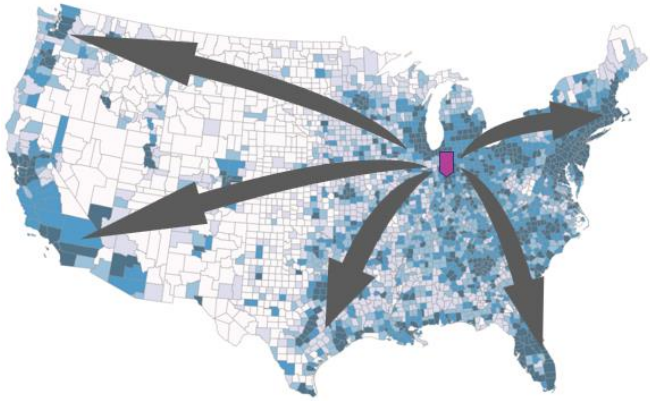
PERSPECTIVE THERAPEUTICS

Mythbusting: "Centralized production is better than networked production"

Networked production is more reliable and utilizes existing logistics for distributed supply

Single centralized manufacturing facility

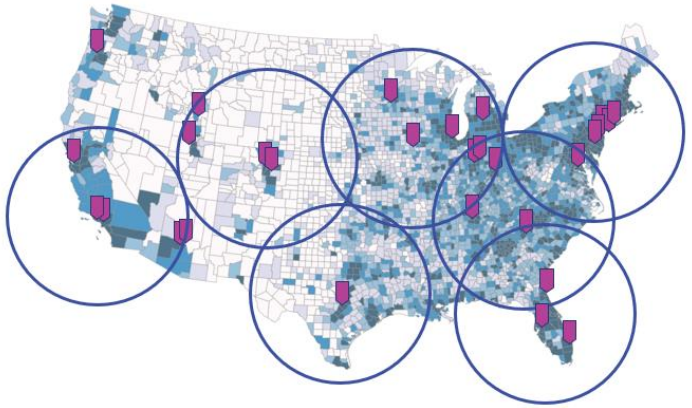
- Suitable for longer half-life isotopes (eg ^{177}Lu, ^{131}I, ^{225}Ac, ^{67}Cu)
- Allows for national/international production
- Shipping of finished product typically requires air and road transport
- Single point of failure (eg Novartis' PLUVICTO® production issues)



VS

National network of manufacturing facilities

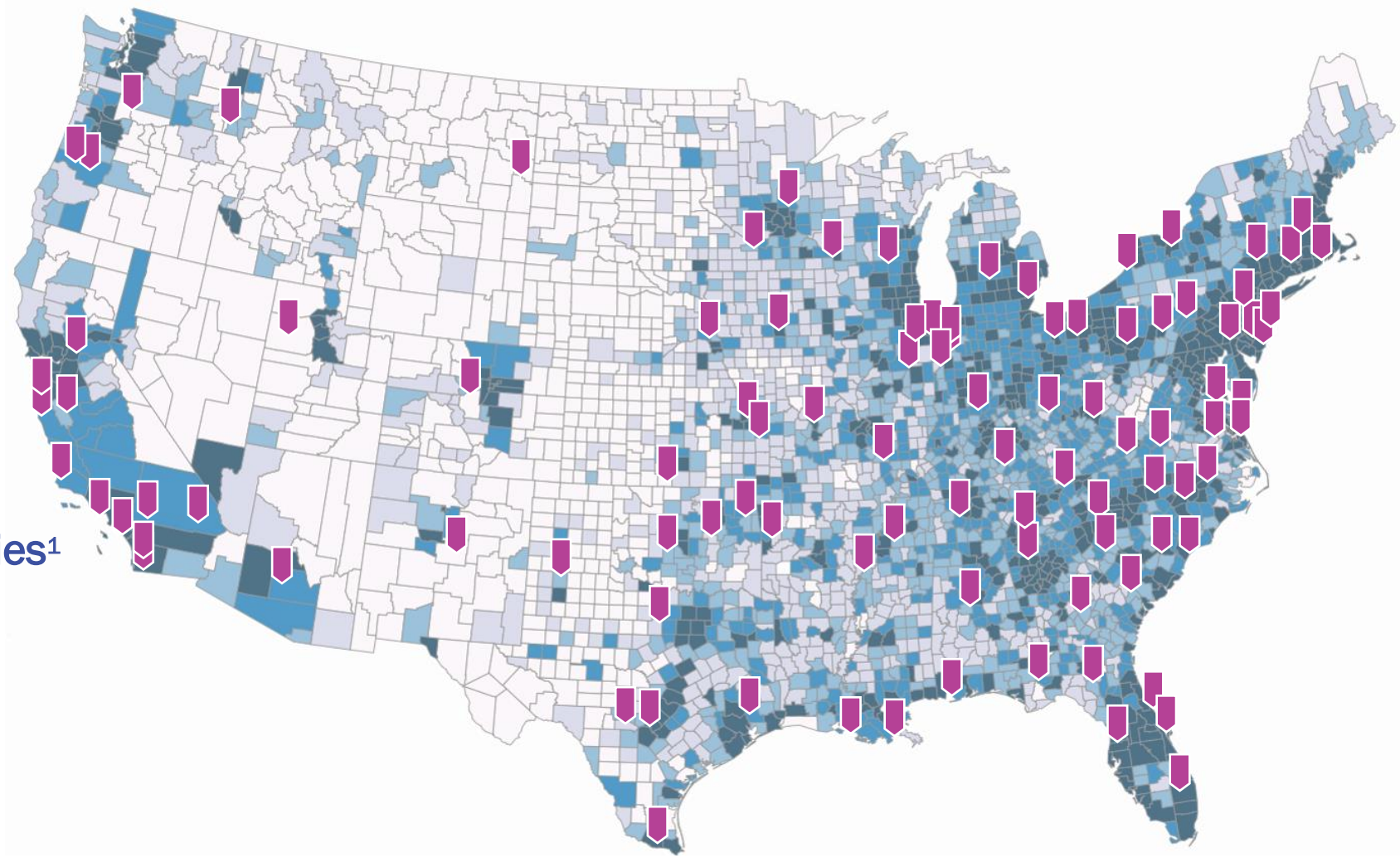
- Suitable for shorter half-life isotopes (eg ^{212}Pb, ^{211}At)
- Requires multiple manufacturing sites for regional finished product
- Shipping of finished product typically road transport
- No single point of failure
- Allows for flexibility and redundancy, improving reliability of supply
- Redundancy fills in to meet demand



[1] Company estimates

Infrastructure Modeling: Commercial History of PET Pharmacy Network Development

Nuclear medicine capability filled in to meet demand as clinical adoption of ultra short half-life PET agents widened



PET Pharmacies[1]

