



PERSPECTIVE
THERAPEUTICS

Corporate Presentation

August 2024

NYSE: CATX



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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 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

Strong Financial Position

Funding into mid-2026

Cash, cash equivalents and short-term investments as of June 30, 2024	\$292.9 million
Share count as of June 30, 2024	67.4 million
Outstanding common stock warrants & options as of June 30, 2024	7.4 million
Outstanding pre-funded warrants as of June 30, 2024	3.2 million

Based on Perspective's current plans, which include advancing current clinical programs based on readout, progressing multiple pre-IND assets towards clinical trials, as well as acquiring and developing several regional manufacturing sites, the Company expects to have sufficient funding into mid-2026.

Platform Expansion Engine

Three Lead Programs in Clinic and Broad Proprietary Pipeline

Program	Tumor Type	Discovery	Human Clinical Imaging	First in Human Therapy	Phase 1/2	Phase 3
VMT- α -NET	Neuroendocrine cancers	[Progress bar]				
	Pheochromocytomas, paragangliomas	[Progress bar]				
	Small cell lung cancer	[Progress bar]				
VMT01/02	Melanoma (MC1R imaging & therapy)	[Progress bar]				
PSV359 (Novel peptide)	Multiple (FAP imaging & therapy)	[Progress bar]				
PSV40X (Radio-hybrid)	Prostate (PSMA imaging & therapy)	[Progress bar]				
Program 5 (Novel peptide)	Prostate, Breast	[Progress bar]				
Pre-targeting Platform (mAbs)	Solid and hematological tumors	[Progress bar]				
Other Programs (Novel peptides)	Solid and hematological tumors	[Progress bar]				

Delivering Momentum Across Solid Tumor Programs

Platform for consistent generation and development of new assets

Program	Target	Tumor Types	Nominate Candidate	IND Filing	Initiate Cohort 1	Enrolled Cohort 2	Preliminary Update	RP2D ² Status
VMT- α -NET	SSTR2	Neuro-endocrine Tumors	☑	☑	☑	☑	☑ (Investigator led research ¹)	Update to timing expected late 2024
VMT01/ VMT02	MC1R	Metastatic Melanoma	☑	☑	☑	☑	Expected 2H 2024	ICI combo study with nivolumab results expected 2025
PSV359	FAP- α	Multiple solid tumors	☑	Expected late 2024	Expected 2025			
Various Discovery Programs	PSMA	Prostate	Expected late 2024					
	Undisclosed	Breast						
	Undisclosed	Lung						

Key future milestones & expected timelines

Cohorts 1&2

Initial results: 2H 2024
Duration of results: 2025

Cohort 3;

Pending FDA interaction

Cohorts 1&2

Initial results: 2H 2024
Duration of results: 2025

Combination cohorts

Initial dosing: 2H 2024
Initial results: 2025

6 | ¹Investigator led research in India in patients with neuroendocrine tumor and medullary thyroid carcinomas.

²RP2D = recommended Phase 2 dose; ICI = immune check point inhibitor.

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 Puhmann, 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

Radiopharmaceuticals are a Pillar of Oncology Treatment

Unique Mechanism of Action Offers Pan-Cancer Opportunities

Molecularly Targeted Radiation

Radioligands can precisely deliver radiation directly to cancer cells reducing off-target effects
Proven pillar of cancer treatment

Perspective's platform technology is optimized for greater efficacy and fewer side effects

Optimized Patient Selection

Molecular imaging companion diagnostics enable visualization of the therapeutic target
Enables the selection of patients who may best respond to therapy

Perspective's elementally matched isotopes are paired for imaging and therapy

Monotherapy Activity and Combination Synergies

Ability for both monotherapy and combination treatments
Potential synergies with DNA damage response and immune checkpoint inhibitors

Perspective's targeted alpha therapy delivers potent and immunostimulatory radiation to tumor

Outpatient Friendly

Modern medical isotopes enable radiopharmaceuticals to be administered outside of hospitals
Treatments are easily-accessible globally with several hundred therapeutic locations in the U.S alone

Perspective's short half-life isotopes simplify patient administration and waste management

Unique Business Opportunity

Radiopharmaceutical theranostic product development is highly-specialized and technical
Greater expertise needed than for standard medicines potentially creating higher barriers to entry

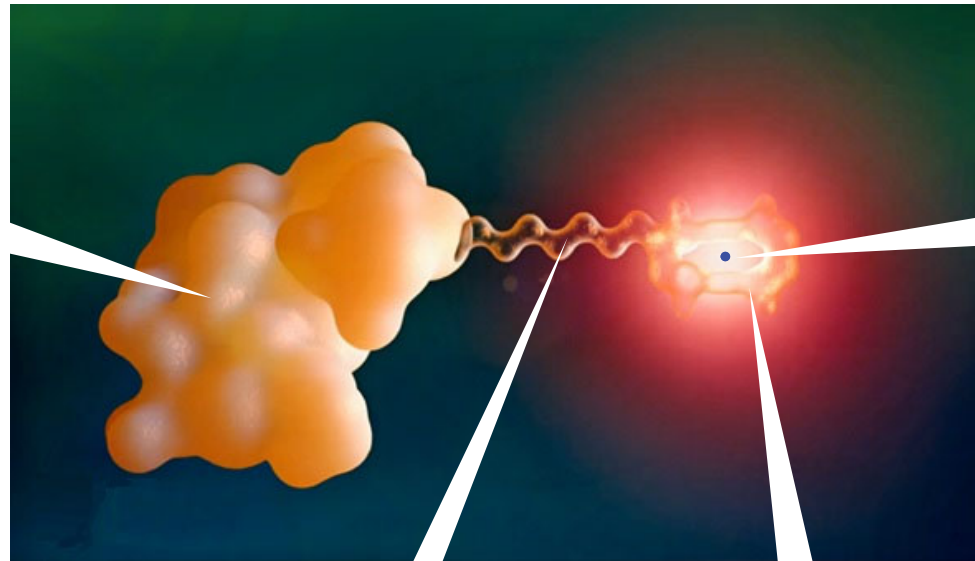
Perspective aims to develop patent-protected and best-in-class intellectual property

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

Lead-212 (²¹²Pb): The Optimal Therapeutic Isotope

Alpha Particles Provide Numerous Benefits Over Currently Used Beta Particle Radiotherapies

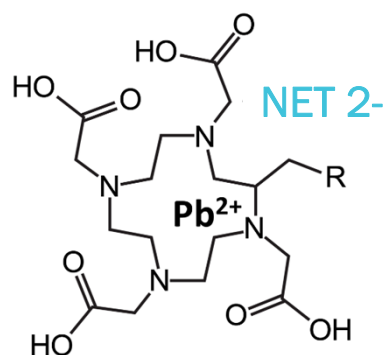
- With a much higher atomic mass, **alpha (α)** particles generate more energy and travel a shorter distance compared to beta (β) particles, making them more cytotoxic, while reducing their off-targeting effects on healthy tissue
- Alpha radiation causes direct lethal double-stranded DNA breaks, vs indirect single-stranded breaks in beta (β) radiation
- Cell death expected – NO resistance
- Greater therapeutic efficacy expected to improve outcomes with better safety

	Lead (²¹² Pb)	Iodine (¹³¹ I)	Lutetium (¹⁷⁷ Lu)	Actinium (²²⁵ Ac)	Implication ¹
Emission Profile	Alpha	Beta	Beta	Alpha	Potent
Half Life	0.46 days	8 days	6.7 days	10 days	High dose-rate
Off Target Toxicity Risk	Low	Very high	Low	High	Best
Supply	High	High	Low	Low	Abundant
Cost of Production	Low	Low	High	High	High margin

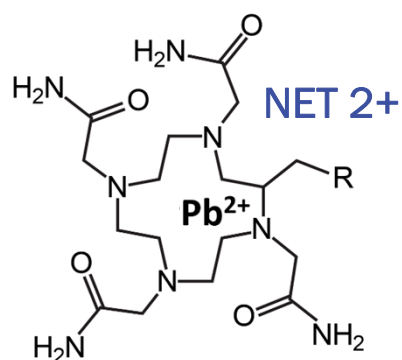
Chelator Optimized for $^{212/203}\text{Pb}$

Perspective's Enabling Technology for Pb-based Radiopharmaceuticals

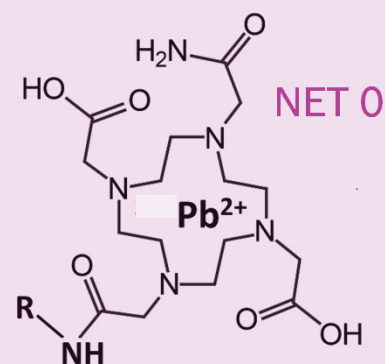
DOTA



TCMC



PSC¹



Commercially Available

Perspective's Chelator

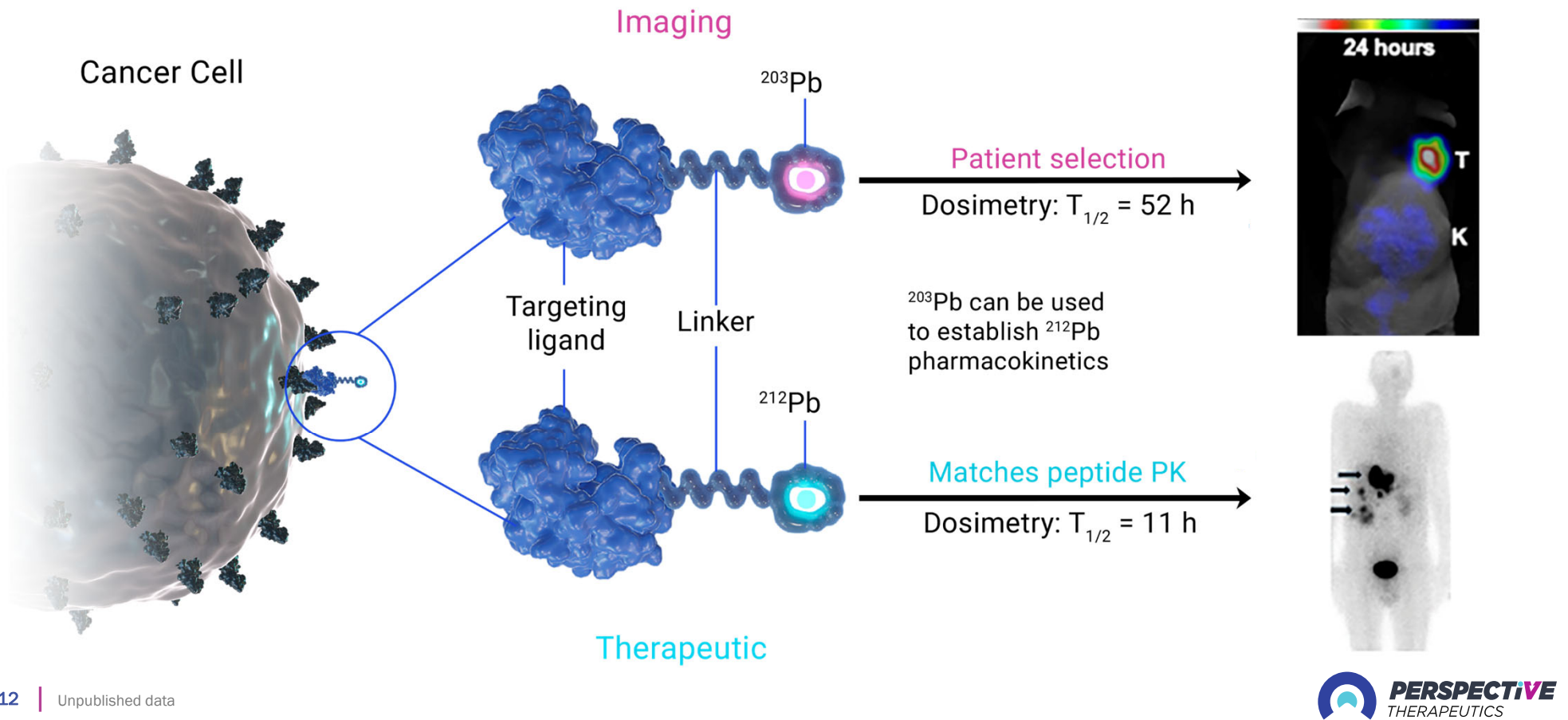
Perspective's Proprietary Chelator:

- Designed specifically for Pb isotopes
- Optimized for rapid renal clearance through neutralized formal charge
- Improves radiolabeling, receptor binding & internalization
- Generic chelators leak the ^{212}Bi alpha-emitting daughter up to 36%²

Generic chelators have not been optimized for Pb isotopes, potentially compromising safety, efficacy and manufacturing efficiency

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

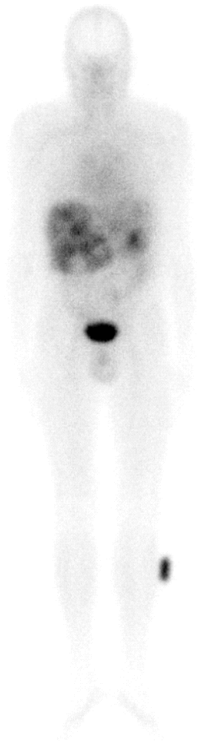
Identical Distribution of ^{203}Pb and ^{212}Pb for Imaging and Treatment, Respectively



Neuroendocrine Tumors: VMT- α -NET

Targeting the somatostatin receptor to treat rare neuroendocrine-type cancers

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

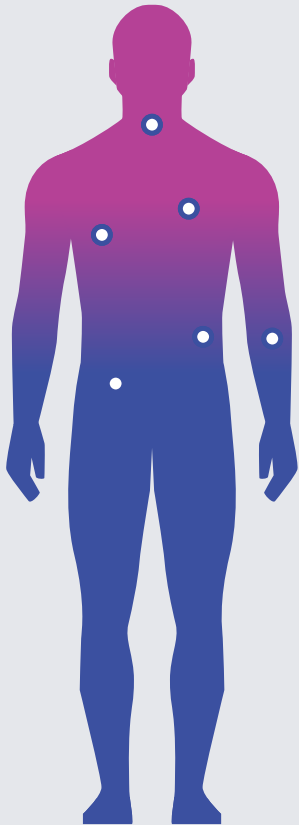
Initiated therapy (2022) investigator led study in India – data on 13 patients presented at SNMMI in June 2024

Fast Track Designation for first line therapy received October 2022
Therapeutic trial in PRRT naïve setting currently recruiting throughout 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 PRRT naïve patients

SSTR2 is an Attractive Target for Identifying and Treating Tumors

Expressed Across Several Tumor Types



Neuroendocrine tumors (NETs)

- Neuroendocrine cells are specialized cells that secrete hormones and other bioactive substances
- Neuroendocrine cells are found throughout the body
- Often grow in the pancreas or other areas of the gut, such as the stomach, small intestine, rectum, colon or appendix

SSTR2 is expressed widely in various tumors

- Meningioma
- Pituitary adenomas
- Nasopharyngeal carcinoma
- Thyroid cancer
- Breast cancer
- Small cell lung cancers
- Merkel cell carcinoma
- Melanoma

Potential Superiority of Perspective's Platform Technology vs Generic Compounds

Decreased Off-Target Toxicity, Increased Tumor Uptake and Retention in Preclinical Studies

Key Takeaways



SSTR2 tumor model demonstrates superiority of VMT- α -NET to generic compounds



8-fold improved tumor uptake with decreased kidney retention



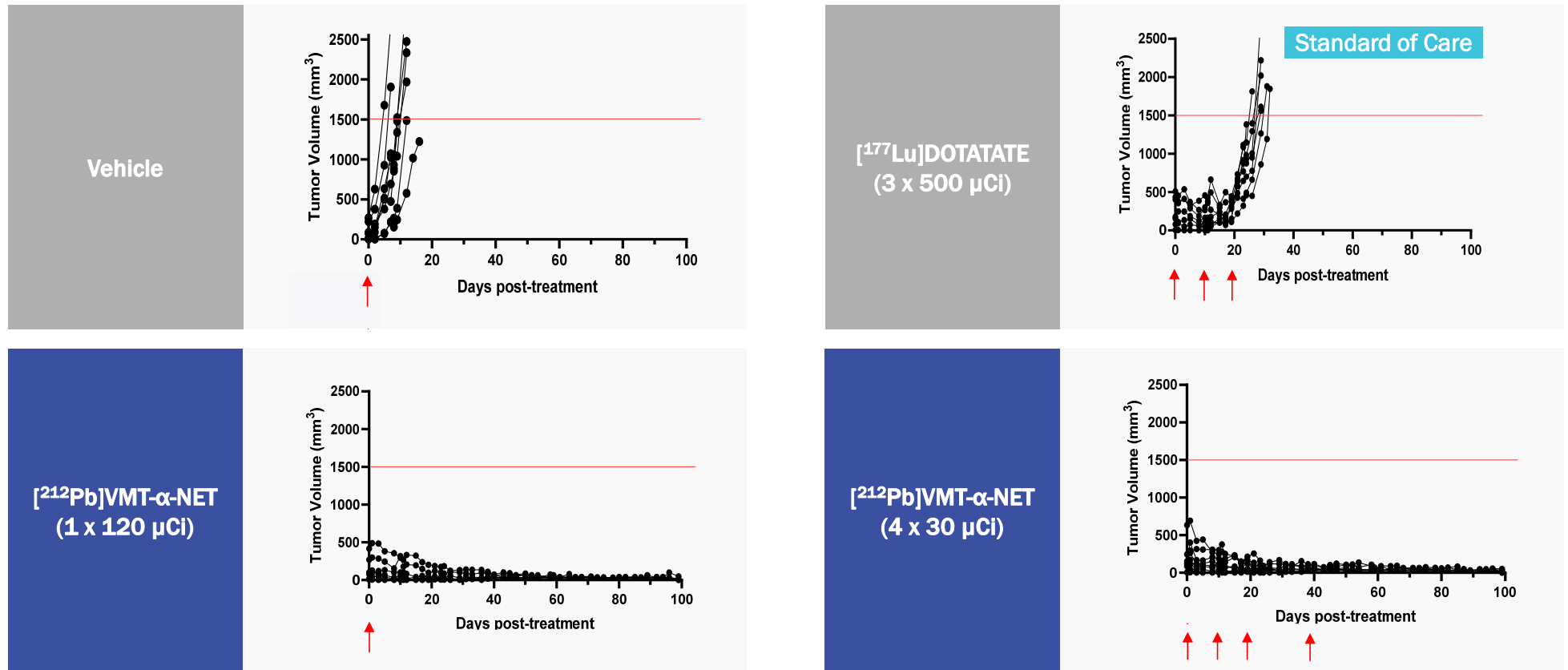
Tumor

Kidneys

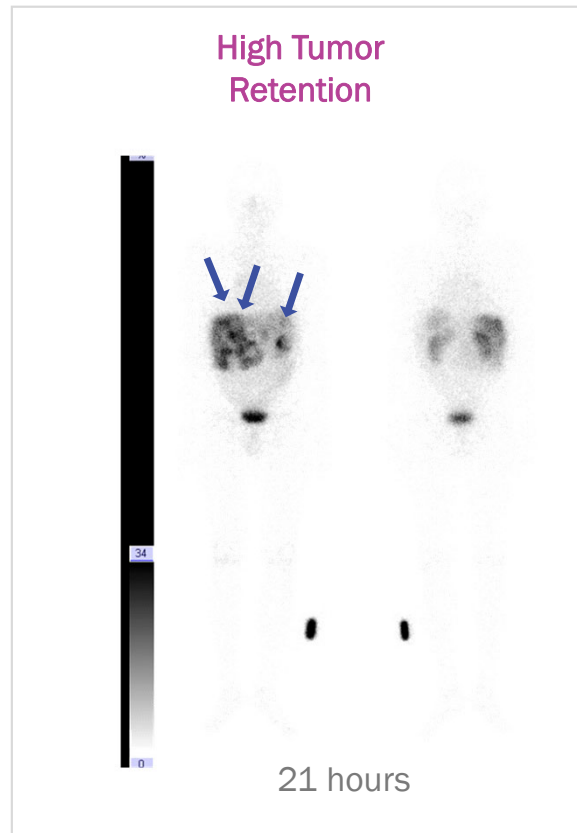
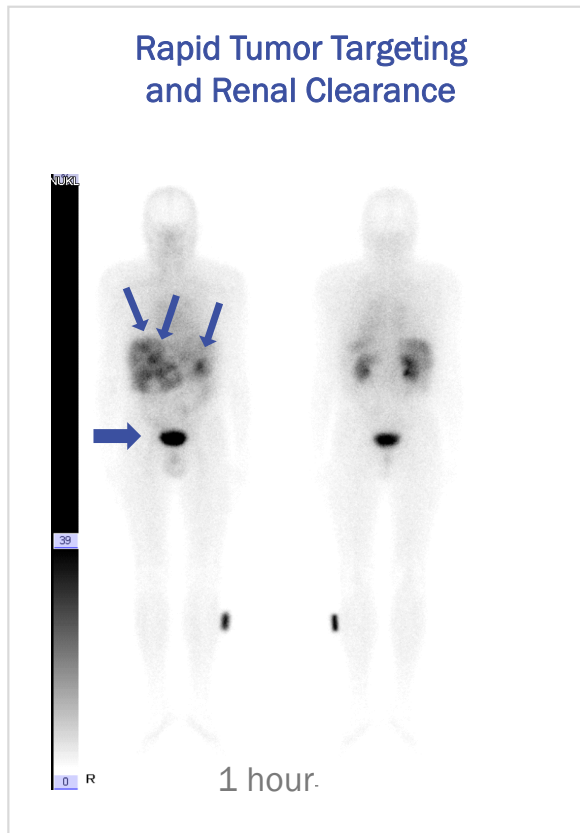