2004: 41

2014: 78

2024: 101

[1] Company estimates

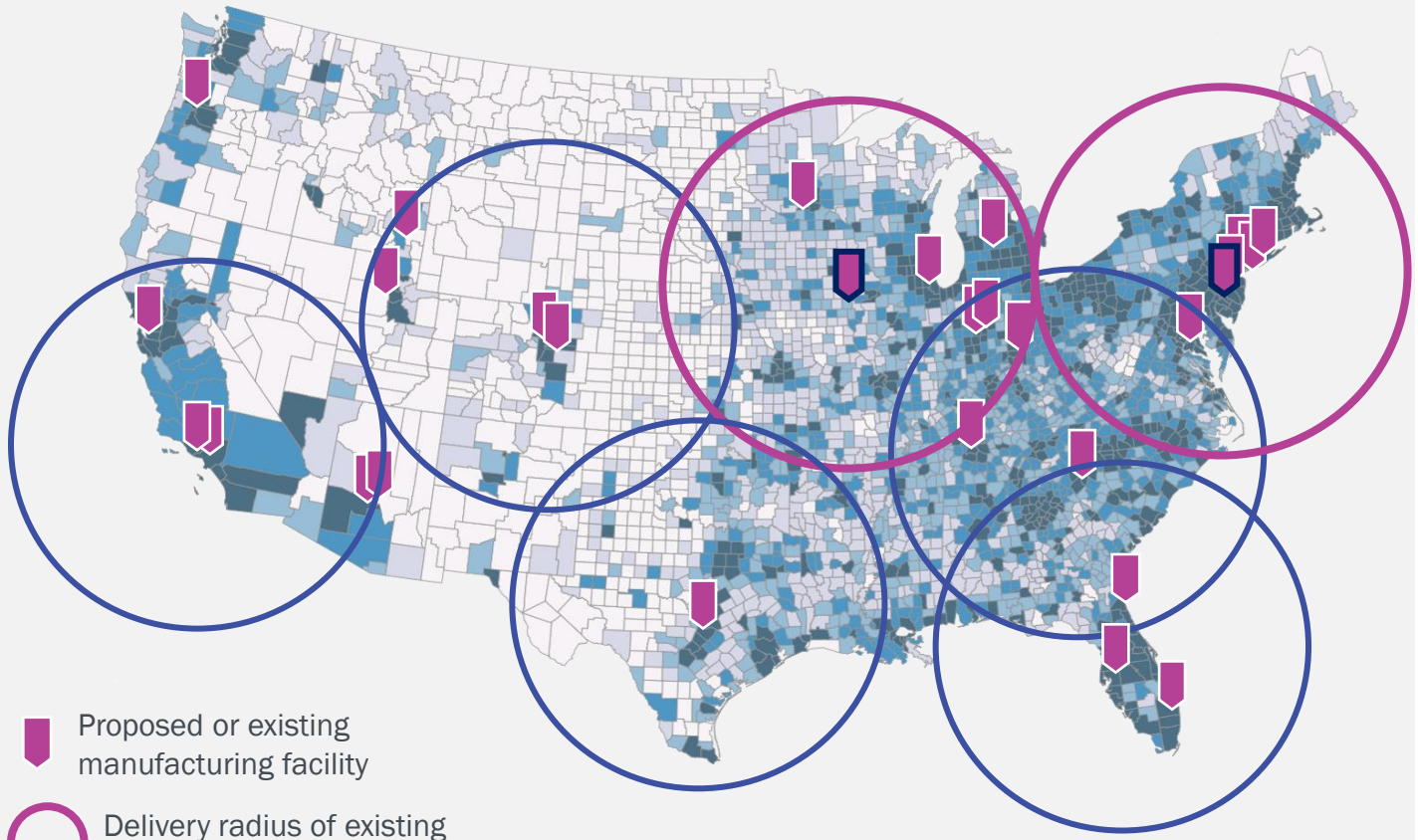
PERSPECTIVE THERAPEUTICS

Regional Manufacturing Allows Commercialization of ^{212}Pb-labeled Finished Products

The "network effect" ensures reliable supply for intermediate half-life therapeutics

Location	Radius 11 hr – 400 miles
Coralville, IA	51 m
Somerset, NJ	75 m
Los Angeles, CA	46 m
Austin, TX	32 m
Atlanta, GA	57 m
Orlando, FL	25 m

- Top 6 sites cover nearly 300 million people within a one half-life (11 hr) delivery radius[1]
- Products can also be driven further or flown as necessary



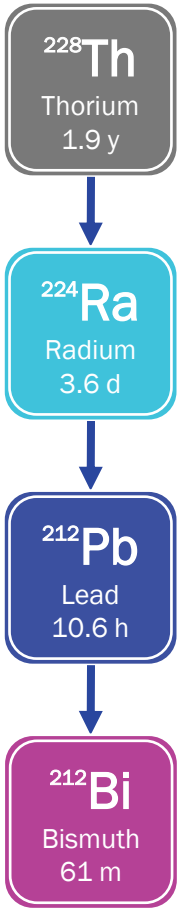
Circles represent distribution radii for facilities producing or **scheduled to produce within next 18 months**

[1] Company estimates

PERSPECTiVE THERAPEUTICS

Mythbusting: "^{212}Pb is Hard to Get" – Isotope Production Process

^{212}Pb isotope decay chain dictates supply, purification, manufacturing & logistics



Plentiful Supply:
Naturally occurring, or
produced as a waste product

- Multiple global suppliers including natural decay
- 2-year half-life allows stockpiling
- Ownership of ^{228}Th reduces 3rd party supply risk

Chemical separation from ^{228}Th:
Allows for Ra-based generators
of ^{212}Pb

- Half-life allows global distribution
- Weekly delivery of ^{224}Ra enables daily ^{212}Pb
- 3.6-day half-life allows local stockpiling

Chemical separation from ^{224}Ra:
Isotope used for manufacturing
finished product

- Regional finished product manufacture
- Multi-dose batch process reduces cost
- Leverages existing networks for logistics

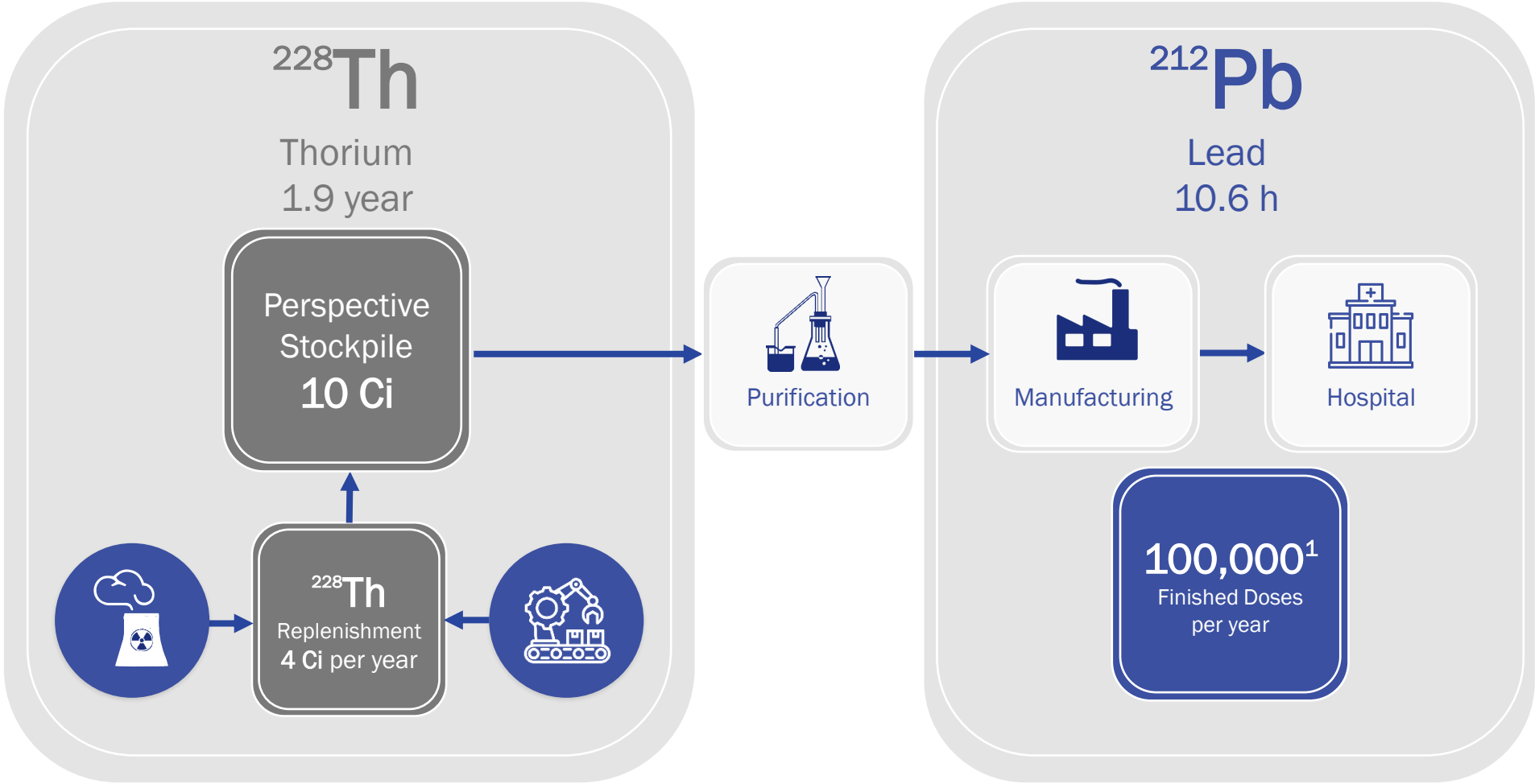
High dose-rate alpha-emitting
therapeutic isotope

- ^{212}Pb acts as *in vivo* "nanogenerator" of alphas
- Perspective's chelator retains ^{212}Bi in drug

PERSPECTIVE THERAPEUTICS

Mythbusting: "^{212}Pb is Hard to Get" – Dose Modeling

Replenishable ^{228}Th stockpile ensures supply of commercial quantities of ^{212}Pb for finished dose manufacture[1]

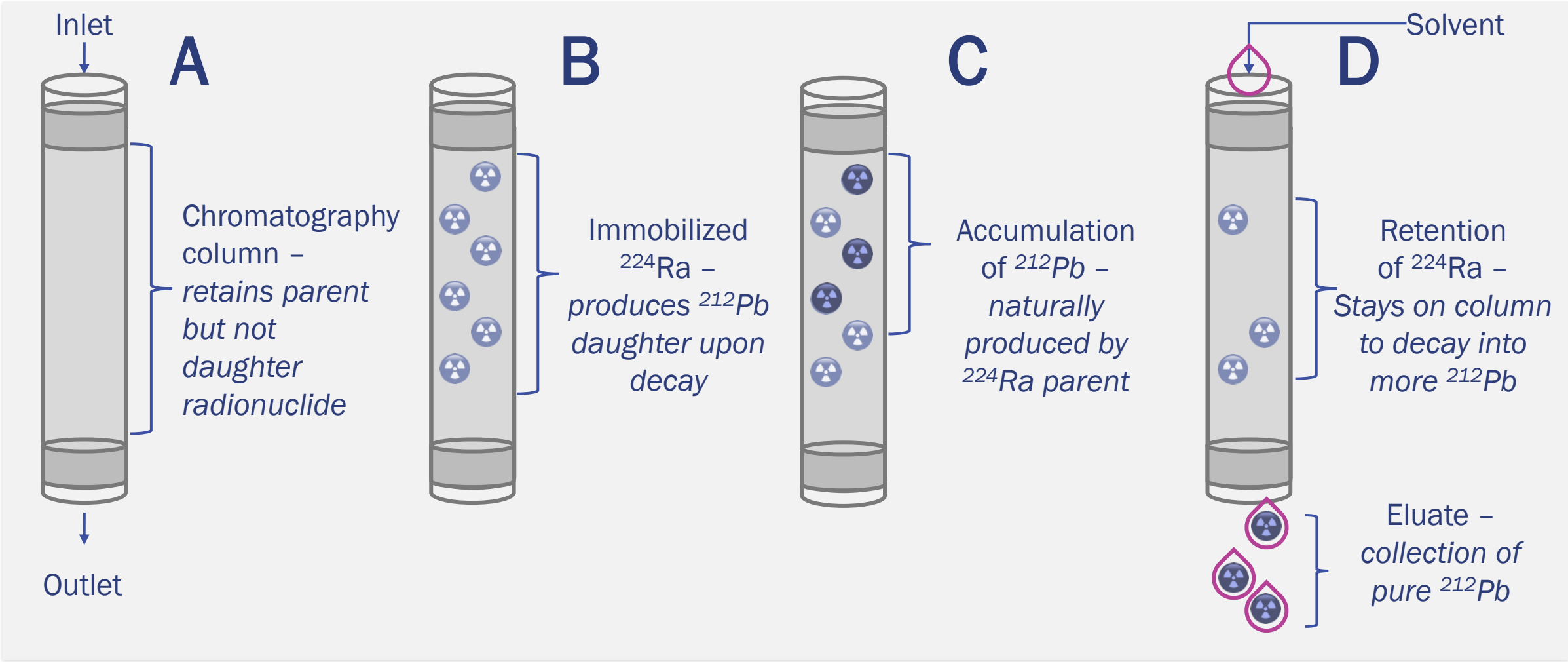


[1] Approximations based on company estimates

PERSPECTIVE THERAPEUTICS

^{212}Pb Isotope Purification Without Just-in-Time Irradiation

Simple chemical separation technology of natural decay products de-risks supply chain

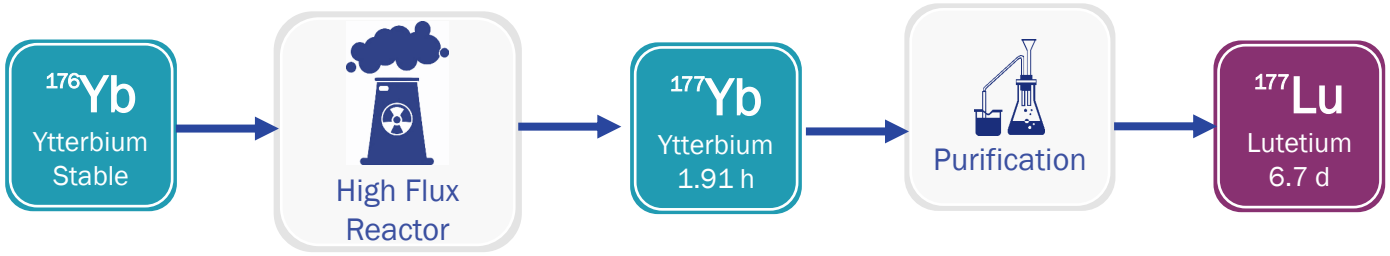


PERSPECTIVE THERAPEUTICS

Contrast with ^{177}Lu Therapeutic Isotope Production and Supply Methods

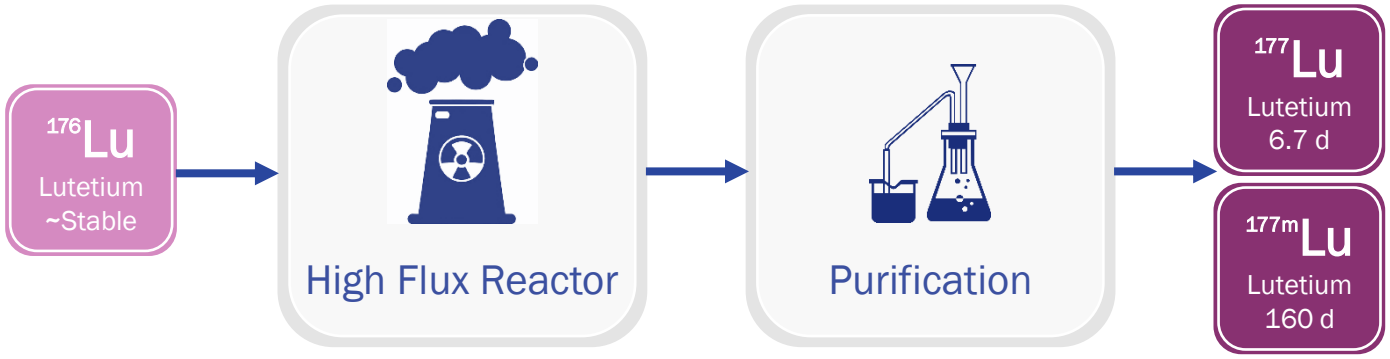
Supply reliant upon constant on-demand production on high flux nuclear reactors

Route 1: Production of n.c.a ^{177}Lu *via* ^{176}Yb through neutron irradiation on a nuclear reactor



- Low production yield
- Difficult radiochemical separations post irradiation due to lower yields
- Requires large quantities of enriched ^{176}Yb (12.9% abundance)
- Currently a shortage of ^{176}Yb

Route 2: Production *via* ^{176}Lu through neutron irradiation on a nuclear reactor



- Produces long-lived contaminant ^{177m}Lu ($T_{1/2}$ = 160 d) unsuitable for medical use