VMT- α -NET Shows Significant Improvement vs Standard of Care in Preclinical Models

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



^{203}Pb SPECT Imaging Reveals Favorable VMT- α -NET Properties¹

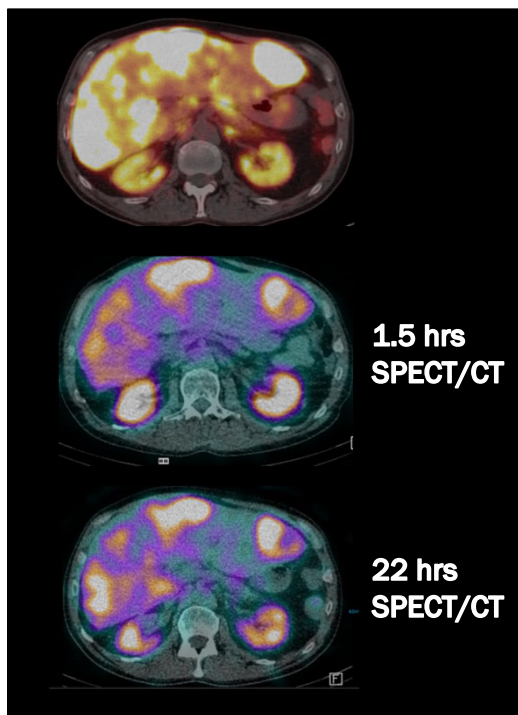


- Tumors visible within 1 hour indicates rapid binding to SSTR2 target
- High intensity above background implies excellent therapeutic window
- Unbound drug in bladder within 1 hour for excretion
- Low renal retention due to neutral charge on proprietary Pb-specific chelator

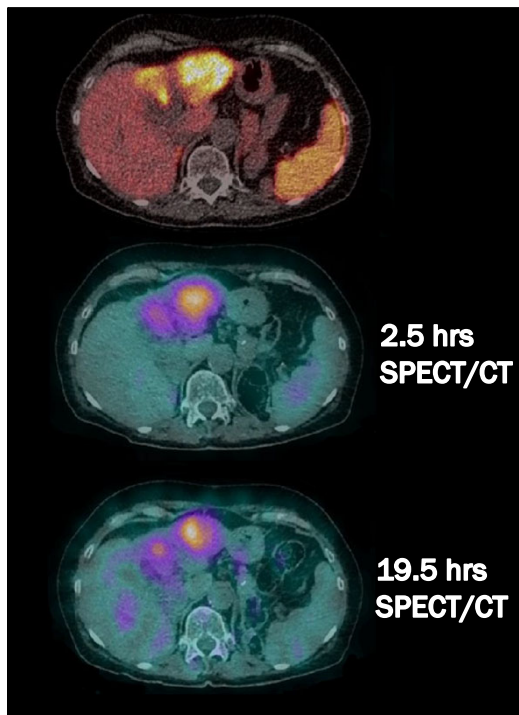
^{212}Pb SPECT/CT Imaging Confirms VMT- α -NET Tumor Uptake

Diagnostic and Therapeutic Show Same Uptake and Retention Characteristics

^{203}Pb SPECT/CT Imaging¹
Pt#001



^{212}Pb SPECT/CT Imaging²
Pt#009



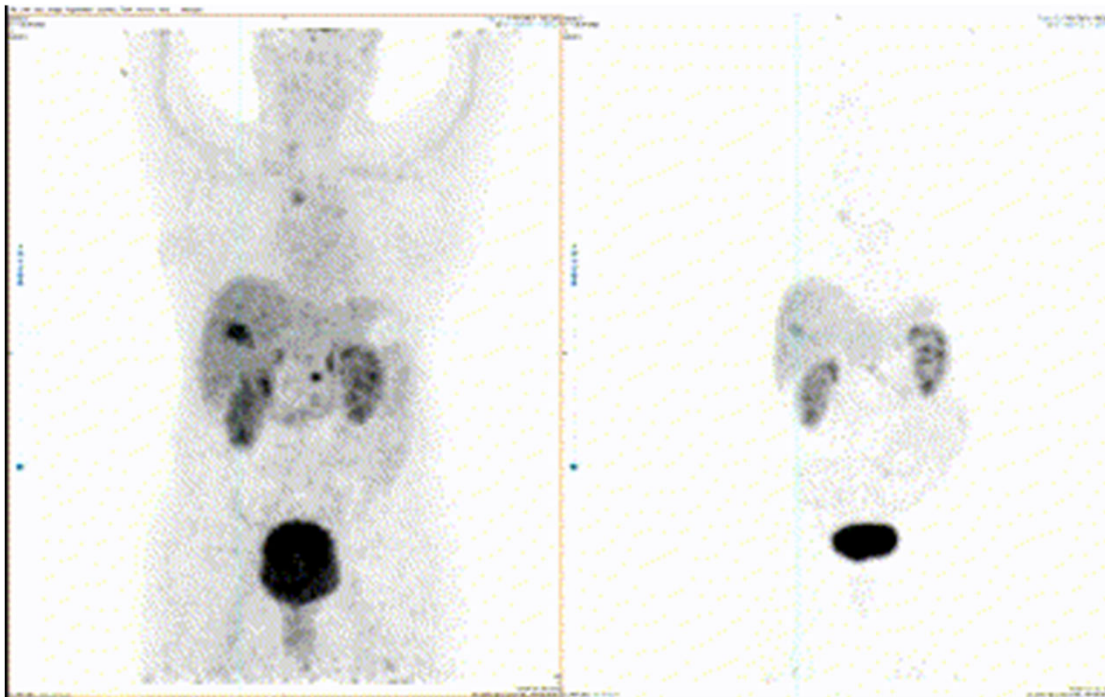
- Both ^{203}Pb and ^{212}Pb can be imaged directly using SPECT
- SPECT/CT shows very rapid tumor uptake and retention of [^{212}Pb]VMT- α -NET
- After 24 hours more than 80% of alpha particles will be generated
- This high alpha dose rate is ideally matched to the biological clearance of the VMT- α -NET peptide

Significant Response After Single Dose of [²¹²Pb]VMT-α-NET

Metastatic NET Pancreas with Adrenal Crisis – Maximum Intensity Projection (MIP)

Tumor Before Treatment

Tumor After 1 Dose



- ⁶⁸Ga-DOTA-NOC PET images at base line and post 1st dose of [²¹²Pb]VMT-α-NET
- MIP suggesting strong reduction of intensity (thoracic lesions) and decreasing tumor volume (Partial Response)

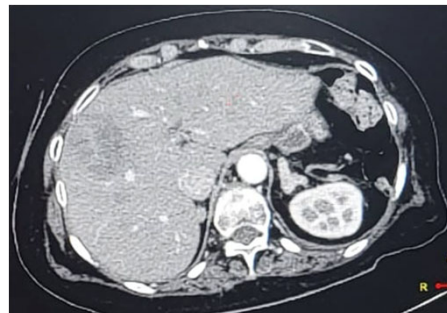
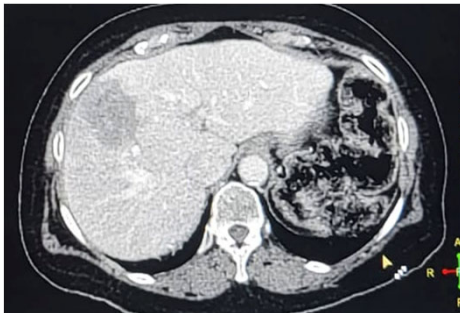
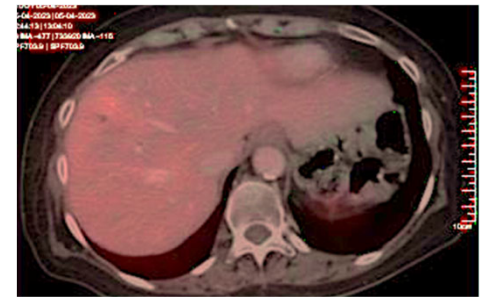
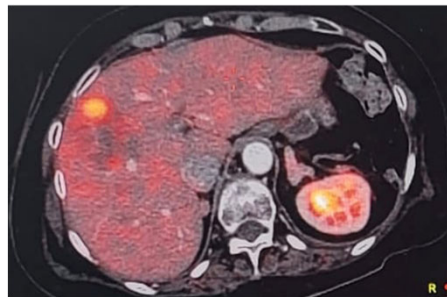
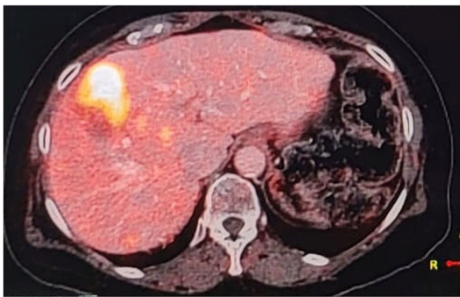
Significant Response After Single Dose, Almost Complete Response After 3 Doses

Metastatic NET Pancreas with Adrenal Crisis

Tumor Before Treatment

Tumor After 1 Dose

Tumor After 3 Doses



(S.ACTH)¹– 790 pg/ml

S.ACTH – 96 pg/ml



Treating Physician:

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

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

Results as of May 31, 2024 for Ongoing Investigation in India

Current Status

- Patients with prior lines of therapy, late-stage, anatomically different NETs (mean age: 51 years; 6 females)
- 13 patients administered [²¹²Pb]VMT-α-NET
- 6/13 patients continuing on therapy
- 2 patients completed all 6 treatments
- 45 total [²¹²Pb] VMT-α-NET doses administered to date

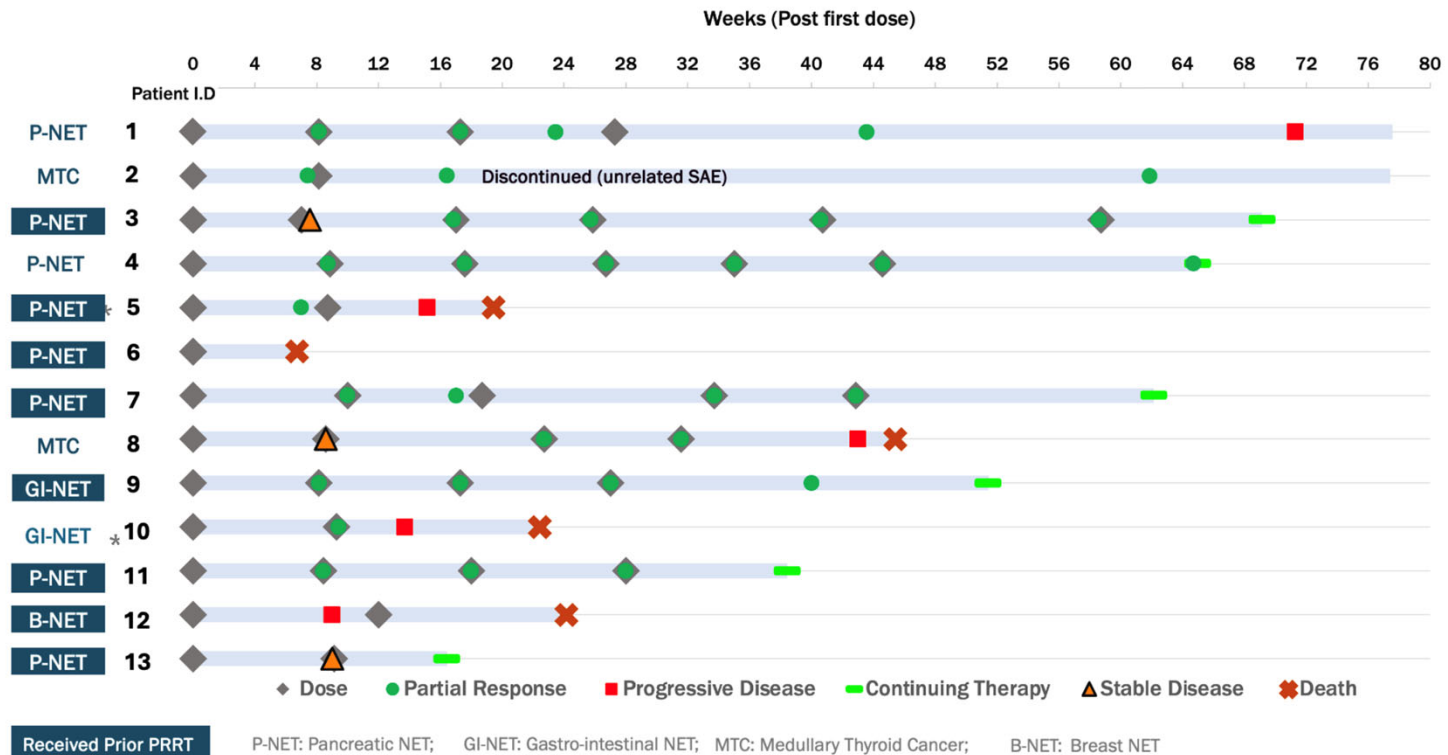
Response

- Interim Overall Response Rate (ORR) seen in 10/13 (76.9%)
- Partial Response Rate 8/13 (61.5%)
- Unconfirmed Partial Response 2/13 (15.4%)

Safety

- 5 fatal adverse events have been reported so far
- Death from underlying disease/progressive disease (N=4), sudden cardiac arrest (n=1)
- (Non-Fatal) Myelodysplastic Syndrome (n=1) , no causal relationship found. Subject BCR-ABL1 gene positive. On Imatinib maintenance, remains well
- No other substantial high grade hematological toxicity
- Alopecia is moderate and transient and appears to be related to SSTR expression in the hair follicles.
- Dysphagia is moderate and transient, etiology uncertain

High Partial Response Rate in Patients with SSTR+, Late-Stage Refractory NETs Interim Results as of May 31st 2024

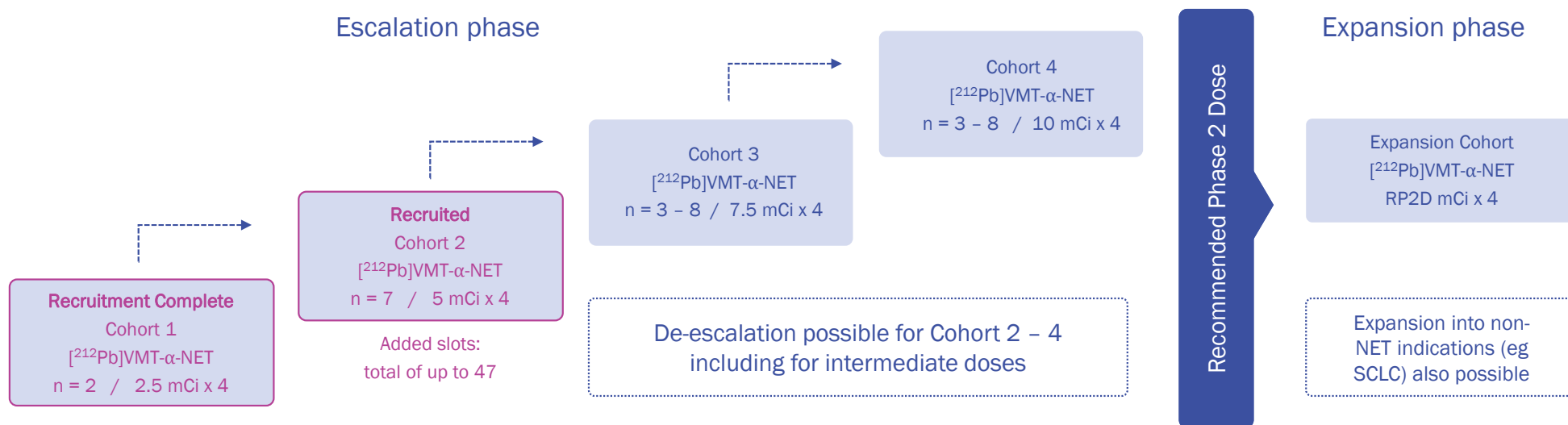


* Unconfirmed PR (uPR) by RECIST 1.1



Trial Design: [²¹²Pb]VMT-α-NET mTPI-2¹ Phase 1/2a For Neuroendocrine Tumors

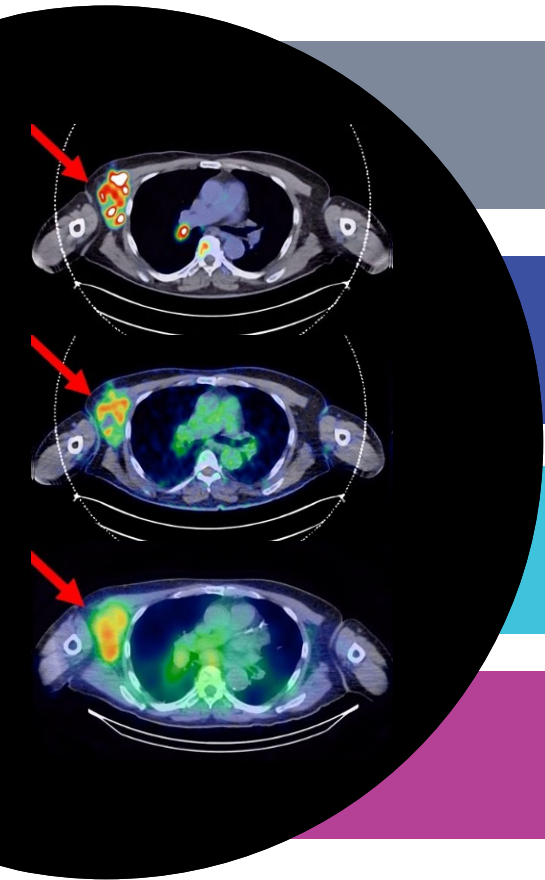
Primary Objective:	To determine the MTD/MFD of [²¹² Pb]VMT-α-NET (RP2D)	Imaging:	FDA approved SSTR2 PET/CT
Population:	Unresectable or metastatic SSTR2-positive NETs PRRT naïve (“First line”)	Therapeutic Dose:	2.5–10 mCi dose escalation with fixed dosing every 8 weeks for up to 4 cycles
Design Methodology: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