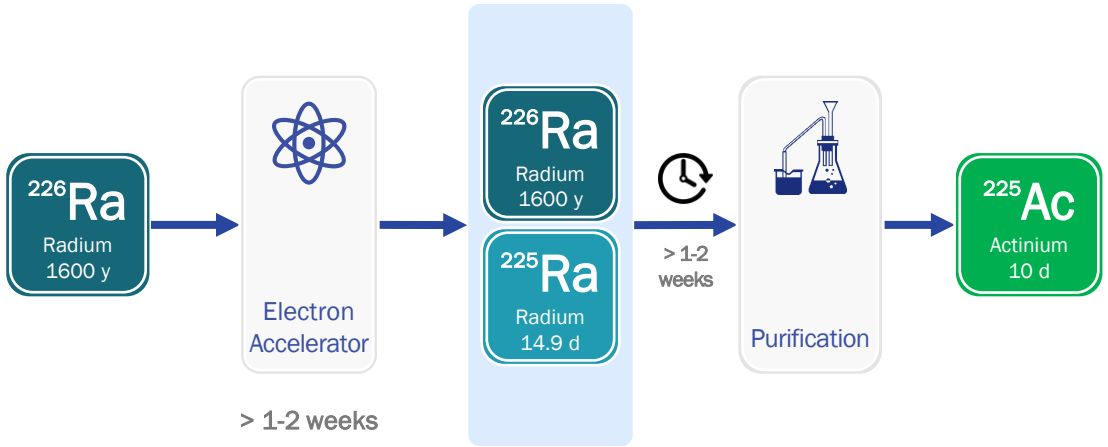
Sources: Dash et al, Nucl Med Mol Imaging 2015; Vogel et al, Eur J Nucl Med Mol Imaging 2021

PERSPECTIVE THERAPEUTICS

Contrast with ^{225}Ac Manufacturing Methods from ^{226}Ra Source

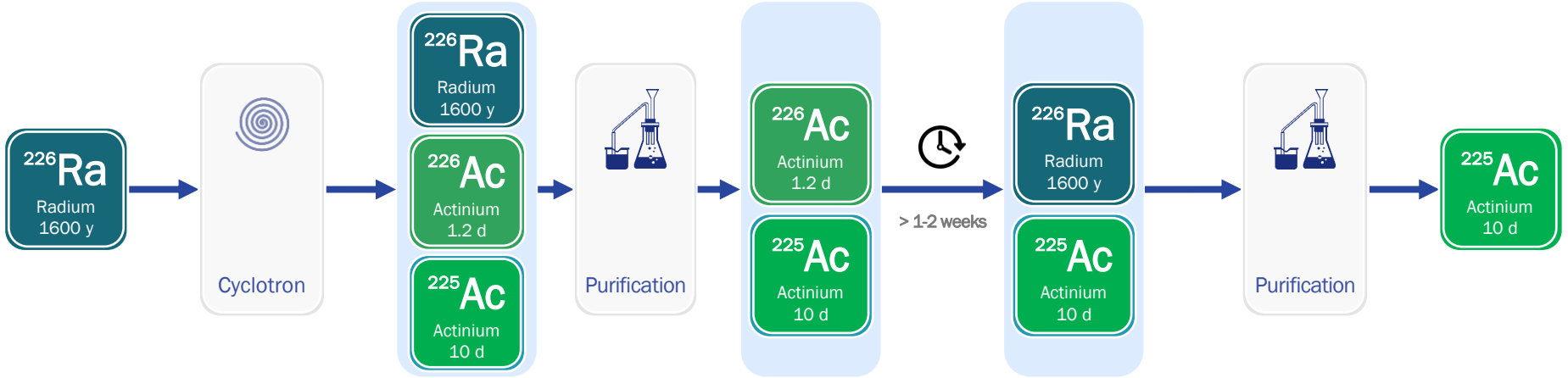
Supply reliant upon constant on-demand production on capital-intensive equipment

Route: Gamma irradiation via electron accelerator (rhodotron) ^{226}Ra(γ,n)^{225}Ra



- Requires capital intensive rhodotron
- ^{226}Ra ($T_{1/2}$ = 1600 y) safety hazard
- Produces gaseous ^{222}Rn ($T_{1/2}$ = 3.8 d)
- Co-production of Ci quantities of ^{224}Ra, producing difficult to shield ^{208}Tl

Route: Proton irradiation via cyclotron ^{226}Ra(p,2n)^{225}Ac



- ^{226}Ra ($T_{1/2}$ = 1600 y) safety hazard
- Gaseous byproduct ^{222}Rn ($T_{1/2}$ = 3.8 d)
- Co-production of ^{226}Ac results in significant loss of ^{225}Ac to ensure purity
- ^{226}Ac decays into ^{226}Ra

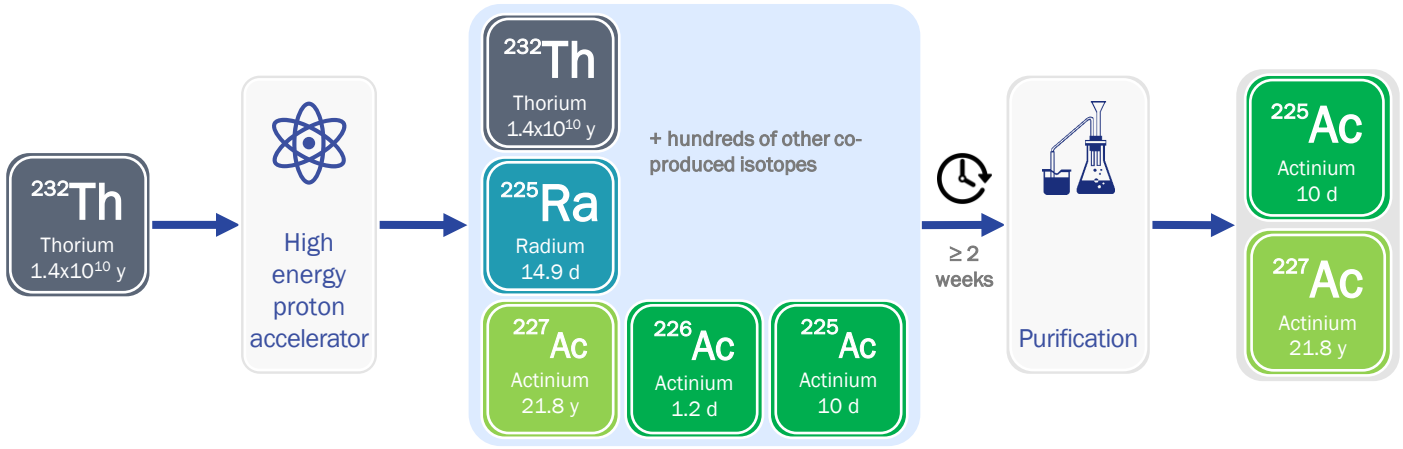
Sources: Diamond et al, J. Appl. Phys. 2021; Nagatsu et al, Eur J Nucl Med Mol Imaging 2021

PERSPECTIVE THERAPEUTICS

Contrast with ^{225}Ac Manufacturing Methods from ^{232}Th Source via Spallation

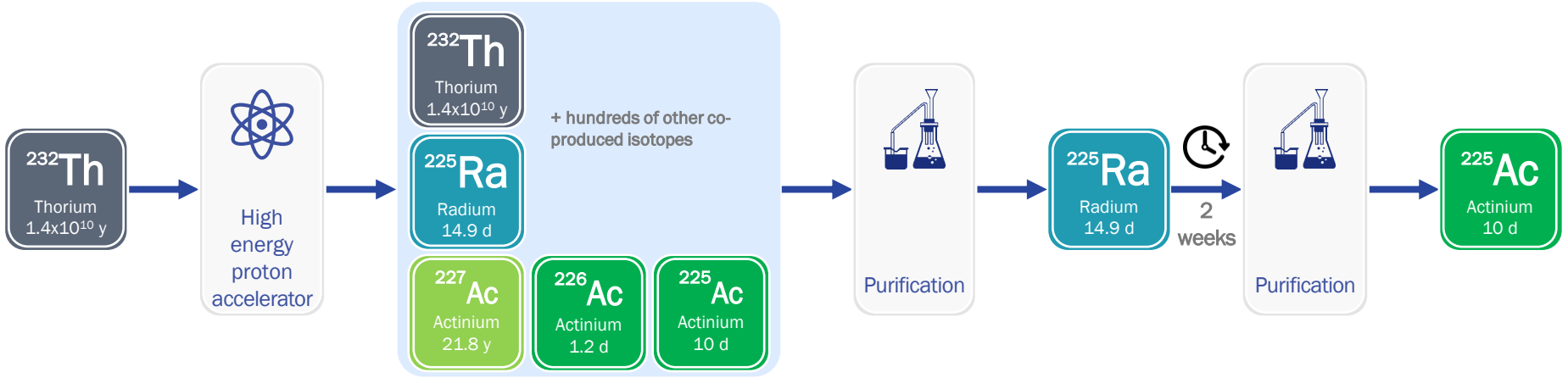
Supply reliant upon constant on-demand production on capital-intensive equipment

Route: Direct production via Th-232 spallation



- Requires high energy proton accelerator >70 MeV
- Co-production of ^{227}Ac (21.8 y) makes ^{225}Ac unsuitable for wide scale medical applications due to hazards posed to medical workers

Route: Indirect production via Th-232 spallation



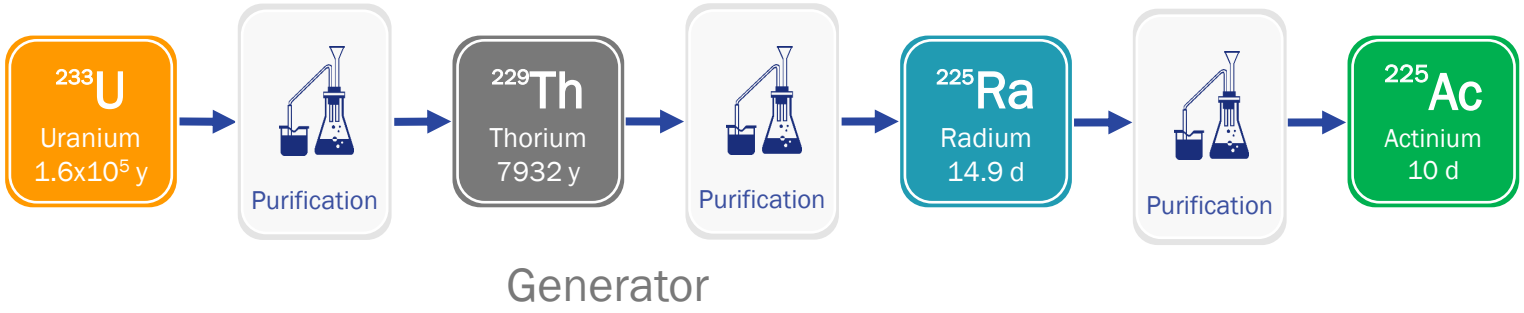
- ^{225}Ac directly produced not usable
- ^{225}Ra production yield low
- Requires high energy proton accelerator (large cyclotron or LINAC)

Sources: Griswold et al, Applied Radiation & Isotopes 2016; Robertson et al, Inorganic Chemistry 2020

Contrast with ^{225}Ac Manufacturing Methods via ^{233}U/^{229}Th Generator

Supply reliant upon highly regulated limited fissile stockpile and capital-intensive equipment

Route: Production via purification from ^{233}U



- ^{233}U is fissile and highly regulated
- ^{233}U supply is limited
- Long ^{229}Th half-life complicates frequent processing required for generator
- Only 4000 dose per year currently available

Summary of ^{177}Lu and ^{225}Ac Production Method Limitations

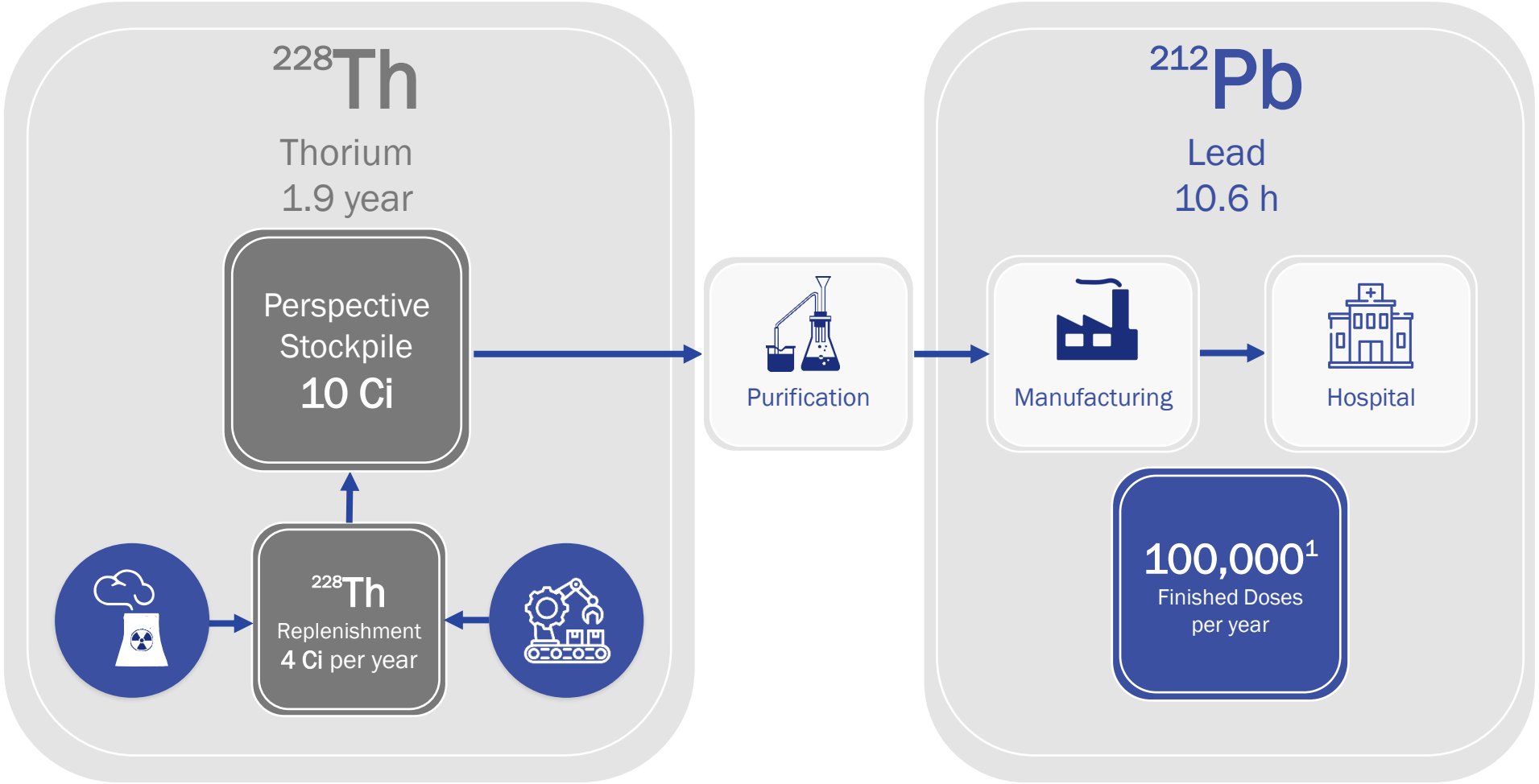
All ^{177}Lu and ^{225}Ac production routes suffer from at least one of the following:

- Capital intensive infrastructure
- Unacceptable impurities
- Low yields
- Frequent handling of ^{226}Ra
- Shortage of target material

Sources: Robertson et al, Current Radiopharmaceuticals 2018

Mythbusting: “^{212}Pb is Hard to Get” – Dose Modeling

Replenishable ^{228}Th stockpile ensures supply of commercial quantities of ^{212}Pb for finished dose manufacture[1]