Melanoma Program: VMT01/02

Using the melanocortin receptor MC1R to target melanoma for imaging and therapy

VMT01 Development Status



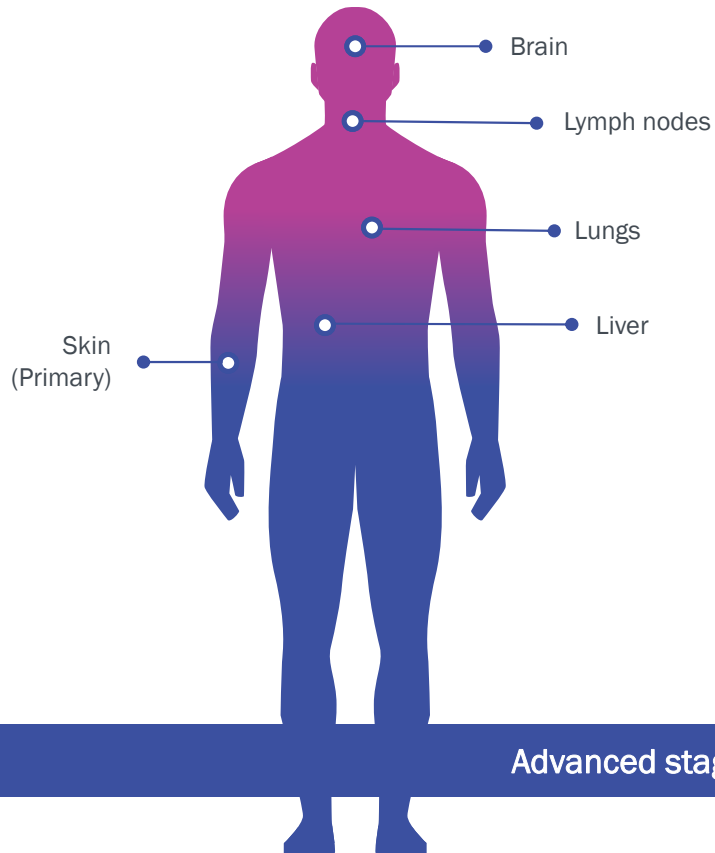
Targeting melanocortin 1 receptor (MC1R) which is over-expressed in melanoma

US Therapeutic Dose Escalation Trial recruiting currently throughout the US
Expected to Receive Orphan Drug Designation and Fast Track Application

Preclinical data shows synergistic effect with Immune Checkpoint Inhibitors
Planning underway for VMT01/ICI combination in second line setting

Phase 1 imaging study at Mayo Clinic Rochester indicates feasibility of patient selection using [^{203}Pb]VMT01 and [^{68}Ga]VMT02

Metastatic Melanoma



[²¹²Pb]VMT01 target indication:

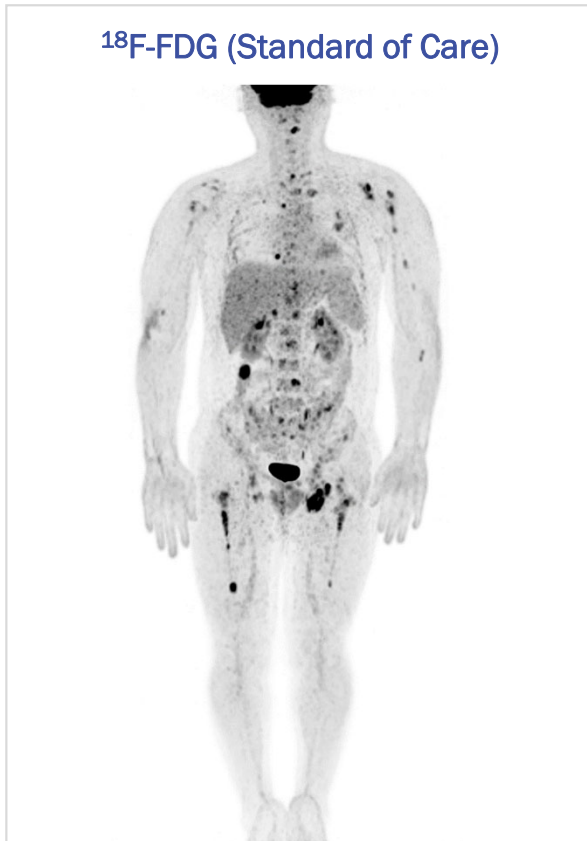
MC1R-positive melanoma

- Projected market opportunity for melanoma of \$8 billion+ in 2028¹
- Significant unmet need in the U.S.:
 - ~100K new diagnoses annually²
 - ~8,000 people die from melanoma every year²
- Treatment depends on the stage of tumor
- Approaches may include surgery, radiation, chemotherapy and immunotherapy
- 5-year survival rate for metastatic melanoma is only 22.5%³

Advanced stages of disease occurs throughout the body requiring aggressive systemic treatment

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

Diagnostic Peptide Demonstrates Similar Uptake to FDG in Tumors



Patient information:

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

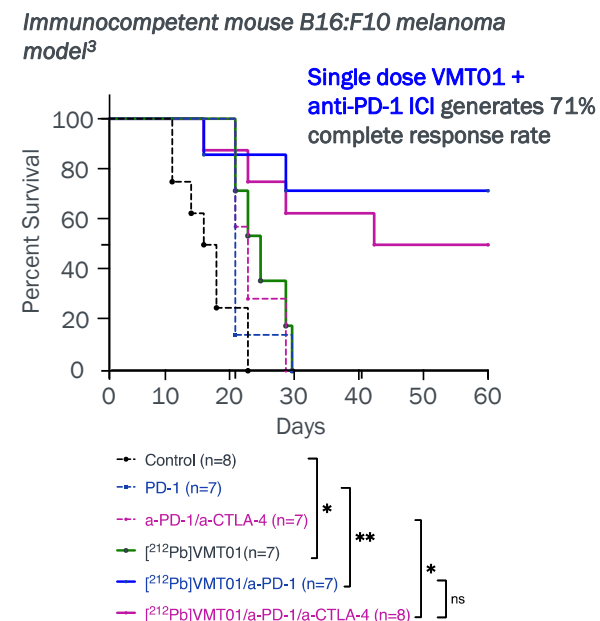
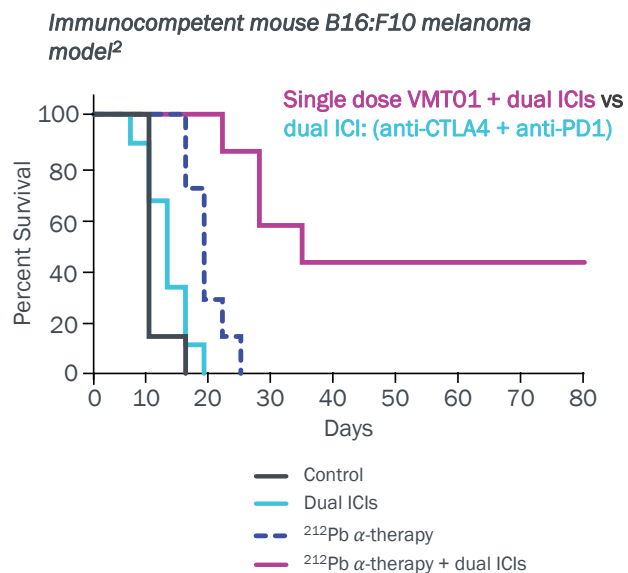
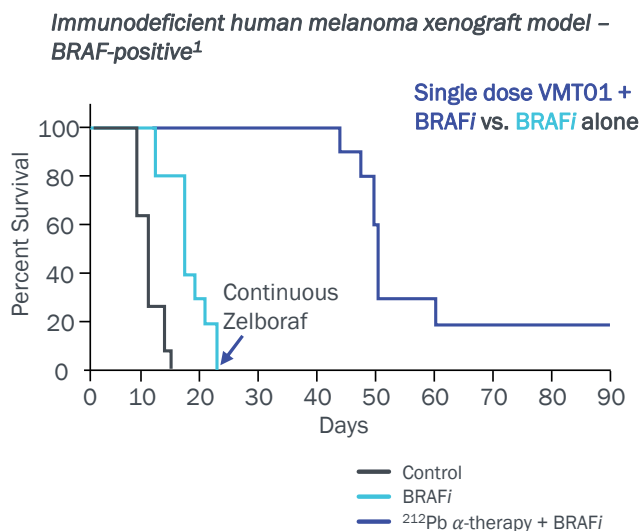
Clinical Collaborator:

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



[²¹²Pb]VMT01 in Combination: Synergistic Responses in Preclinical Studies

Single dose of VMT01 in combination significantly arrested melanoma tumor growth and extended survival



Key Takeaways

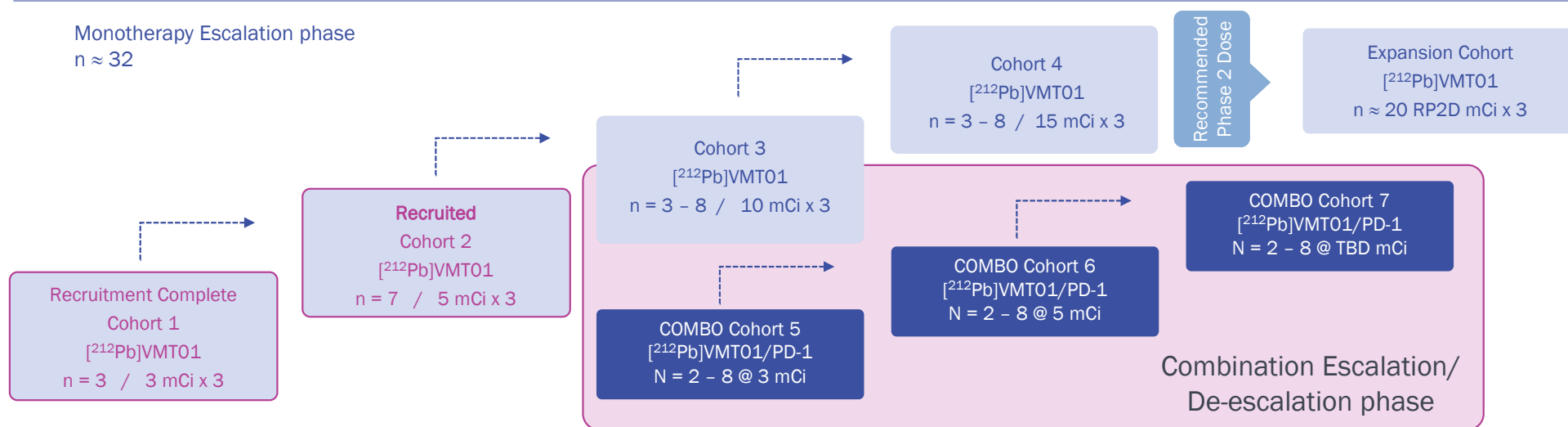
- High response rates in multiple tested models
- >70% complete and durable response if combined with PD1 immunotherapy in a model highly resistant to checkpoint inhibitors³
- Combination with immune checkpoint inhibitors induced synergistic anti-tumor effect

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

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

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

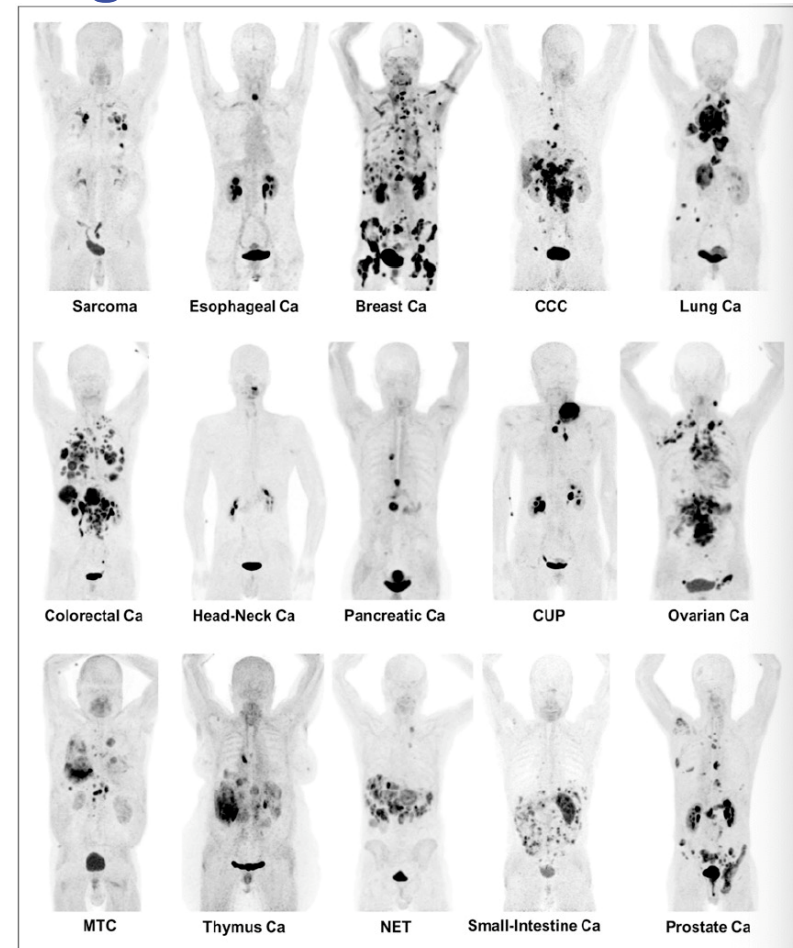
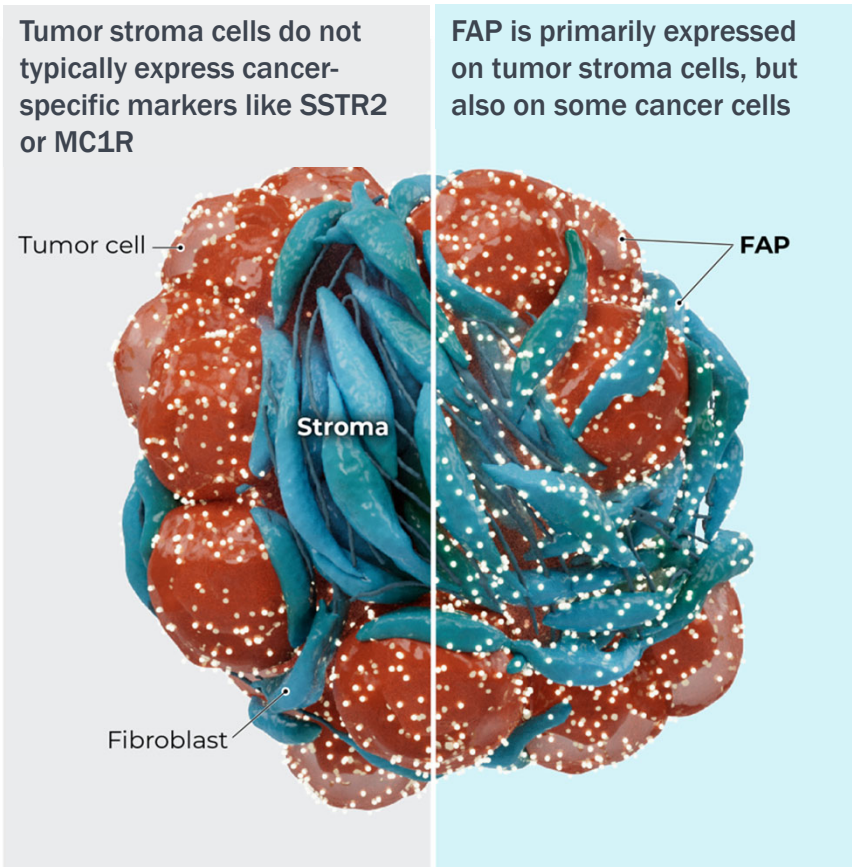
Primary Objective:	To determine the MTD/MFD of [²¹² Pb]VMT01 (RP2D) in combination with PD-1 inhibitor (nivolumab)	Imaging:	[²⁰³ Pb]VMT01 SPEC/CT
Population:	Enroll ~52 subjects Unresectable or metastatic MC1R-positive melanoma After 1L SOC	Therapeutic Dose:	3 – 15 mCi dose escalation of [²¹² Pb]VMT01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



Pan Cancer Target: PSV359

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

Fibroblast Activation Protein α is a Pan Cancer Target

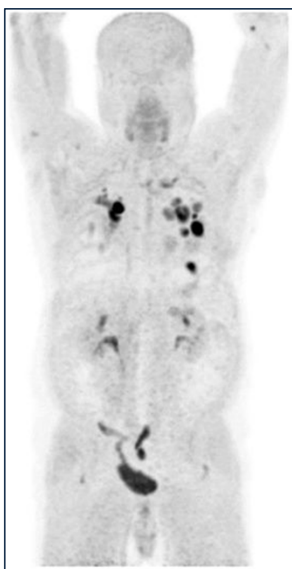


Kratochwil et al., JNM, 2019

Fibroblast Activation Protein α is a Pan Cancer Target¹

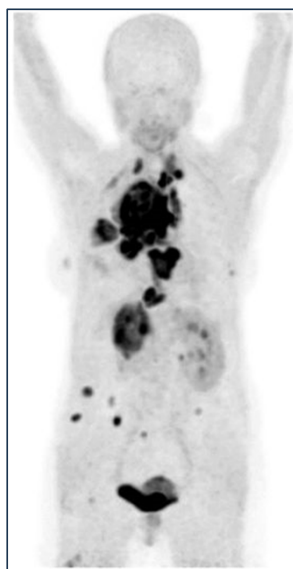
Multiple imaging products in development such as ⁶⁸Ga-FAPi, but significant therapeutic opportunity remains

Expression of FAP- α on Tumor Cells



Sarcoma

Expression of FAP- α on Tumor Stroma Cells

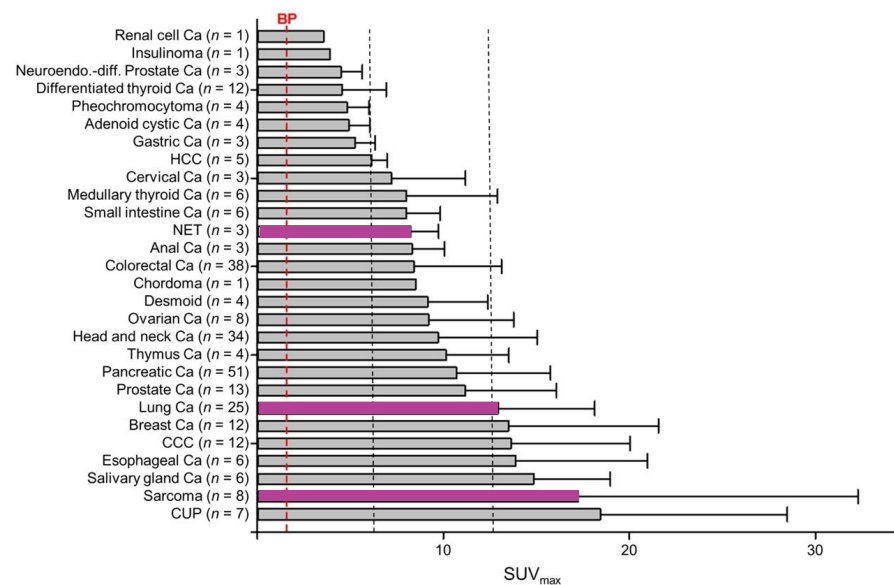


Lung Cancer



NETs

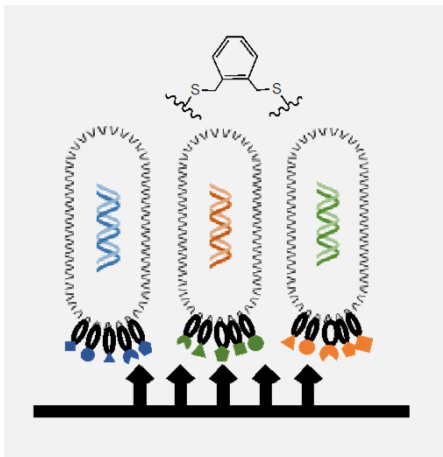
Average SUV_{max} of ⁶⁸Ga-FAPi PET/CT Across 28 Different Cancer Types



Fibroblast Activation Protein α -targeted Novel Compound Development

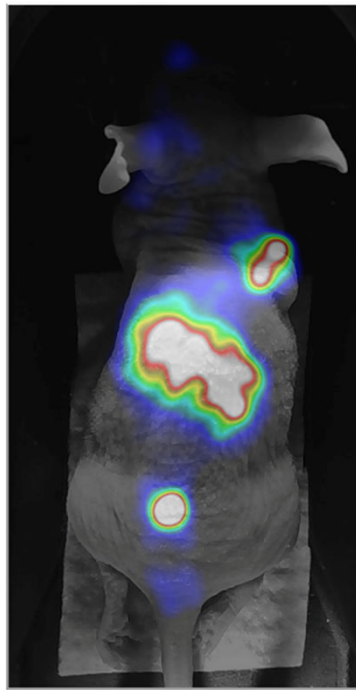
In-house peptide synthesis and in vivo capability allows rapid iteration and optimization of novel compounds

Phage display screening

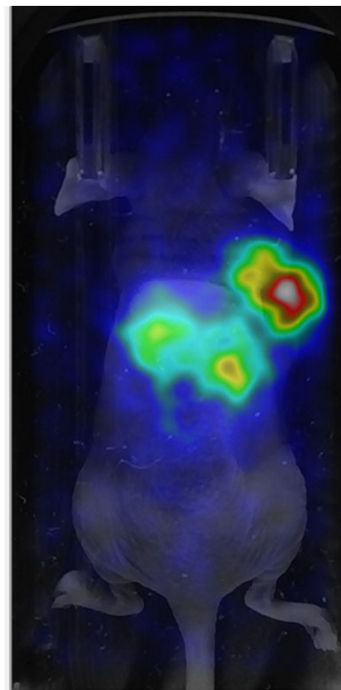


- Phage display followed by affinity maturation
- Bioconjugate chemistry and further optimization
- In vitro and in vivo binding assays identified lead candidates¹

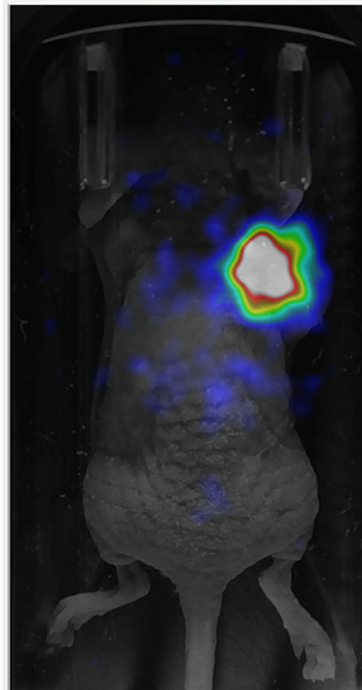
Compound 3-30



Compound 3-42



Compound 3-59

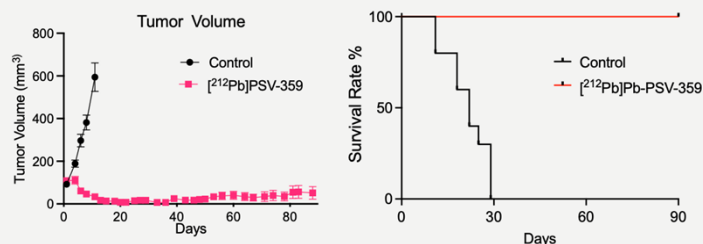
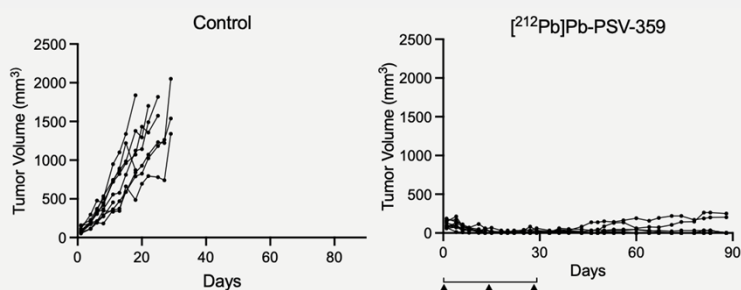


[²¹²Pb]PSV359 Demonstrates Preclinical Efficacy in Human Fibrosarcoma Model

Compares favorably against other therapeutic products in development²

Preclinical [²¹²Pb]PSV359 Targeted Alpha Therapy¹

hFAP-HT1080 Fibrosarcoma Model – Expressing hFAP-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



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

Dirk Zboralski¹ · Aileen Hoehne¹ · Anne Bredenbeck¹ · Anne Schumann¹ · Minh Nguyen² · Eberhard Schneider¹

Summary Table

Treatment	MTV, Day 0 (mm ³ , mean ± SD)	MTV, Day 9 (mm ³ , mean ± SEM)	MTV, Day 23 (mm ³ , 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 ¹⁷⁷Lu-FAP-2286 and ¹⁷⁷Lu-FAPI-46

40-day results

Comparison against other FAP-targeted therapies in development indicates promise of [²¹²Pb]PSV359 in preclinical setting

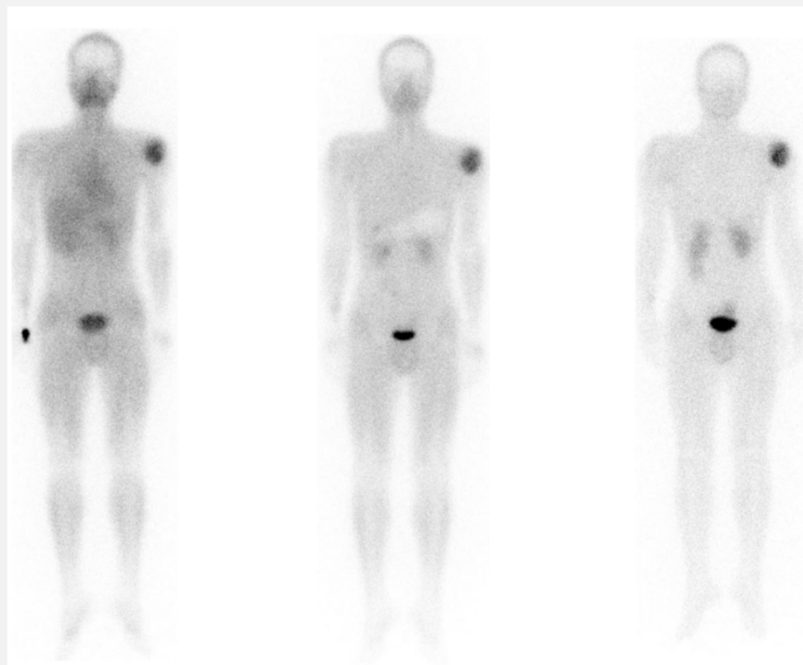
FIH Imaging of [²⁰³Pb]PSV359 in Different Types of Cancers

Patient 1 Chondroblastic Osteosarcoma



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

[²⁰³Pb]PSV359

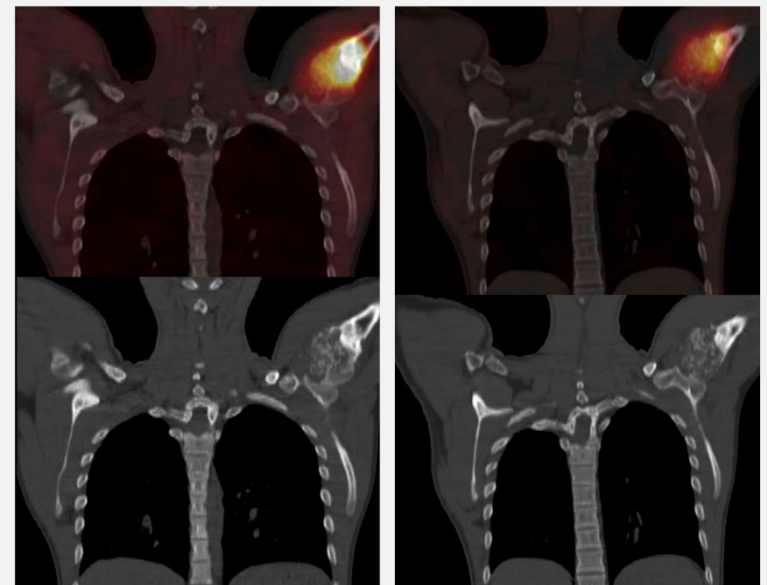


1 hr

4 hr

18 hr

[²⁰³Pb]PSV359 SPECT/CT



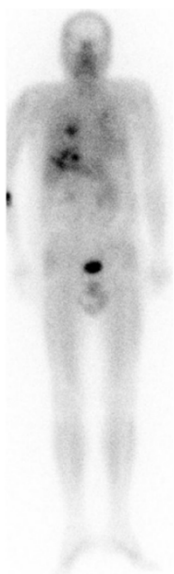
4 hr

18 hr

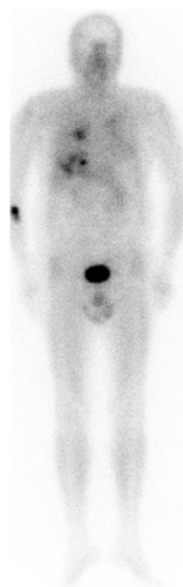
Lesion in head of left humerus

Patient 2 Neuroendocrine Tumor

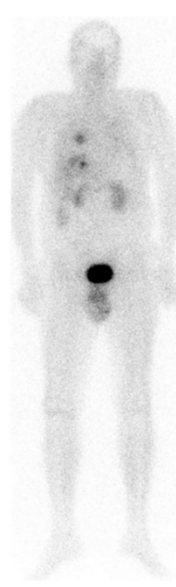
[²⁰³Pb]PSV359



1 hr



4 hr



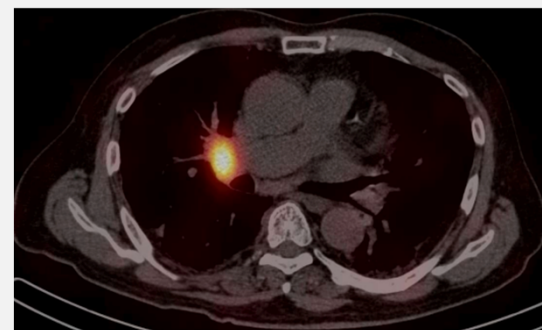
18 hr

[²⁰³Pb]PSV359 SPECT/CT

4 hr



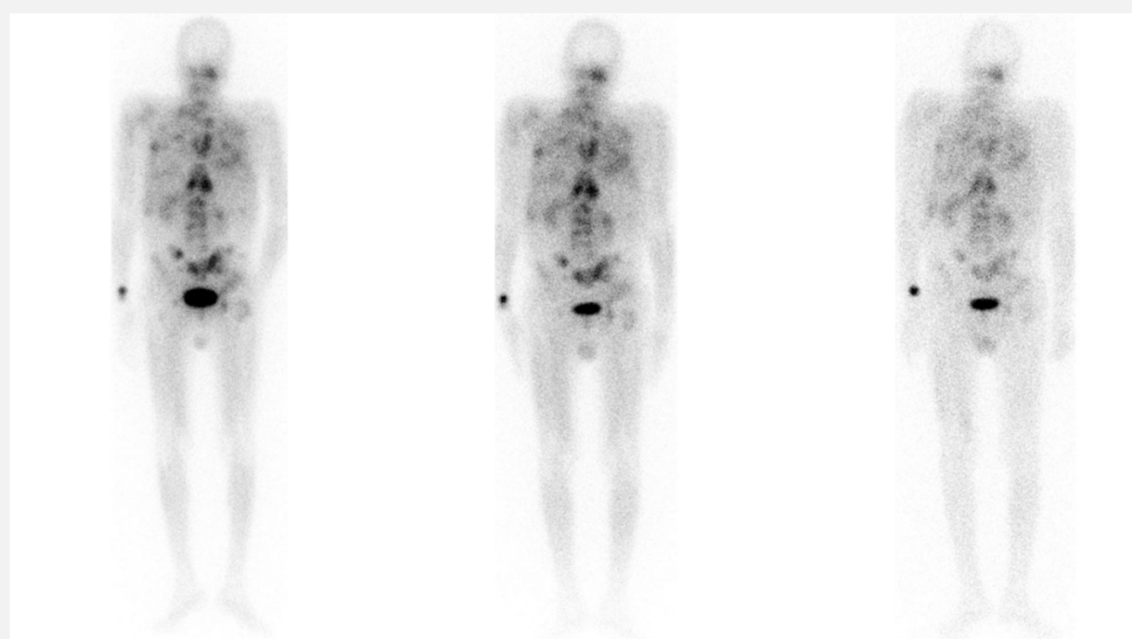
18 hr



Lesion in head of left humerus

Patient 3 Lung Adenocarcinoma

[²⁰³Pb]PSV359



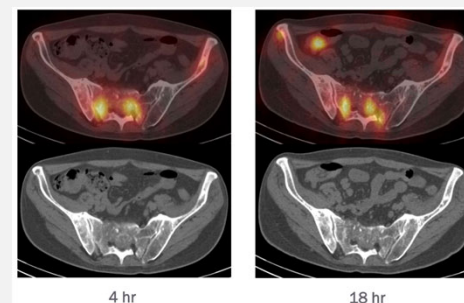
1 hr

4 hr

18 hr

[²⁰³Pb]PSV359 SPECT/CT

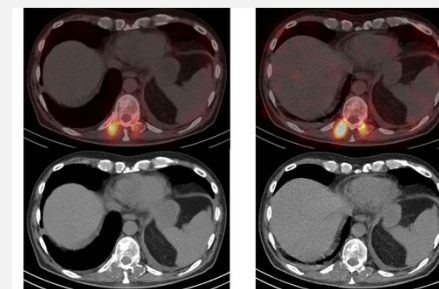
Lytic lesion in sacrum



4 hr

18 hr

Lytic lesion in thoracic vertebra

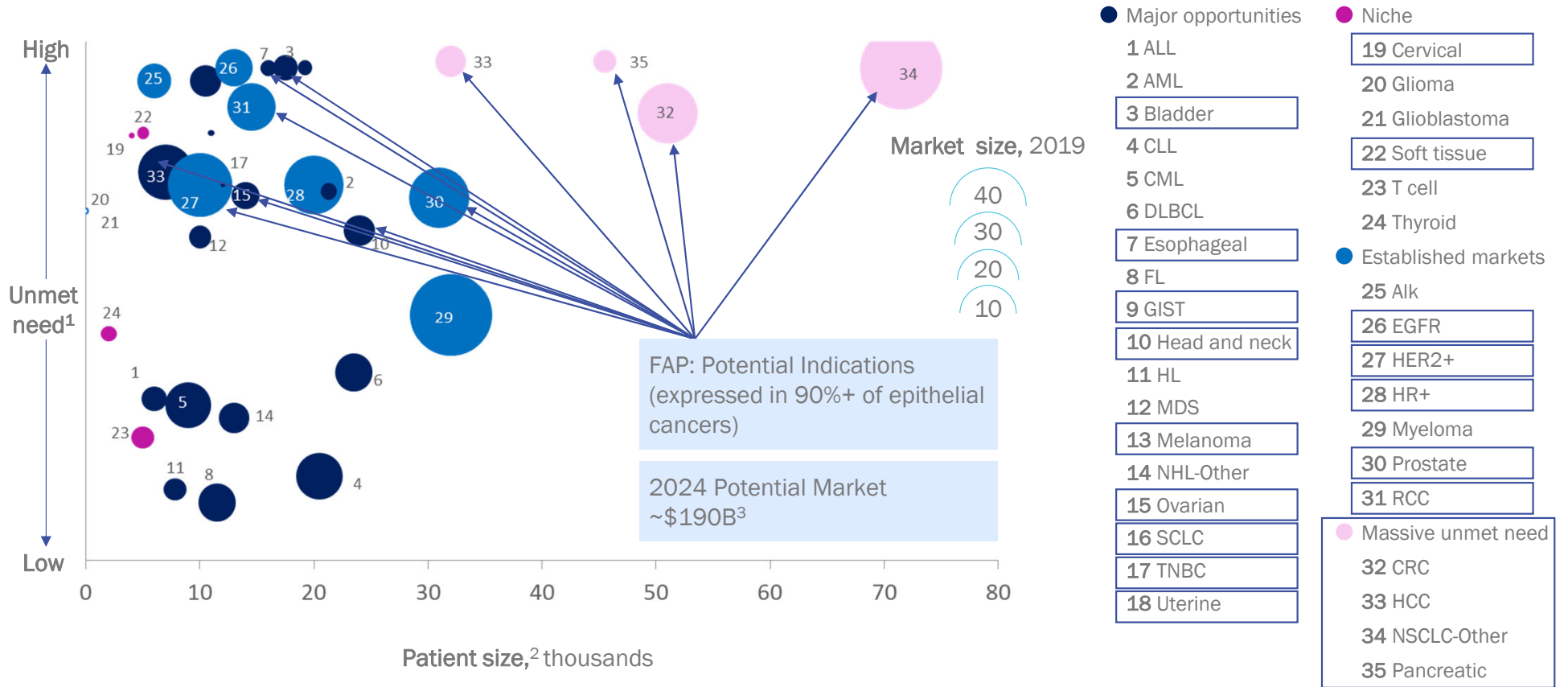


4 hr

18 hr

Fibroblast Activated Protein α is a Pan Cancer Target with Significant Market Potential

Tumor types with large patient populations and high unmet need



¹Unmet need defined as one minus five-year survival rate (overall for heme, metastatic for solid).

²Patient size calculated as annual incidence for heme, and larger of mortality and metastatic incidence for solid.