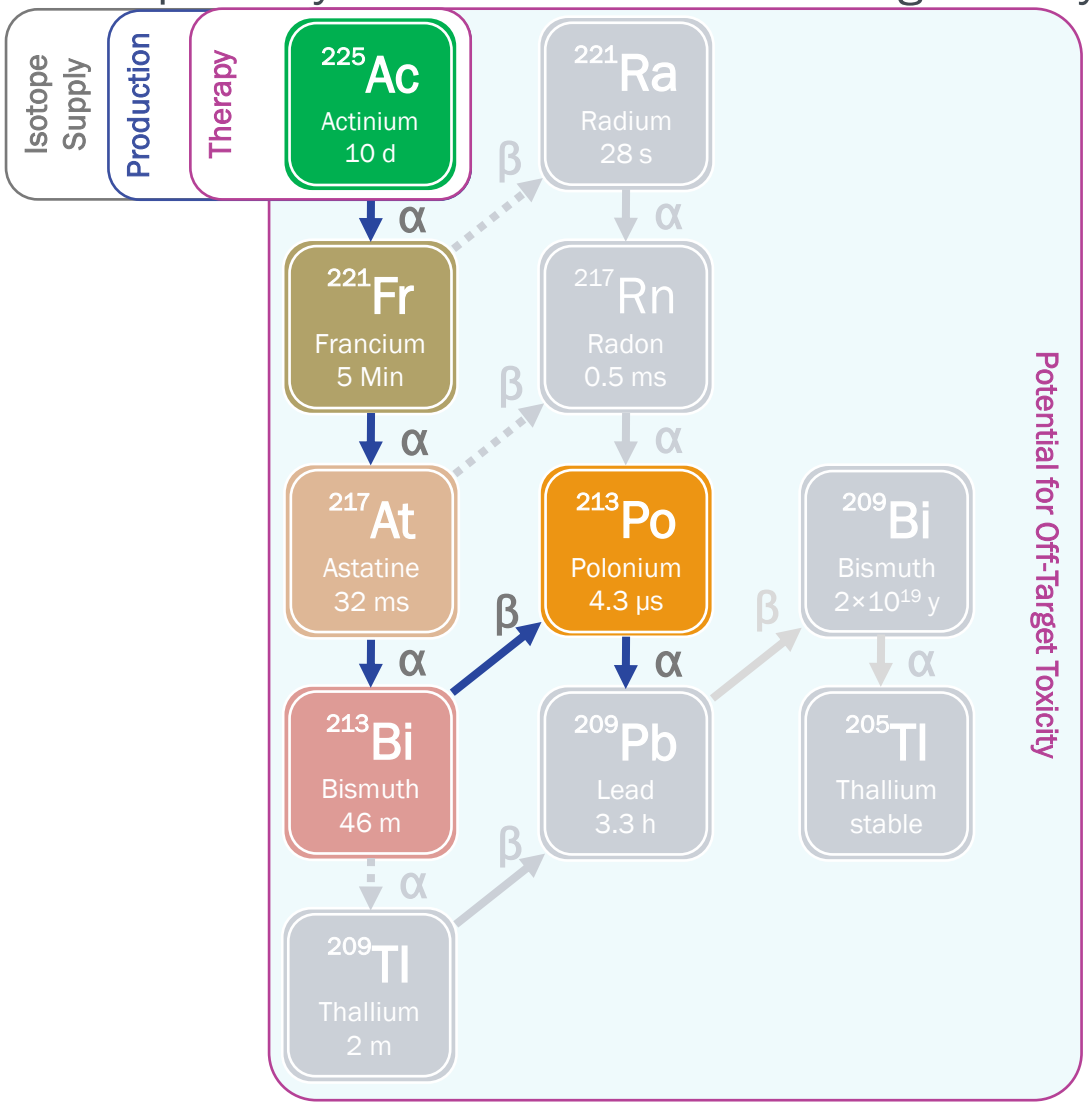


[1] Approximations based on company estimates

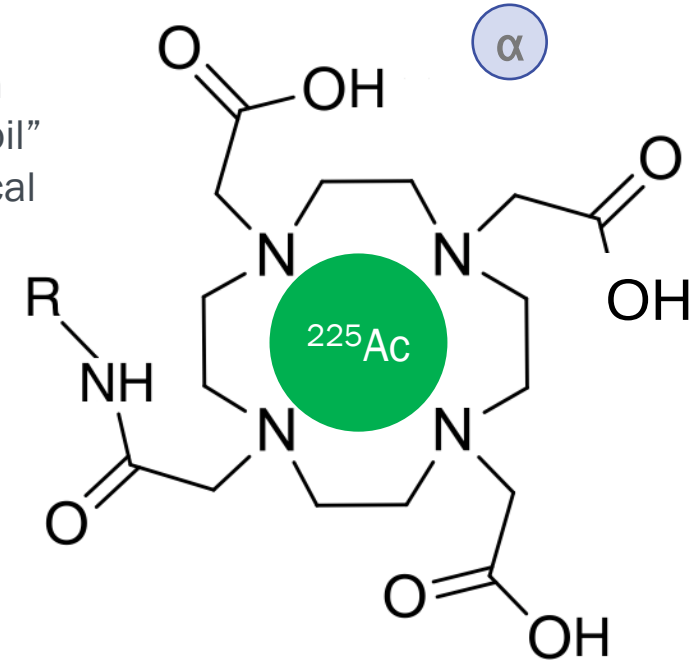
PERSPECTIVE THERAPEUTICS

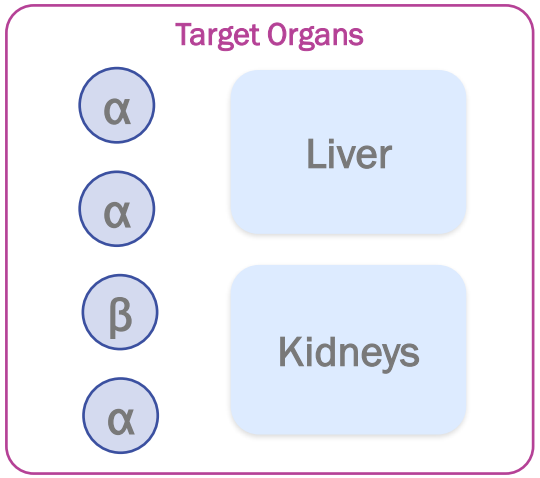
Mythbusting: "Daughters from ^{225}Ac-225 don't redistribute"

^{225}Ac Isotope Decay Chain and Potential for Off-Target Toxicity



Alpha-particle emission imparts sufficient "recoil" energy to break chemical bonds