³Modified from EvaluatePharma® July 2020, Evaluate Ltd.; Surveillance, Epidemiology, and End Results (SEER) Program

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 in 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

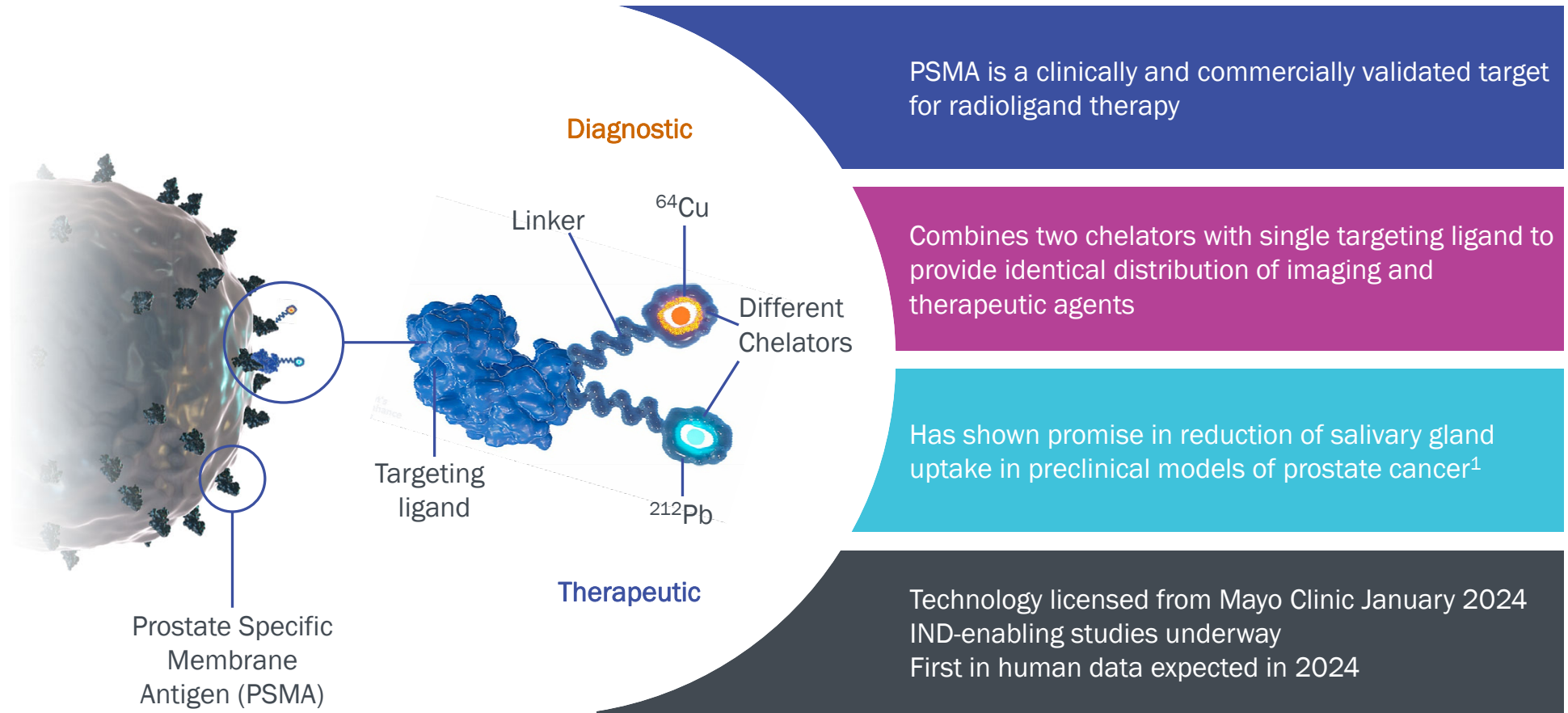


Prostate Cancer Program: PSV401

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

Prostate Cancer Program: PSV40X

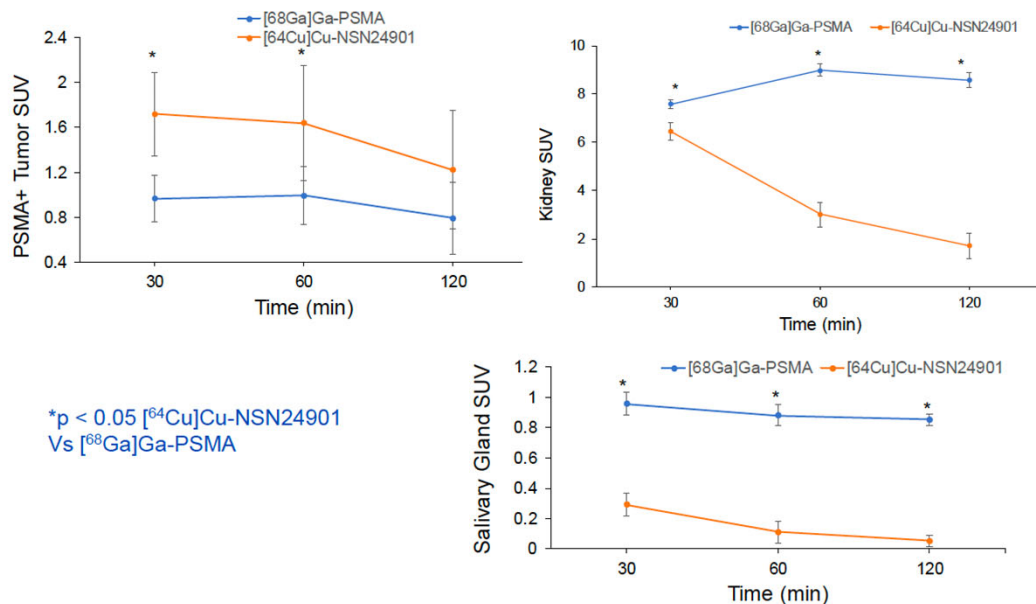
A differentiated PSMA-targeted radiohybrid molecule for dual PET imaging and targeted alpha therapy



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 [⁶⁸Ga]PSMA-11 and [⁶⁴Cu]PSV404 (“NSN24901”) in Tumor, Kidney and Salivary Gland of LNCaP Tumor Athymic Nude Mice



*p < 0.05 [⁶⁴Cu]Cu-NSN24901 Vs [⁶⁸Ga]Ga-PSMA

- 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

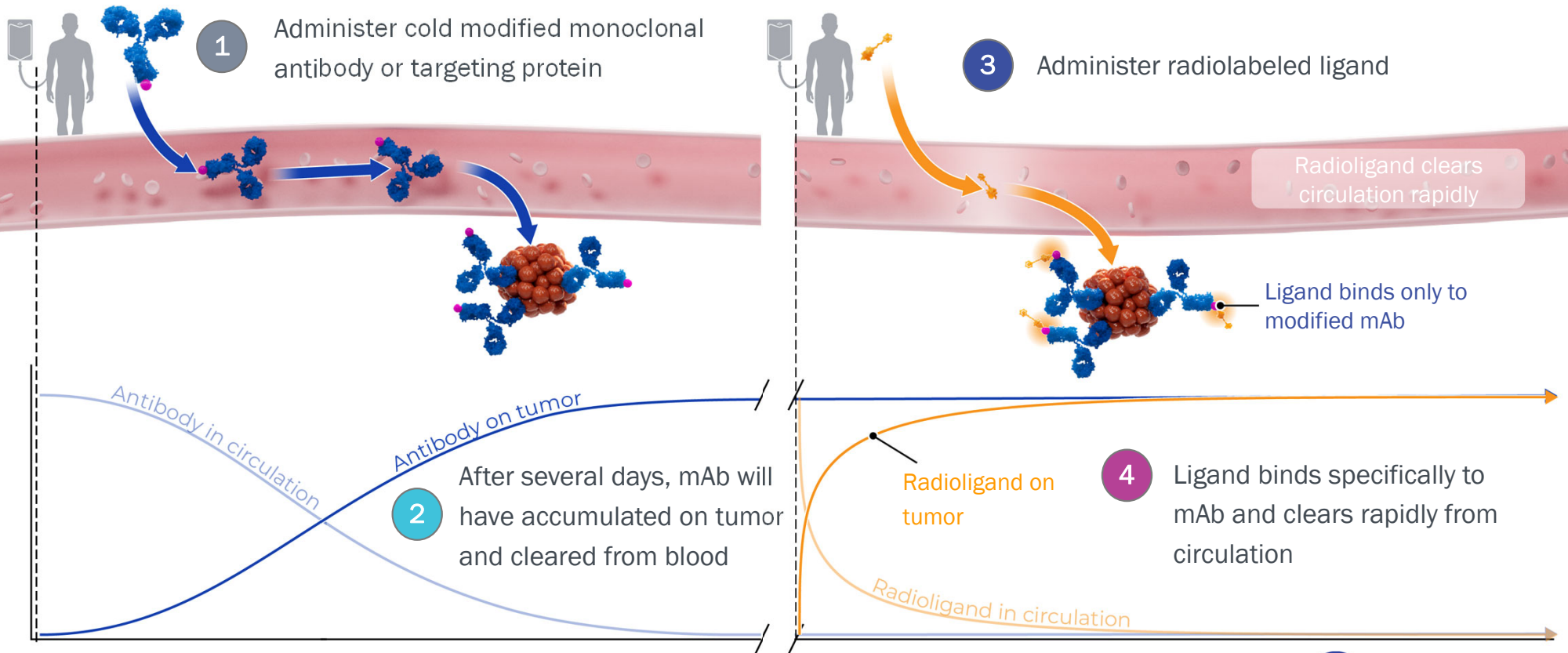
©2012 MFMR | slide-16

Pre-Targeting Platform

The Next Generation of Targeted Alpha Particle
Radiopharmaceuticals

Pre-Targeting Platform Background

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






Manufacturing, Production and Logistics of ^{212}Pb -labeled Therapeutics

The Path to Commercial Supply

^{212}Pb is Plentiful, Storable, Scalable & Suitable for Distributed Logistics

The supply chain is lower-risk and more robust than other therapeutic isotopes

Isotope Source	Isotope Purification	Product Manufacturing
 <p>Naturally occurring in mining waste Also produced in industrial nuclear processes Can be made on demand if needed</p>	 <p>Parent isotope Thorium-228 can be stored (2 yr half-life) ^{212}Pb purified from ^{228}Th or ^{224}Ra source in simple separation step</p>	 <p>VMT-α-GEN ^{212}Pb generator technology scales for commercial production Extremely pure isotope allows straight forward manufacturing process</p>
<p>All other therapeutic isotopes require capital-intensive infrastructure manufacturing processes (irradiation)</p>	<p>VMT-α-GEN enables shipping of isotope and purification of ^{212}Pb in one package</p>	<p>10.5 hr half life of ^{212}Pb allows for robust regional distribution of finished radiopharmaceuticals</p>

Isotope Decay Chain Dictates Supply, Purification, Manufacturing & Logistics

Naturally Occurring Isotope Decay – No Irradiation Processes Required



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



- Multiple global suppliers including natural decay
- 2 year half-life allows stockpiling



Chemical Separation:
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
- Leverages existing networks for logistics



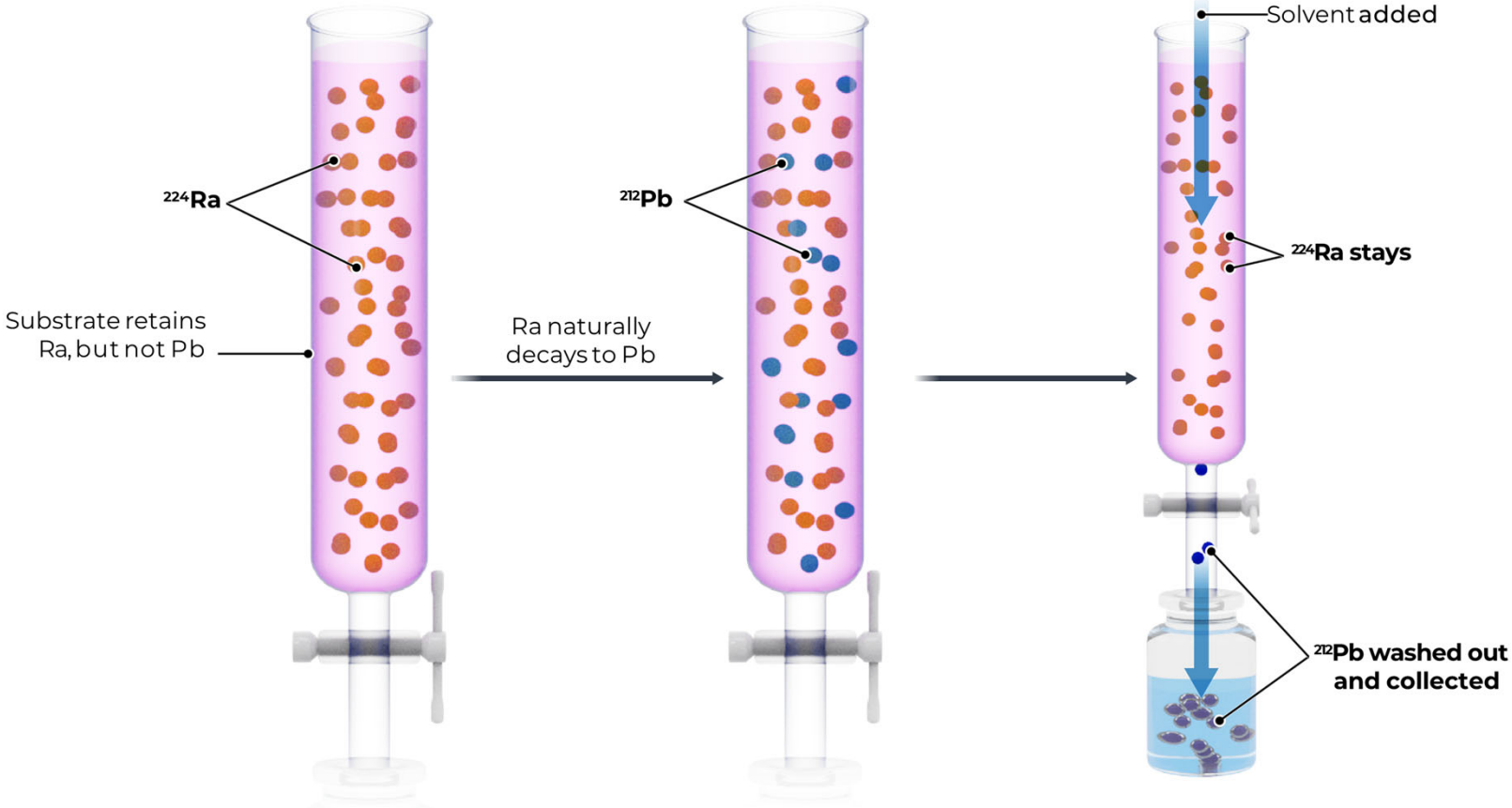
High dose-rate alpha-emitting
therapeutic isotope



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

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

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



^{212}Pb Supply via Reusable Desktop Isotope Generator



VMT- α -GEN

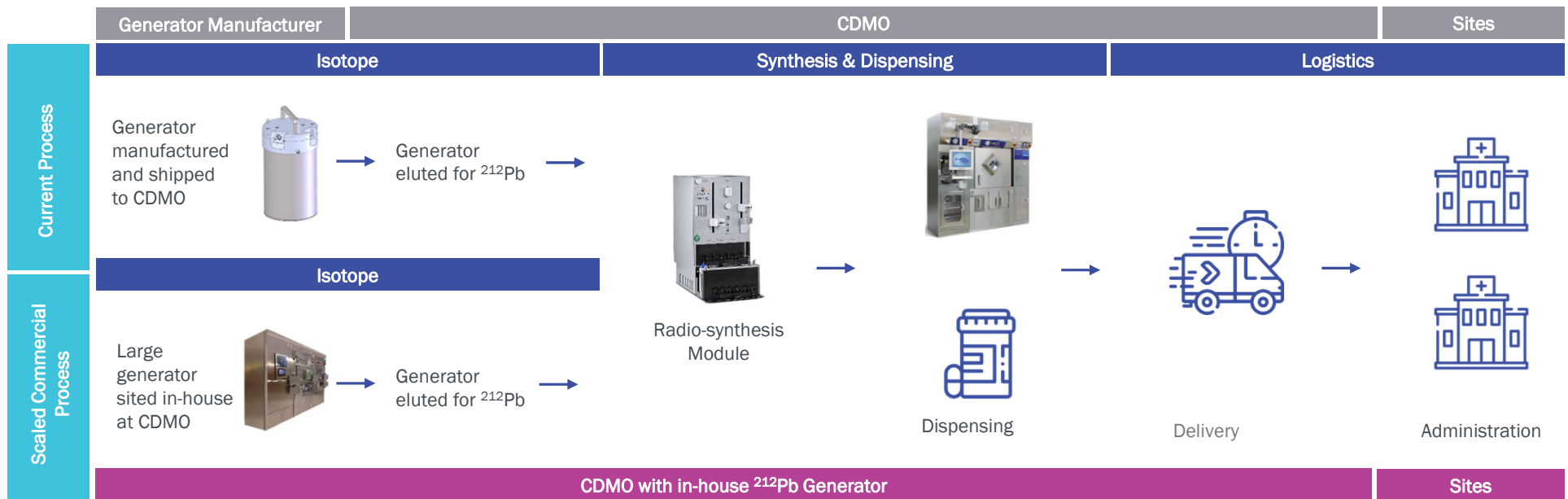
- Extensive feedstock from nuclear and mining waste material
- Long-term supply contract secured with US DOE
- On demand daily doses
 - Auto-regenerates overnight
 - ~1 week shelf life

Small, Elegant ^{212}Pb Isotope Generator

- Integrated lead shielded containment
- Simple inlet and outlet ports
- Radioactive feedstock for nearly 300 generators fits in a small vial

Scalable Manufacturing and Distribution Logistics

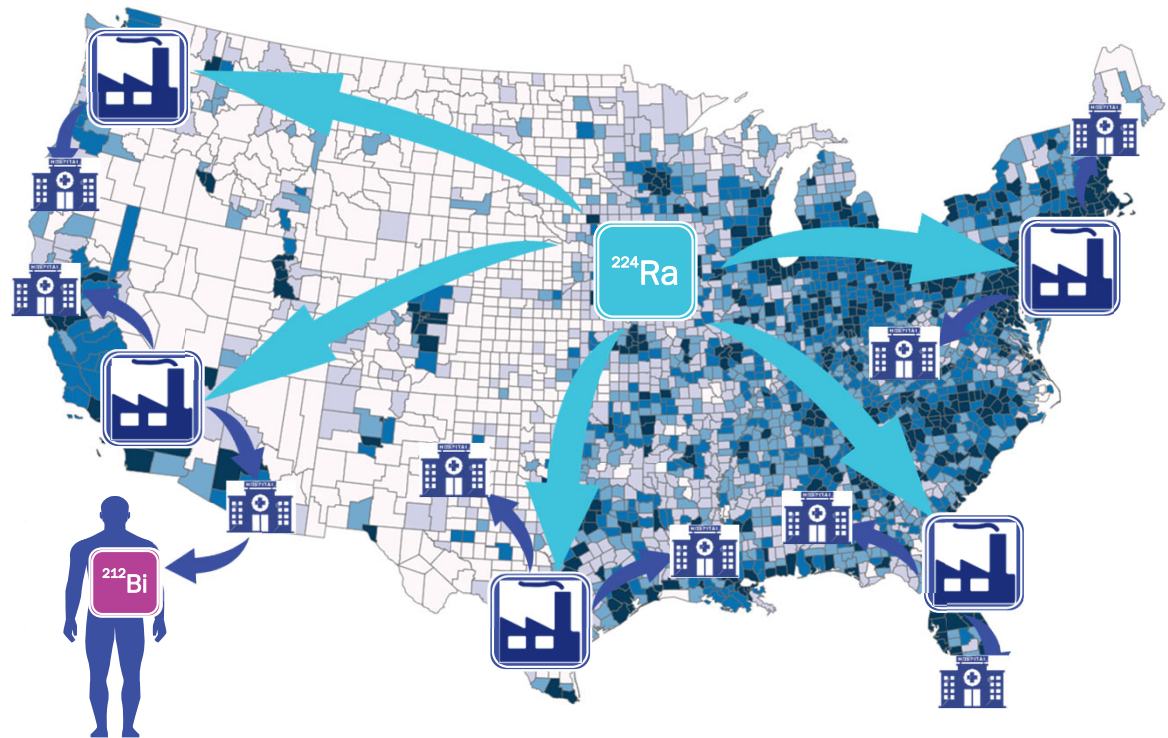
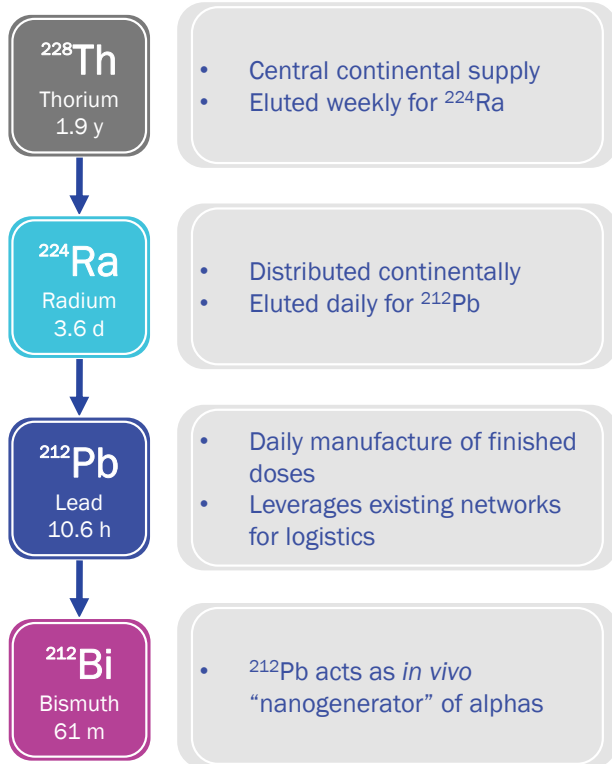
Perspective's plan to flexibly scale manufacturing to commercial levels (100,000+ doses per year)



- Commercial supply will require the use of an isotope production system of larger scale than the current $^{224}\text{Ra}/^{212}\text{Pb}$ generators
- The current isotope separation process remains highly scalable with larger activity levels
- Regional CDMOs will have capabilities to expand capacity as needed as more ^{212}Pb products come on-line

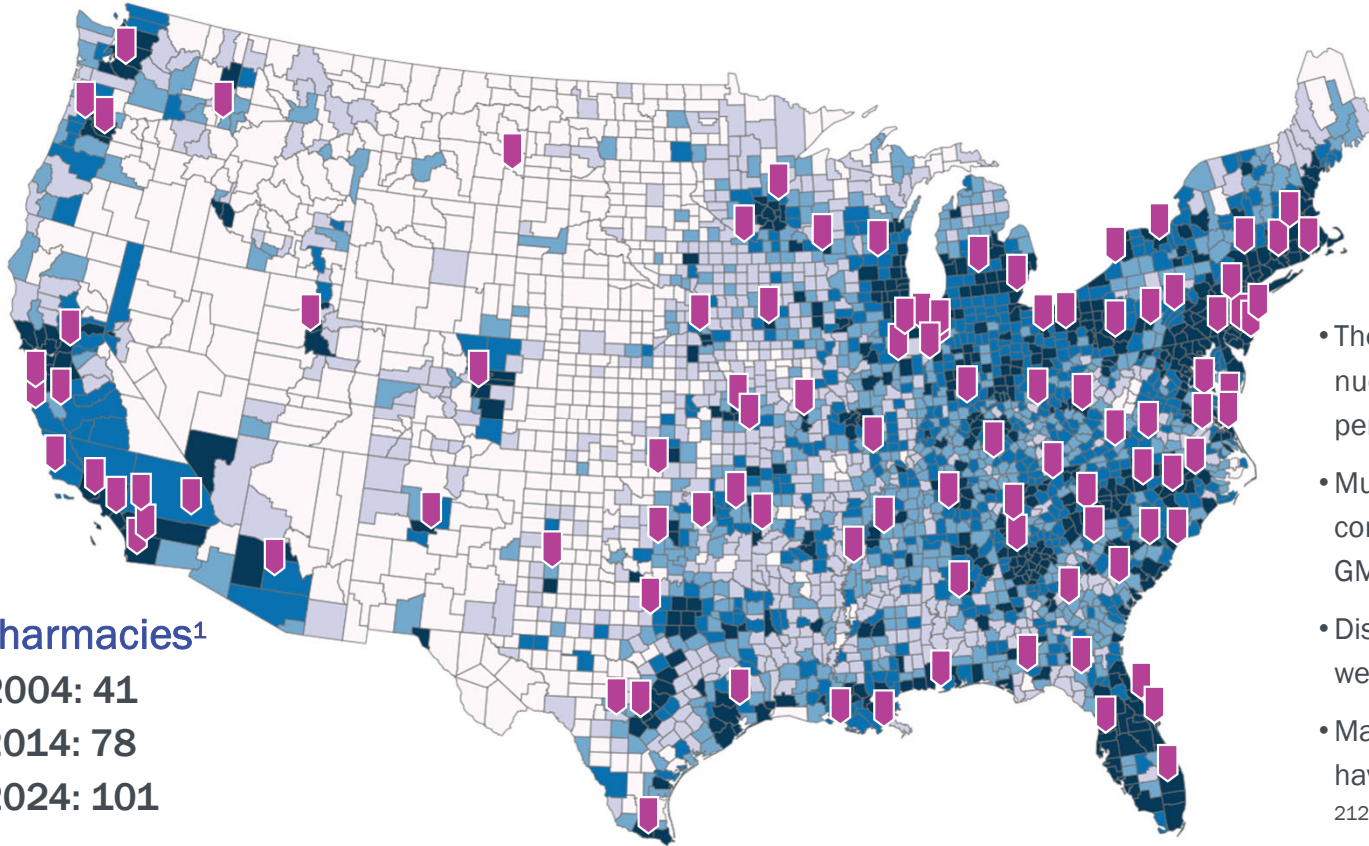
Isotope Decay Chain Dictates Supply, Purification, Manufacturing & Logistics

Naturally Occurring Isotope Decay – No Irradiation Processes Required



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 Pharmacies¹

2004: 41

2014: 78

2024: 101

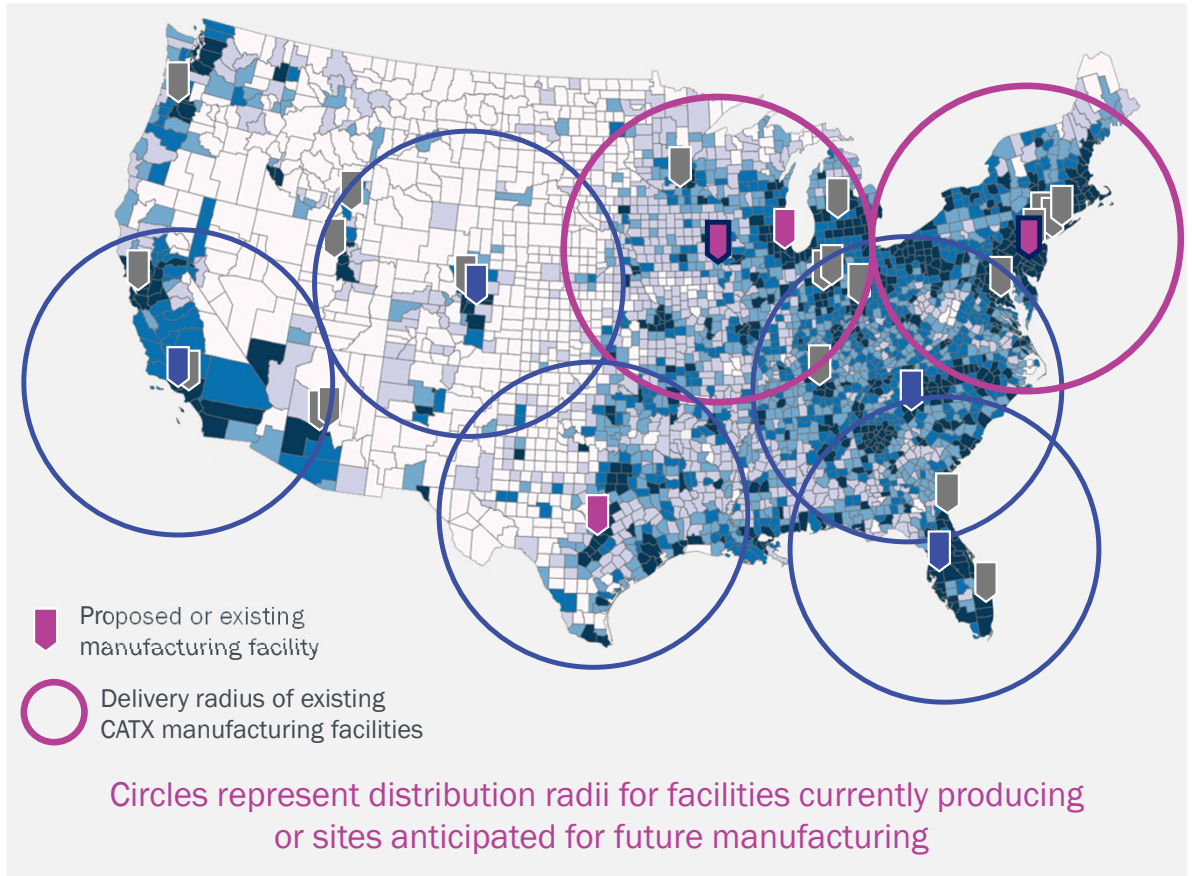
- There were 40+ million diagnostic nuclear medicine procedures performed in the US in 2022
- Multiple networks exist in a competitive environment of 100+ GMP PET radiopharmacies
- Distribution logistics are mature and well-developed
- Many of these diagnostic products have much shorter half-lives than ²¹²Pb

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 radius¹
- Products can also be driven further or flown as necessary



Strong Intellectual Property Portfolio

Perspective-owned/Exclusively-licensed IP

2 Issued Patents (Expiry in 2037, with potential PTE)

Composition of matter and method of use on melanoma targeting peptides with Pb-specific chelator

1 Allowed AU Patent Application (Expiry in 2037)

Composition of matter and method of use on melanoma targeting peptides with Pb-specific chelator

28 pending patent applications (including 5 PCT and 1 provisional)

Composition of matter and method of use on:

- Radiometal separation technology
- Chelators
- SSTR2, MC1R, FAP, and PSMA targeting radiopharmaceuticals
- Pre-targeting technology platform



IP Portfolio covers all aspects of radiopharmaceutical value chain



Potential for Orphan Drug Designation



Potential for U.S. FDA Priority Review Voucher: VMT- α -NET is a candidate for pediatric neuroblastoma indication

Appendix

The image features a white background with a large, abstract graphic on the right side. This graphic consists of several overlapping shapes: a large grey semi-circle at the top right, a white semi-circle below it, a teal semi-circle below that, and a dark blue semi-circle at the bottom right. A solid dark blue horizontal bar spans the width of the page, starting from the left edge and ending at the dark blue semi-circle of the graphic. The word "Appendix" is written in white, bold, sans-serif font on the left side of this bar.



Our Mission

Targeting cancer from the inside out

We are developing game-changing *Precision Medicine Therapeutics* which harness the power of targeted *Alpha-Particle Radiotherapies* that make an impactful difference for cancer patients and the clinicians who treat them.

Who We Are

Perspective Therapeutics (NYSE:CATX) is a clinical stage **precision medicine company**, debuting as a public company in 2023.

With a broad pipeline and **two prioritized lead programs** in clinic, we are disrupting traditional radiation therapy treatment for cancer through developing a new class of **image guided alpha-particle radiotherapies** treatments for the most challenging cancers. With an initial focus on **neuroendocrine tumors (NETs)** and **metastatic melanoma**, we have a robust discovery platform to advance our pipeline into the clinic further.

Perspective's **personalized theranostic approach** arms physicians with companion imaging diagnostics, capturing personalized information about a patient's cancer in the process which can then be used to guide precise radiation therapy, killing cancers from the inside out.

Perspective's core technology hinges on **alpha (α) particle radiation** which deliver large amounts of radioactive energy very specifically to tumors, irreparably damaging DNA and reliably killing the targeted tumor cells.

We believe the use of alpha-particles provides numerous benefits over currently used beta-particle radiotherapies. Alpha-particles generate **more energy** and travel a shorter distance compared to beta-particles, making them **more cytotoxic**, while reducing their effects on healthy tissue.

α -Particles Have Superior Tumor Killing Properties vs. β -Particles

More Powerful Effects Than Approved β Therapy

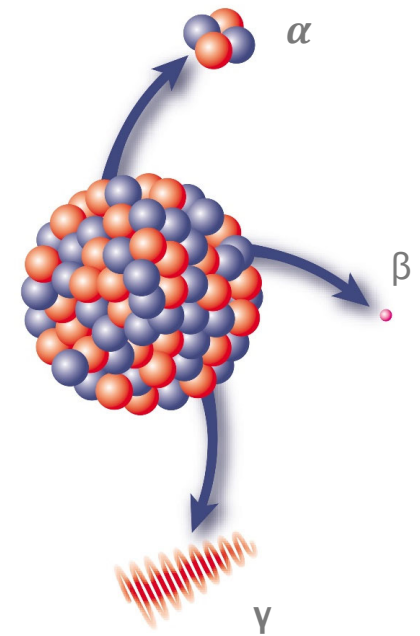
Higher atomic mass
Lethal double-stranded DNA breaks
DNA repair mechanisms overwhelmed

Precision Delivery Provides Targeted Cell Destruction

Deposit energy over 3-5 cell diameters vs. beta particles (up to 200 cells)

Anti-Tumor Immune Response¹

Evidence for antitumor response alone or in combination with immunotherapies
Consistent with “Abscopal effect” observed with external beam radiation therapy



α -particles are >7,000-fold greater in atomic mass

Lead-212 (^{212}Pb): The Optimal Therapeutic Isotope

Greater Therapeutic Energy Expected to Improve Outcome with Better Safety Profile

Alpha particle range (up to 3 cell diameters)

Beta range (up to 200 cell diameters)



The destructive energy of an alpha particle is deposited within several cell diameters.
A beta particle spreads its lower energy over a longer range

Lead (Pb): The Ideal Theranostic Isotope

Ideal Theranostic Requirements

Solutions: ²⁰³Pb and ²¹²Pb & Perspective Chelator

Ideal agreement between imaging and therapeutic compounds

²⁰³Pb and ²¹²Pb matched pair

Readily available isotope

Generator produced

Ideal chelator

Proprietary chelator carries 0 net charge

Rapid clearance from blood

Conjugation to small peptides

High tumor retention @24 hours

High and sustained binding

Short t-¹/₂ gives rapid effect while minimizing environmental impact

Low hospital and patient impact for radiation safety

No unsafe daughter isotopes

Decays to cold Pb

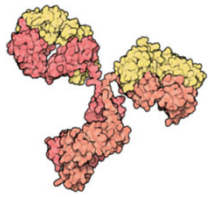
Peptides are Ideal Ligands for Radiopharmaceutical Therapy

Monoclonal antibodies

Kinetics		Production	
Tumor penetration:	Low	Manufacturing:	Complex biological
Clearance:	Hepatobiliary (liver)	CoGs:	High
Biological $\frac{1}{2}$ Life	Long		
Target affinity	High		
Accumulation time:	Extended		
Stability	Questionable		

Peptides

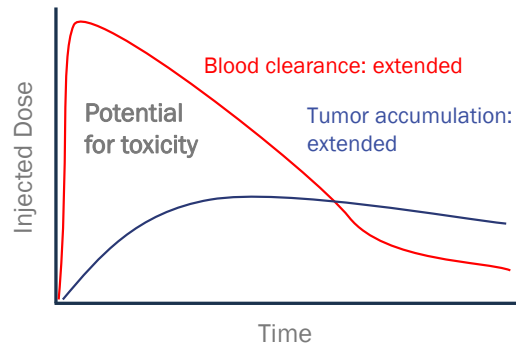
Kinetics		Production	
Tumor penetration:	High	Manufacturing:	Synthetic
Clearance:	Renal (kidneys)	CoGs:	Very low
Biological $\frac{1}{2}$ Life	Short		
Target affinity	High		
Accumulation time:	Rapid		
Stability	Excellent		



←→ 10 nanometers

mAb Size: 150 kDa

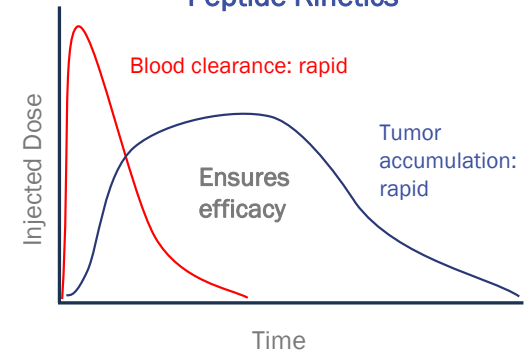
mAb Kinetics



←→ 10 nanometers

Peptide Size: 1.5 kDa

Peptide Kinetics



VMT- α -NET is Developed to Address the Unmet Need in NETs

Current Standard of Care limited to subset of NETs patients

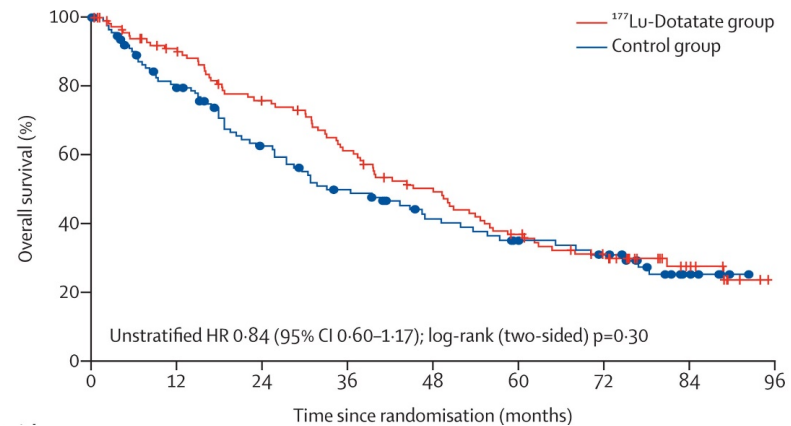
Significant unmet need:

- ~12K new diagnoses annually in the US¹
- ~175,000+ people are living with this diagnosis in the US¹