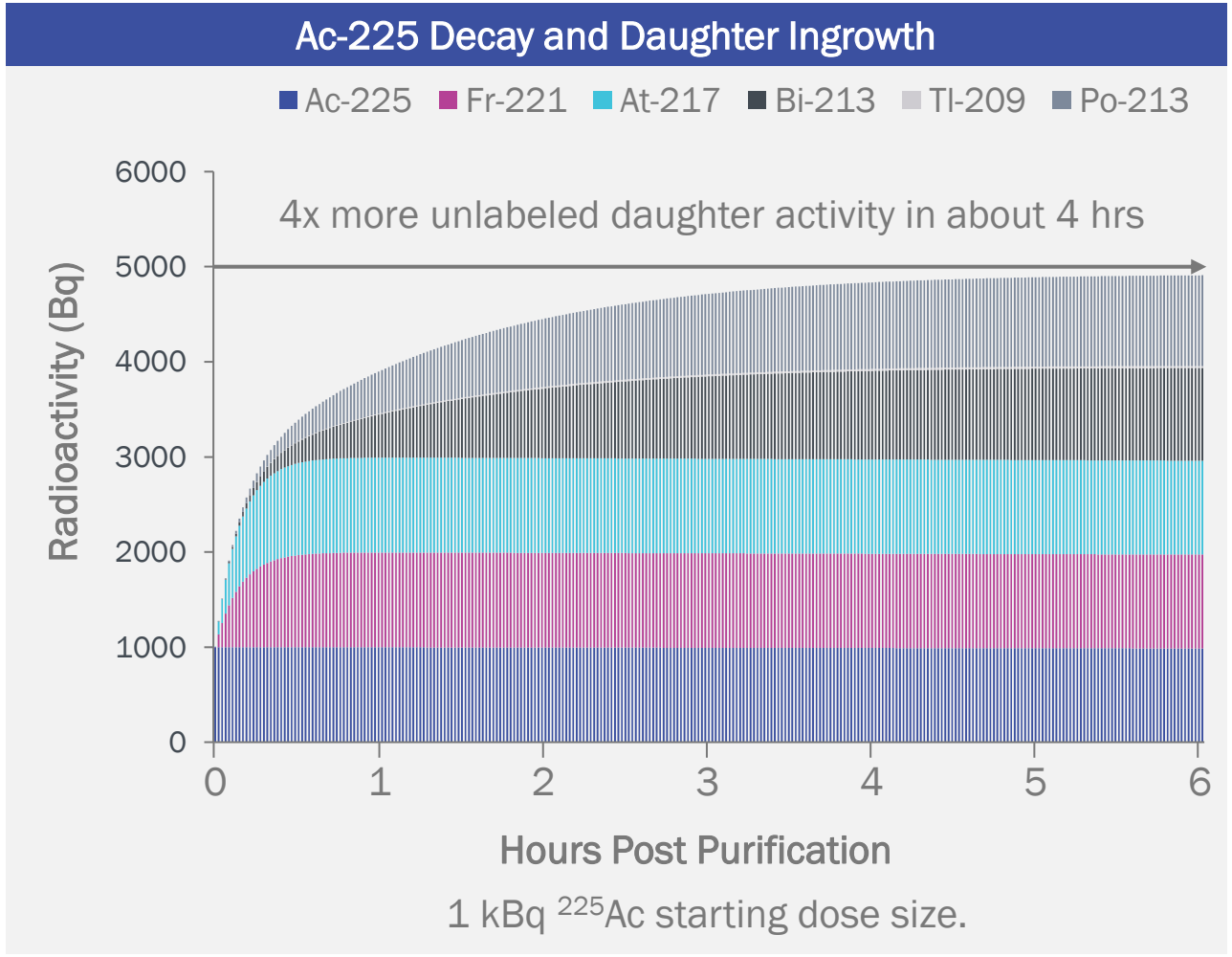


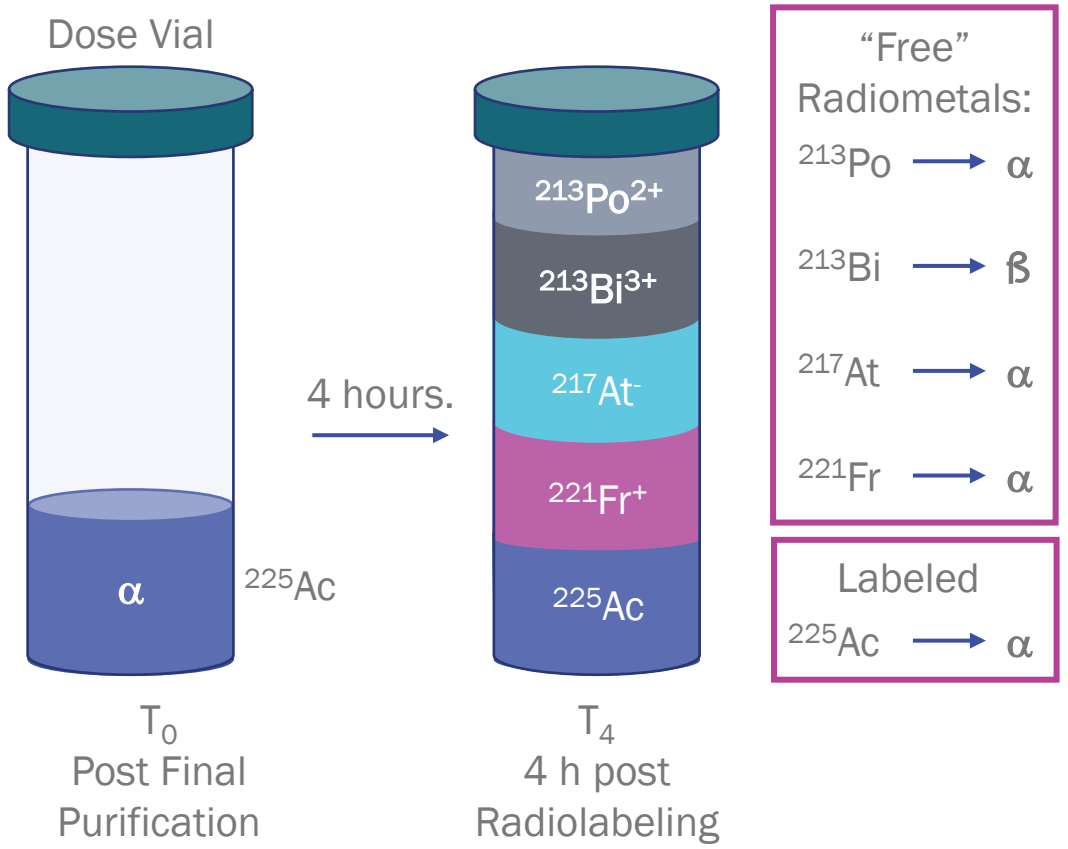


PERSPECTIVE THERAPEUTICS

Mythbusting: "Daughters from ^{225}Ac-225 don't redistribute"

Post final radiolabeling and purification, alpha and beta emitting daughters of ^{225}Ac build up fast in drug product

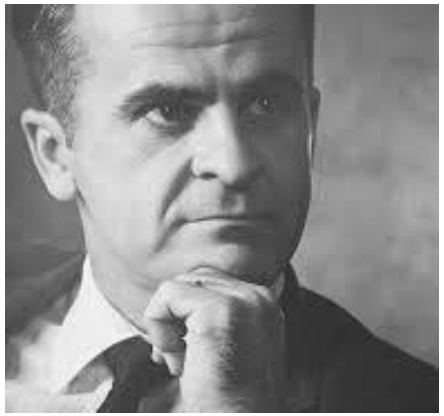




PERSPECTIVE THERAPEUTICS

Mythbusting: “Daughters from ^{225}Ac-225 don’t redistribute”

^{225}Ac daughters follow the laws of physics, chemistry and biology



American Nuclear Chemist
Dr. Gregory R. Choppin

- Chemical bonds cannot contain daughter isotopes following an alpha emission.
- Free metals can diffuse through tissue, even as they are generated in the tumor microenvironment

“Because of the large mass difference between the α-emitting nucleus and the helium atom, almost all of the energy is carried away with the α-particle.

Although the kinetic energy of the daughter nucleus is small in comparison with that of the α-particle, it is large (72,000 eV) in comparison with chemical binding energies (< 5 eV). Thus, the recoiling daughter easily breaks all chemical bonds by which it is bound to other atoms.”