Market Opportunity

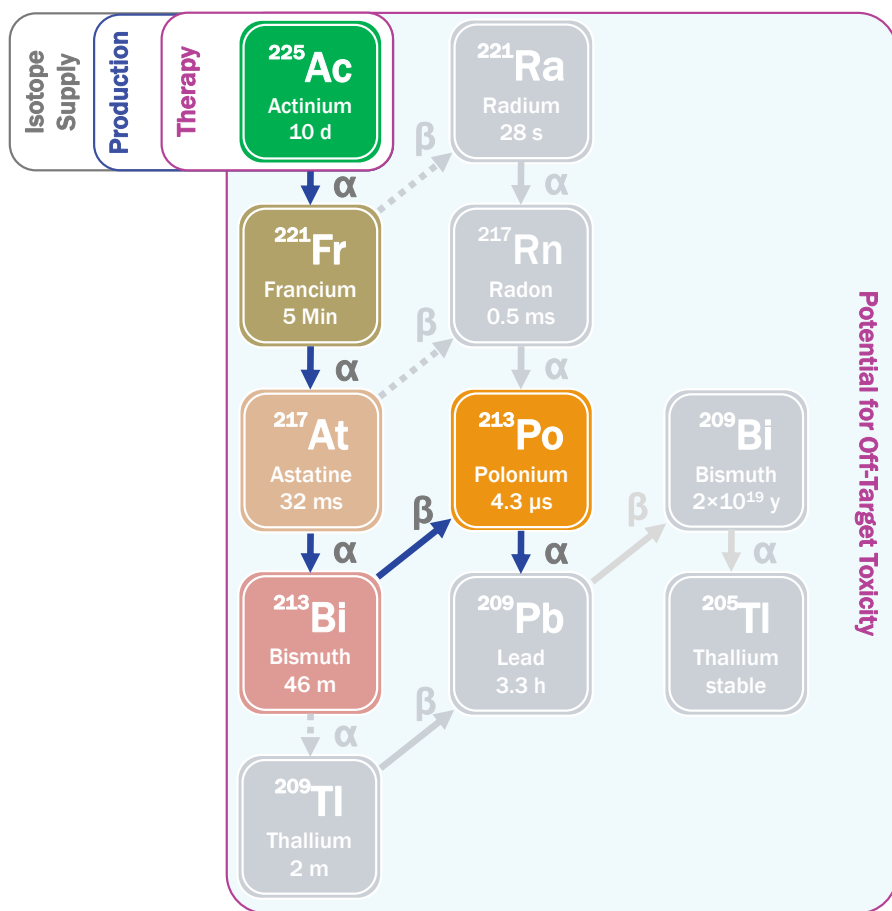
- Projected to be \$2.9 billion+ in 2029²
- Existing radiopharmaceutical treatment LUTATHERA® (Novartis) has an overall response rate (ORR) of **only 13–17%**, and **no overall survival (OS) benefit**³

NETTER-1 Study: Final overall survival⁴

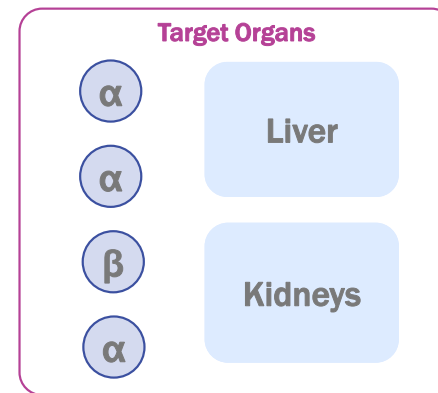
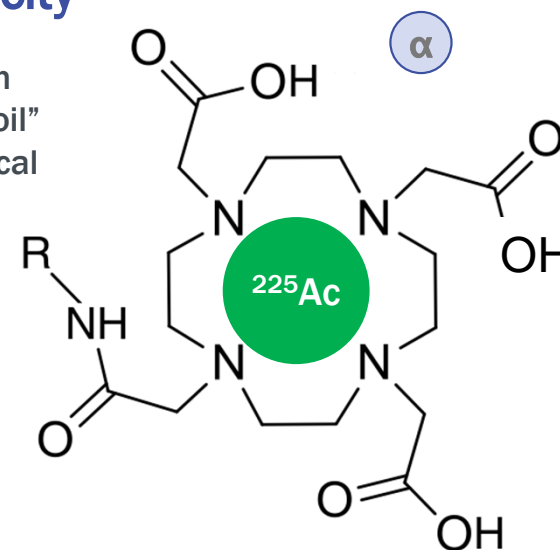
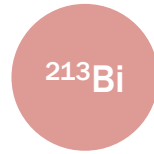


- Treatment depends on the type of tumor. Some approaches may include surgery, radiation, and chemotherapy
- Broad acknowledgment that targeted alpha therapies are needed to improve care⁵

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

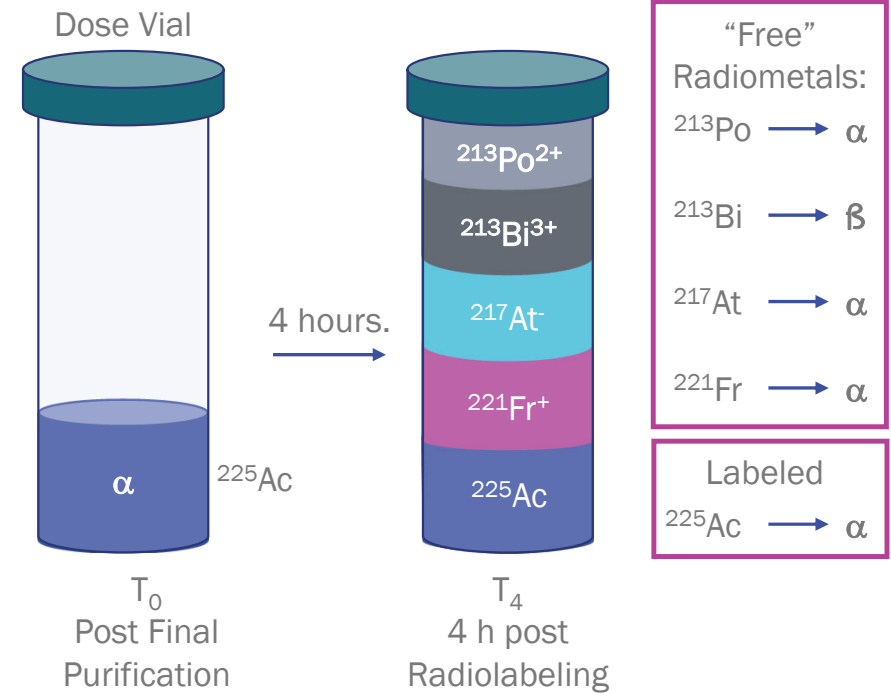
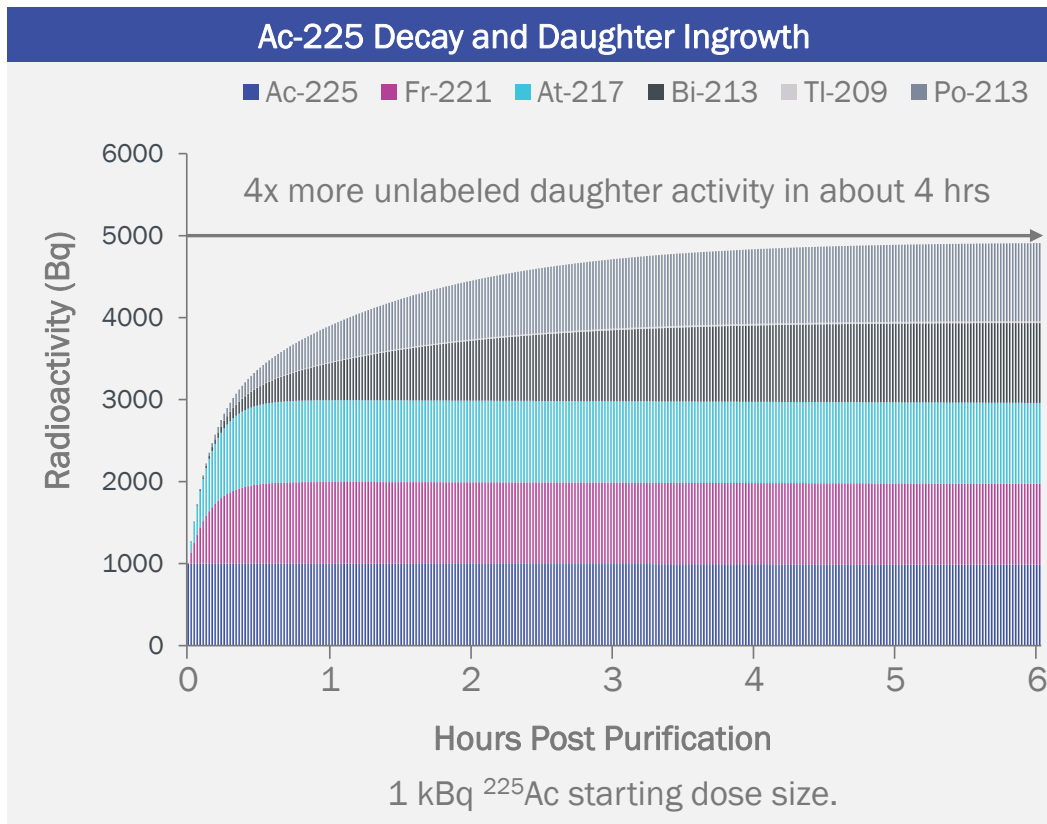


Alpha-particle emission imparts sufficient "recoil" energy to break chemical bonds

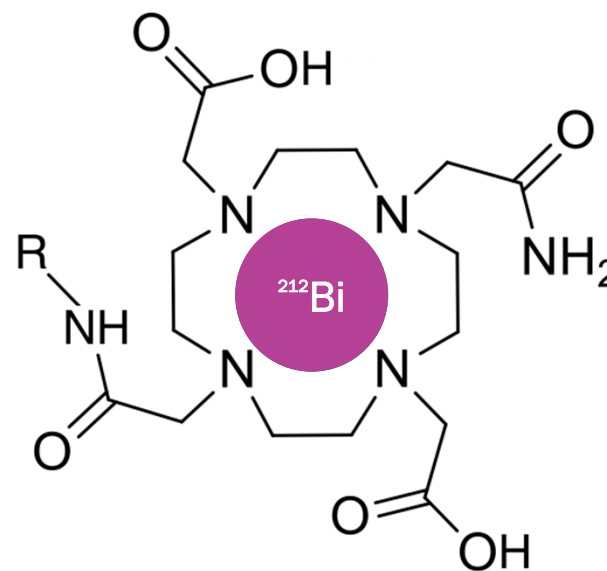
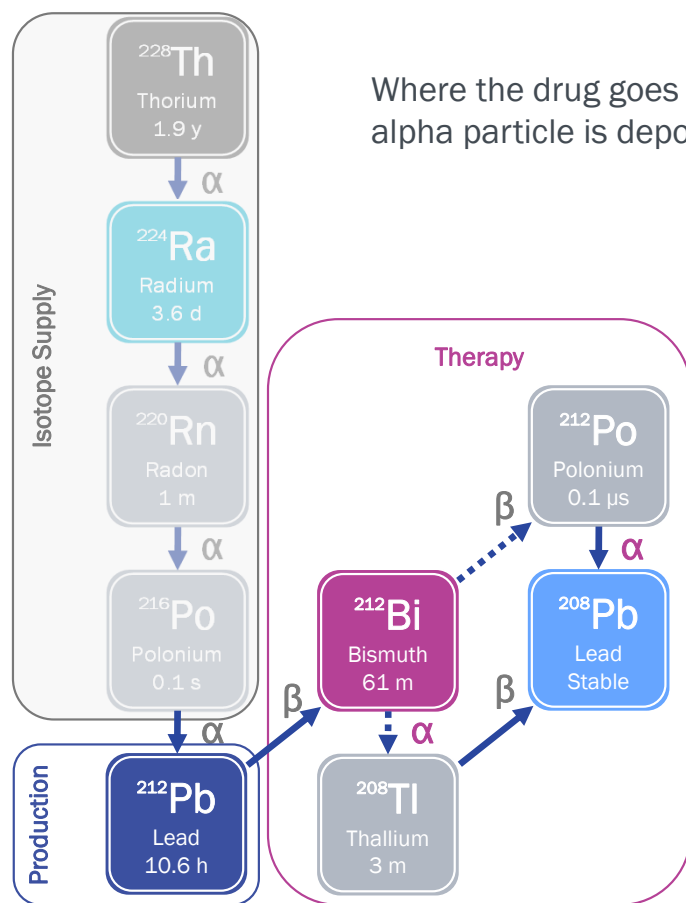


Isotope: Decay chain – Product implications

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



^{212}Pb Isotope Decay Chain and Importance of the Pb-Specific Chelator

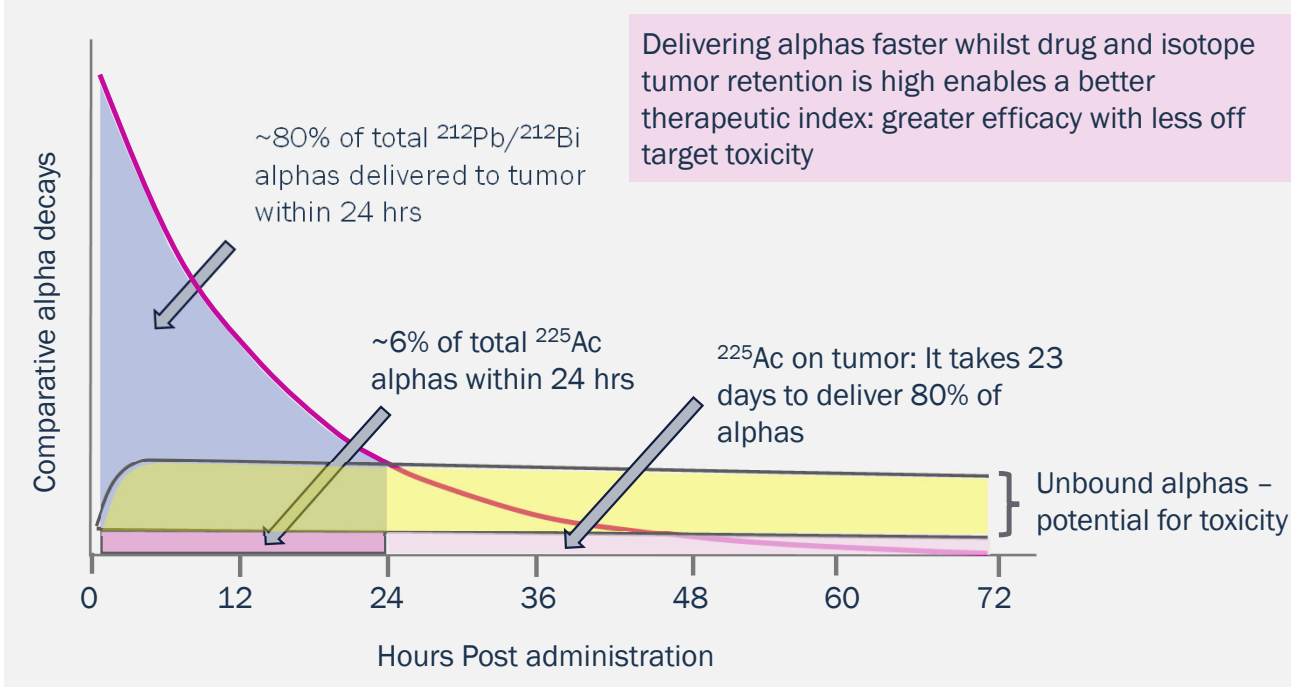


- Perspective's proprietary chelator retains 98% of ^{212}Bi after transition in drug formulation
- Generic chelators leak the ^{212}Bi alpha-emitting daughter up to 36%¹

^{212}Pb Hits Tumors Hard and Fast and Disappears

^{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 Time¹

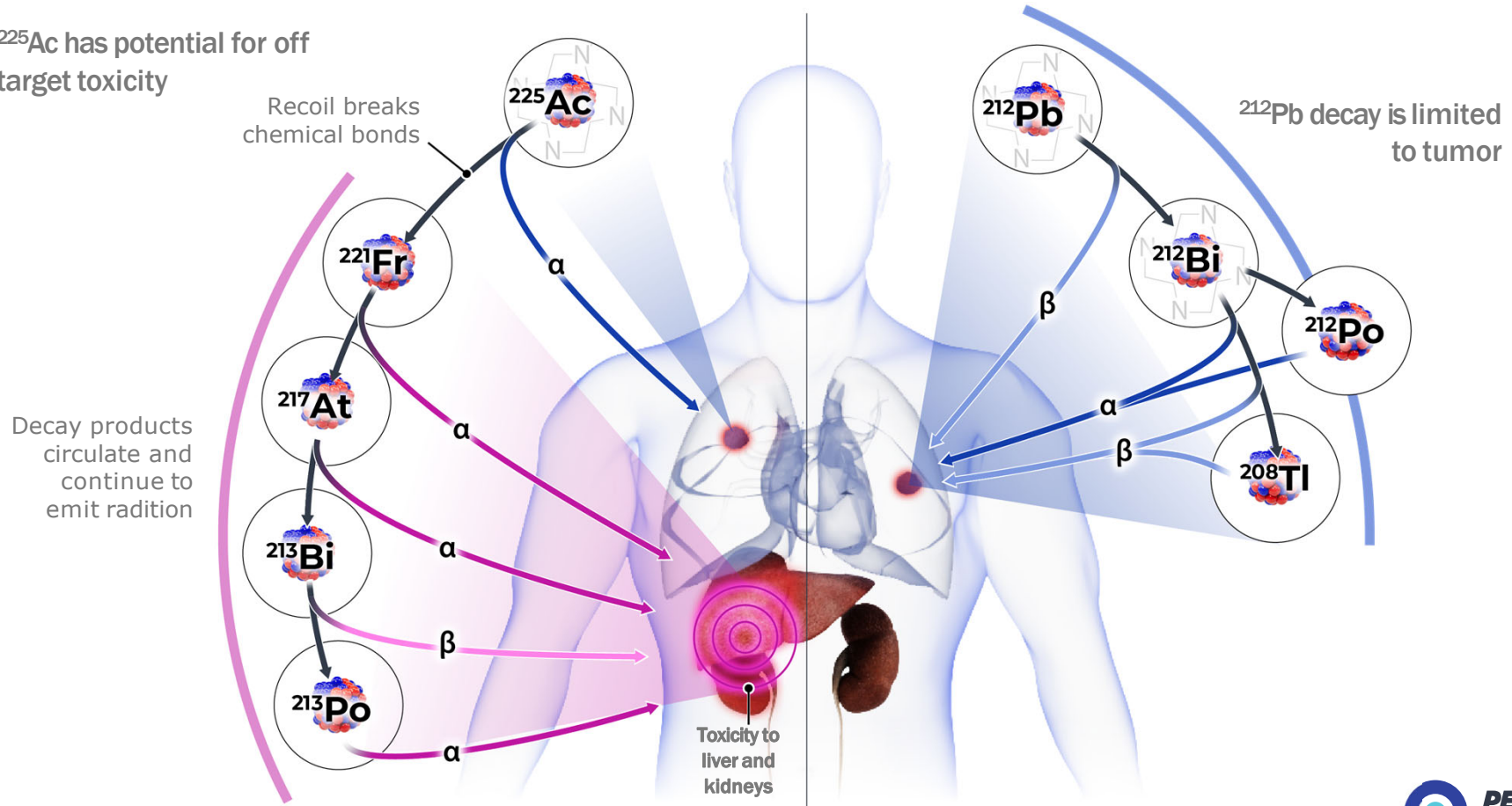


- “Activity” is measured in decays per second, so depends on isotope half-life
- ^{212}Pb will likely be administered at 20 times the ^{225}Ac activity
- ^{225}Ac is administered in smaller activities due to its 10 day half-life and the total alphas decays from its daughters
- Most drugs stay bound to 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

Isotope: Decay chain – Biological Implications

Isotope selection drives potential for off target toxicities

^{225}Ac has potential for off target toxicity



Clinical Trial Principal Investigators

Renowned Experts in Radiotherapy Development



Geoffrey B. Johnson MD, PhD

Chair, Division of Nuclear Medicine



Chair, PET/MR R&D
Associate Professor Departments of Radiology
and Immunology
Mayo Clinic – Rochester, MN



Yusuf Menda MD

Professor of Radiology



Chair, Division of Nuclear Medicine
Project Leader
Neuroendocrine Tumor SPORE
University of Iowa – Iowa City, IA



Vikas Prasad MD

Professor of Radiology



Associate Professor Radiology, Division of
Nuclear Medicine
Washington University in St Louis – St Louis, MO



Zachary Morris, MD, PhD

Professor of Radiation Oncology



Associate Professor, Department of Human
Oncology
The University of Wisconsin – Madison, WI



Appendix: VMT- α -NET

Additional Material and Data from Clinical Investigation at Fortis
Memorial Research Institute, Gurgaon, India