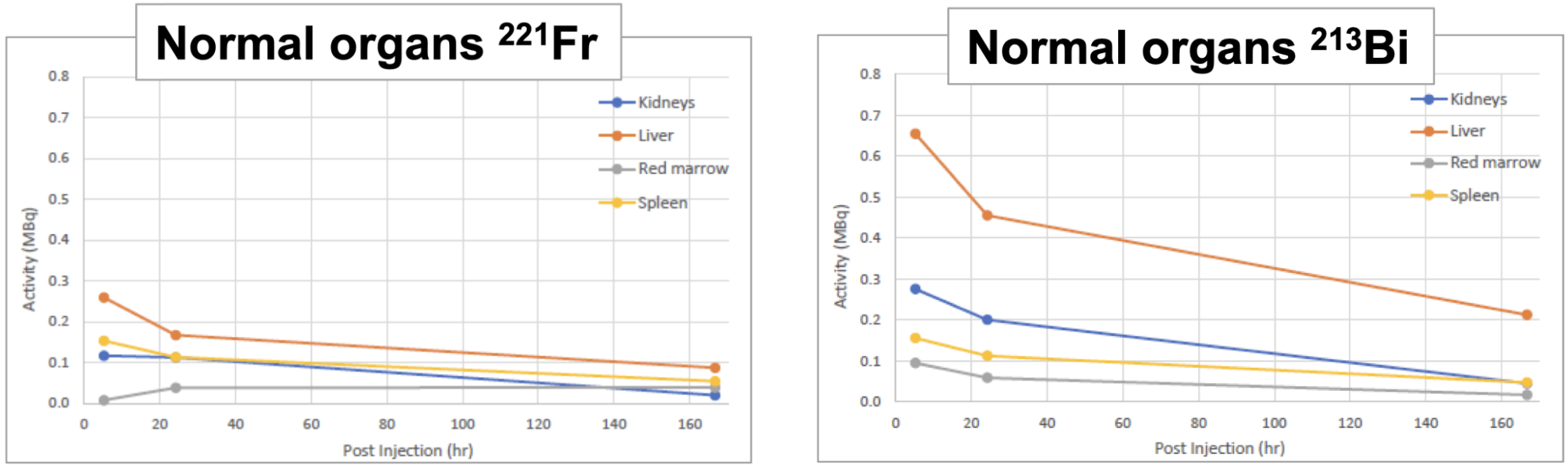
- Gregory R. Choppin, et.al., *Radiochemistry and Nuclear Chemistry (Third Edition)*, 2002

PERSPECTiVE THERAPEUTICS

Mythbusting: "Daughters from ^{225}Ac-225 don't redistribute"

^{225}Ac daughter redistribution – ACTION-1 trial measurement of early and late gamma emissions from healthy tissue

Early (^{221}Fr) and Late (^{213}Bi) Decay



- Extrapolations for radioactivity were seen based on the gamma emissions from the ^{221}Fr and ^{213}Bi daughters
- Higher values in organs were observed with ^{213}Bi than ^{221}Fr, particularly at early time points and in kidneys and liver

This provides evidence of a free isotope bolus with injection AND daughter redistribution during ongoing ^{225}Ac decay over the imaging interval

SNMMI 2023 Oral Presentation. RayzeBio website https://rayzebio.wpengine.com accessed March 11, 2024 (y axis scale matched)

PERSPECTIVE THERAPEUTICS

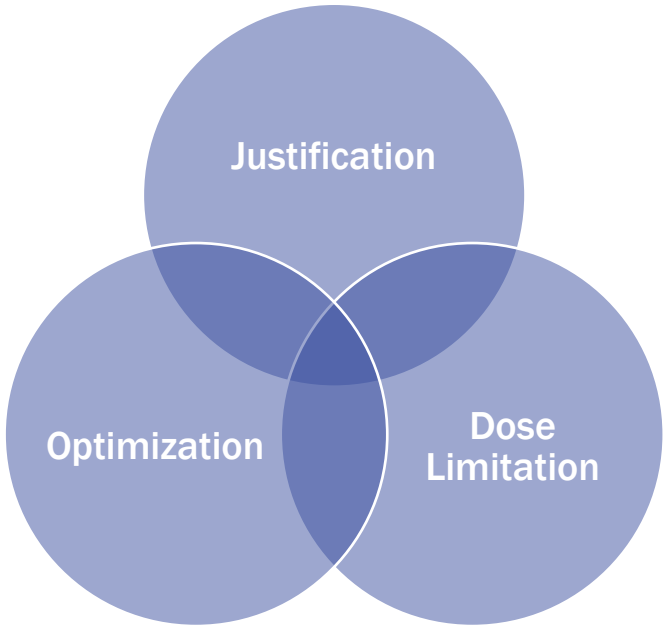
Mythbusting: "Daughters from ^{225}Ac-225 don't redistribute"

^{225}Ac daughters do redistribute in the body

Implication: Threshold exposures for toxicity must be established

IAEA Fundamental Safety Principles

IAEA International Atomic Energy Agency



When introducing a new source of radiation exposure, fundamental principles apply, including the ALARA "as little as reasonably achievable" principle.

Important considerations for alpha-particle therapy:

- *What is the dose rate?*
  - ➢ *Time to full dose delivery is isotope-specific*
- *Where is the radiation deposited in organs?*
  - ➢ *How does that effect function?*
  - ➢ *Dose is not equal within an organ's component parts*
- *What are the long-term effects of radiation exposure of this type?*

PERSPECTIVE THERAPEUTICS

Corporate Update

Corporate Activities Update

2023

- Closed Merger between Isoray Medical and Viewpoint Molecular Targeting
- Completed dosing, interim results presented on compassionate use study with VMT-α-NET
- Initiated US phase 1 study in VMT-α-NET, closed 1st cohort and safe to proceed 2nd cohort
- Initiated US phase 1 study in VMT01 melanoma, closed 1st cohort and safe to proceed 2nd cohort
- Filed new composition matter (FAP)
- Multiple peer reviewed publications

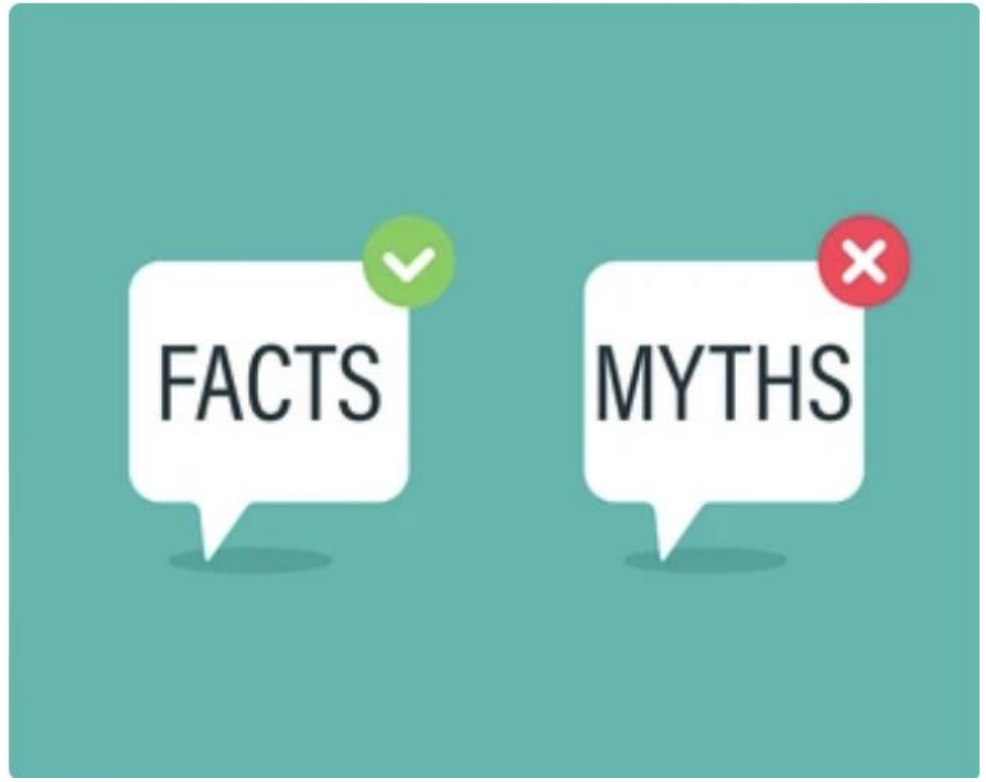
2024

- Strategic partnership with Lantheus Medical
  - Equity investment
  - Licensing options
  - Manufacturing facility
- PIPE and CMPO proceeds give cash runway to 2026 if all programs at full speed
- Brachytherapy business divestiture expected to close 1H24
- VMT-α-NET Compassionate use data expected 2Q24
- VMT01 safety / efficacy data initial readout 3Q24
- VMT-α-NET safety / efficacy data initial readout 3Q24

PERSPECTIVE THERAPEUTICS

Summary of Myths

- "^{212}Pb Doesn't Get Enough Energy Into the Tumors"
- "Regulatory environment doesn't suit ^{212}Pb"
- "Centralized production is better than networked production"
- "^{212}Pb is Hard to Get"
- "Daughters from ^{225}Ac don't redistribute"



PERSPECTIVE THERAPEUTICS

Questions