NET Trials

	¹⁷⁷Lu-DOTATATE	¹⁷⁷Lu-DOTATATE	²¹²Pb-DOTAMTATE	²²⁵Ac-DOTATATE	VMT-α-NET
Study	NETTER-1 ⁽¹⁾⁽²⁾ RCT; randomized 2:1 N = 229	NETTER-2 ⁽⁴⁾ RCT; randomized 2:1 N = 226	Phase I/II ⁽⁵⁾ Single arm N=44	ACTION-1 Phase Ib/III ⁽⁶⁾ Phase Ib: Single arm N=17	Investigator led research ⁽⁷⁾ N=13
Dose Level (administered)	4 x Q8W 200 mCi	4 x Q8W 200 mCi	4 x Q8W 67 μCi/kg → 4.7 mCi/70 kg	4 x Q8W 3.2 uCi/kg → 0.23 mCi/70 kg	4 x Q8W 67 μCi/kg → median 2.9 mCi
Patient Population	SSTR2+, GEP-NETs	SSTR2+, GEP-NETs	SSTR2+, GEP-NETs	SSTR2+, GEP-NETS	SSTR2+ GEP-NETs, B-NETs, MTCs
Prior PRRT	0%	0%	0%	100%	62%
Median time from dx	3.8 years	1.9 months	5 years	5 years	N/A
Performance Status	Karnofsky Performance Scale Median was 90	Karnofsky Performance Scale 83% at 90-100	N/A	ECOG 0 (59%), 1 (41%)	ECOG 0 (38%), 1(31%), 2 (31%)
Histology	Well differentiated G1 (66%), G2 (35%)	Well differentiated G2 (73%), G3 (27%)	Well differentiated G1 (18%), G2 (68%), G3 (7%)	Well differentiated G1 (47%), G2 (53%)	Well differentiated G1 (15%), G2 (85%)
PFS	Median 28.4 vs 8.5 months ⁽³⁾	Median 22.8 vs 8.5 months	74.3% at 24 months	NE (95% CI: 12 months, NE)	Median 16.4 months
ORR (CR/PR)	13% (1%/12%) vs. 4% (0%/4%)	43% (5%/38%) vs. 9% (0%/9%)	56%	29.4% confirmed 41.2% (6%/35%) w/ unconfirmed	62% (0%/62%) confirmed
AEs (>20%)	Nausea, vomiting, fatigue, diarrhea, abdominal pain, multiple laboratory abnormalities	Nausea, diarrhea	Alopecia, nausea, fatigue, appetite↓, diarrhea, dysphagia, lymphocyte count↓, abdominal pain, vomiting, weight↓, blood glucose↑	Nausea, fatigue, weight↓, hyperglycemia, abdominal pain, constipation, vomiting, multiple laboratory abnormalities	>10 events: alopecia, anemia, fatigue, nausea
Grade 3+ (>10%)	Lymphopenia (44%), GGT↑ (20%)	TEAE: 35%	TEAE: 52% Lymphocyte count↓ (25%)	TEAE: 53% Anemia (18%), lymphocyte count↓ (18%), creatinine clearance↓ (12%)	Anemia (2 events)
Other notes	5 Lu-177 treated patients withdrew due to renal-related events	Nephrotoxicities 13 (8.8%) vs. (2.0%)	Dysphagia treated with Botox injection		Transient dysphagia resolved without intervention

(1) US prescribing information; (2) DOI: 10.1056/NEJMoa1607427; (3) NANETS 2021; (4) DOI: 10.1016/S0140-6736(24)00701-3; (5) ASCO 2024; (6) ASCO 2024; (7) SNMMI 2024.

71

No head-to-head studies between the products have been conducted. Given the different study designs and methods, cross-trial comparisons cannot be made.

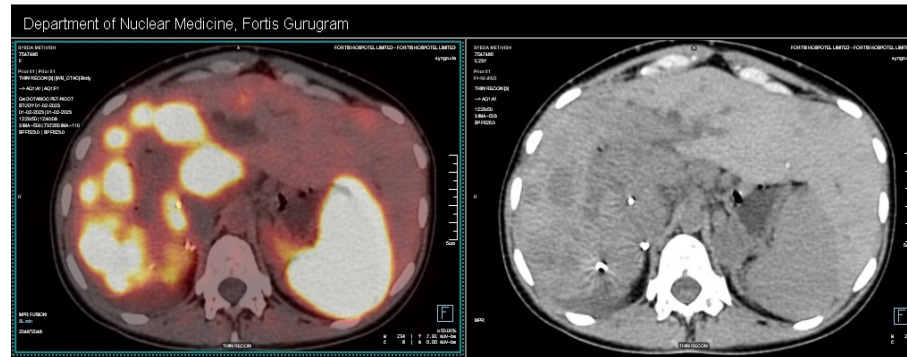
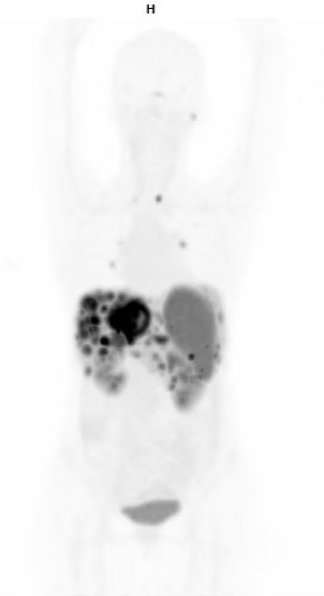
The information on this slide is not intended to promote the products referenced herein or otherwise influence healthcare prescribing decisions. The safety and efficacy of the agents under investigation have not been established. There is no guarantee that the investigational agents will receive regulatory approval or become commercially available for the uses being investigated.



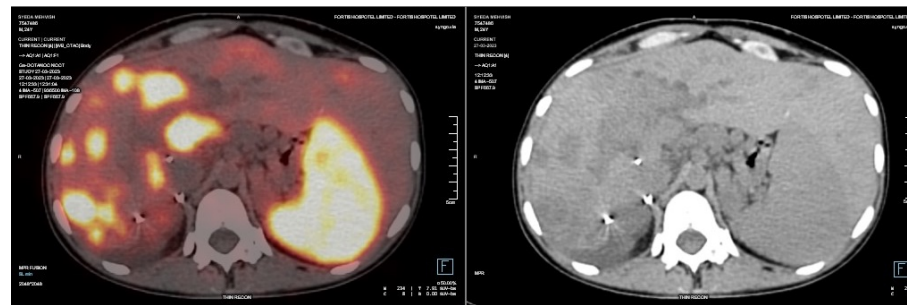
Significant Tumor Response After Two Doses

Patient 3: Metastatic NET Pancreas with Liver Metastases

MIP image Before Treatment

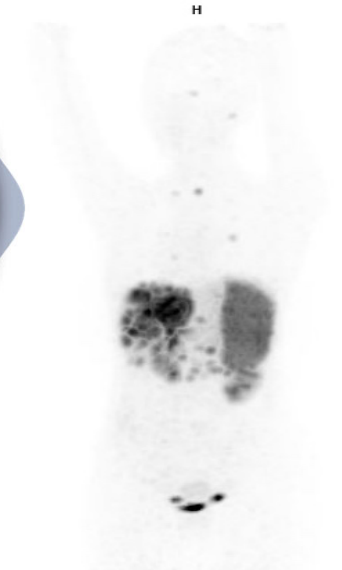


Liver Metastases before treatment



Liver Metastases after treatment with two doses

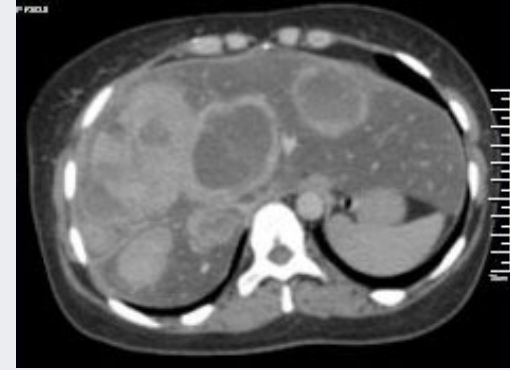
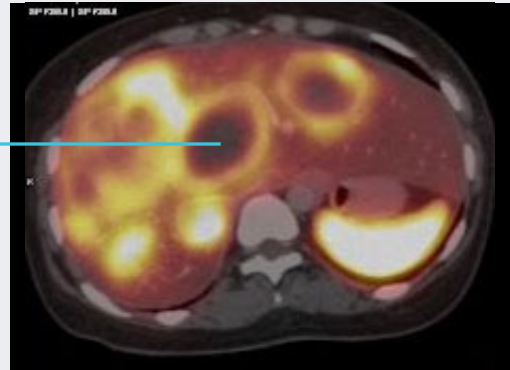
MIP image After 2nd Treatment



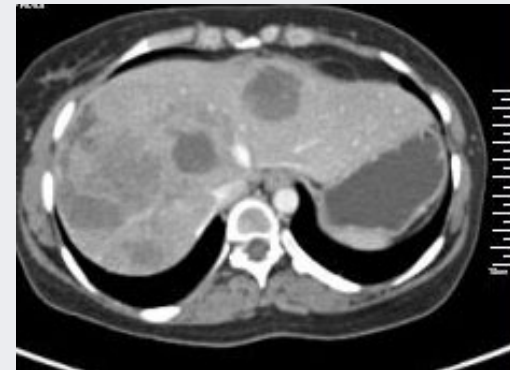
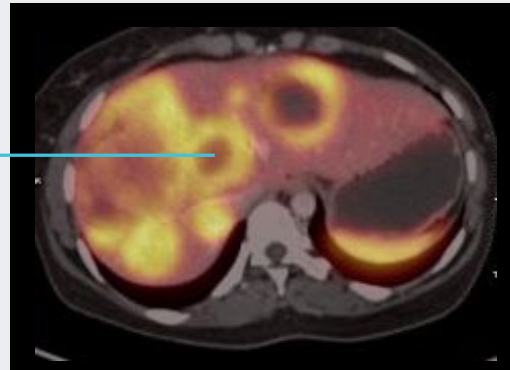
Reduction in Size of Necrotic Masses After 2 Doses

Patient 5: Pancreatic NET

Tumor Before Treatment



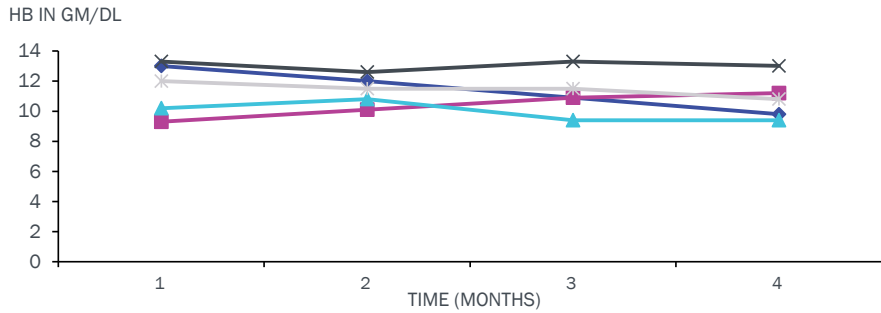
Tumor After Treatment



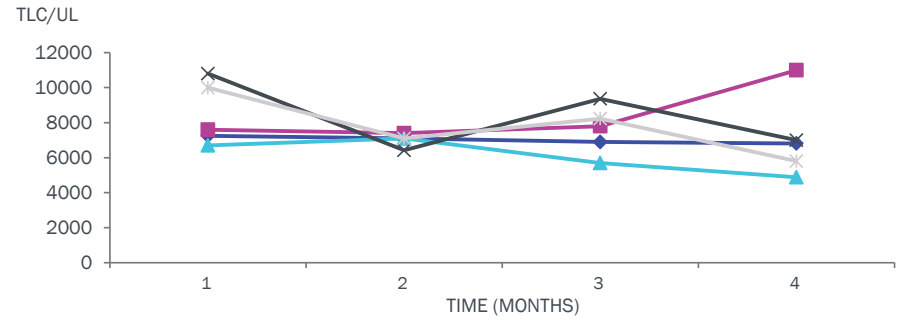
Favorable Safety and Tolerability Profile

Four Months Post-Treatment (5 Patients)

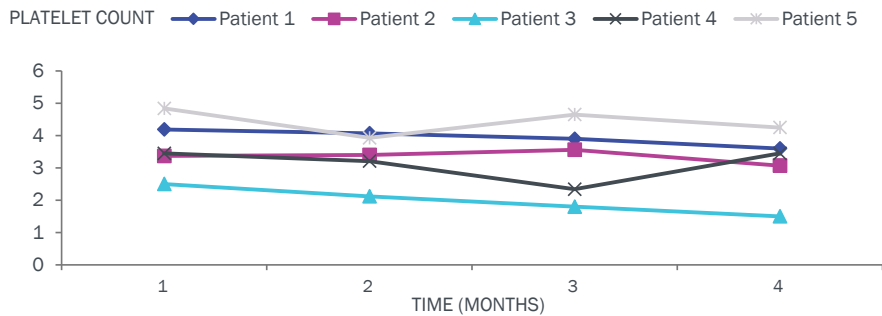
Hemoglobin Levels



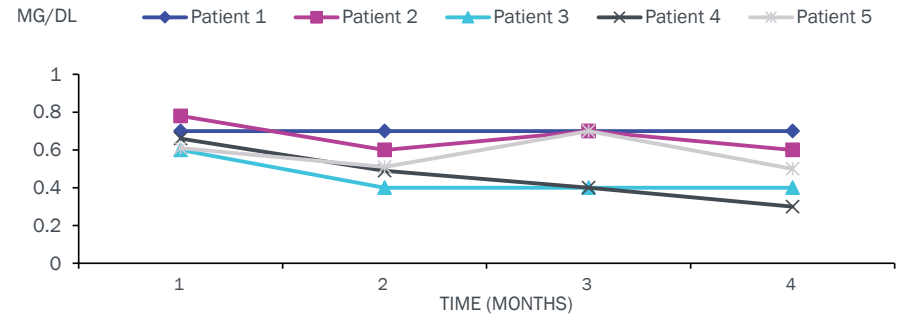
Total Leukocyte Count



Platelet Counts



Serum Creatinine

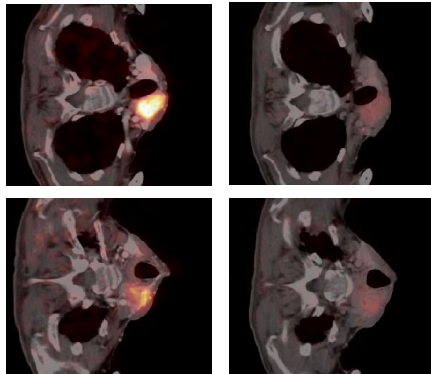


Serious Adverse Event in Patient 2

Myelodysplastic syndrome (MDS) Unrelated to Study Drug



Pre-Therapy



Post-Therapy

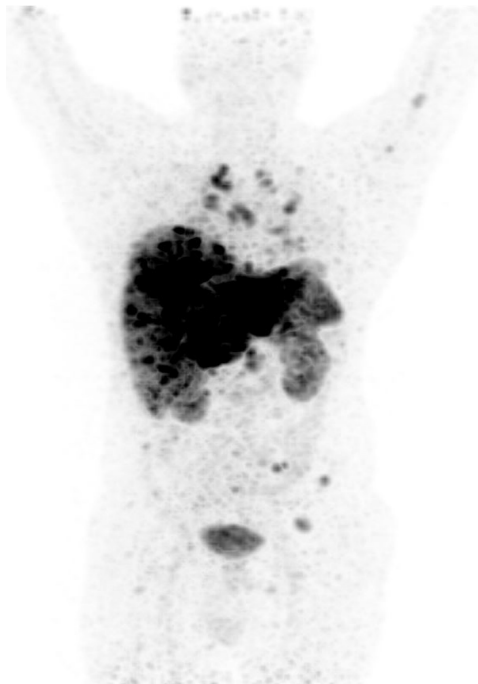
Patient Profile

- 79 year-male
- Metastatic Medullary Carcinoma thyroid
- Disease progression of TKI's
- Received total 3 doses of [^{212}Pb]VMT- α -NET therapy at an interval of 8 weeks (Cumulative dose 9.6 mCi)
- Shows Partial response for disease till date.
- Developed MDS on routine blood investigations
- Found positive for BCR-ABL gene

No causal relationship could be established

Serious Adverse Event in Patient 6

Acute Cardiac Event Unrelated to Study Drug



Significant tumor burden

Patient Profile

- 25 year-male
- Metastatic NET-pancreas
- Long-standing disease (>6 years duration)
- Heavily pre-treated with Inj. Sandostatin and 4 cycles of ^{177}Lu -DOTATATE along with CAPTEM regimen
- Received 1 dose of ^{212}Pb VMT- α -NET therapy (3.5 mCi)
- Acute Cardiac Event (Possible Carcinoid Heart Syndrome)
- Significant Tumor Burden - Possible Disease Progression

No causal relationship could be established



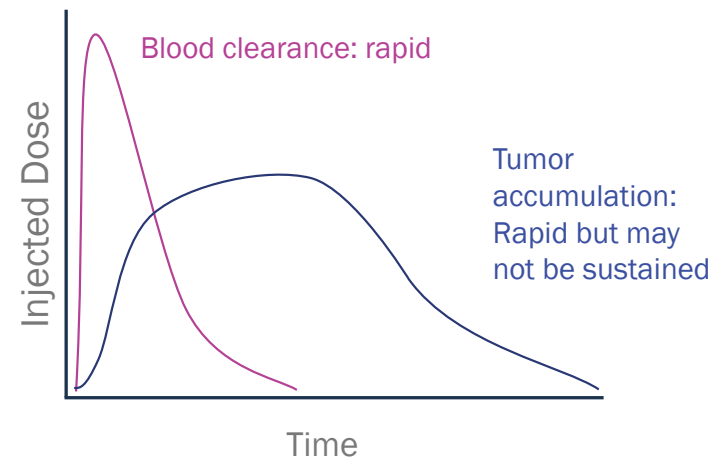
Appendix: Preclinical Programs: Pre-targeted Platform

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 Kinetics¹



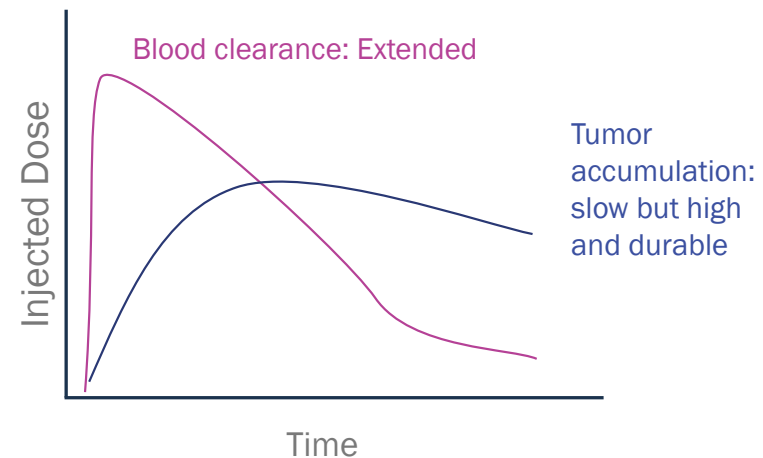
We believe peptides are the ideal targeting vectors for high dose-rate isotopes such as ²¹²Pb, as the biological and radiation half-lives are matched

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 billion²) but some safety issues with Blackbox warnings³
- 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 molecules⁵
- Tumor accumulation can be very high and retention long
- Very long list of targets for mAbs available

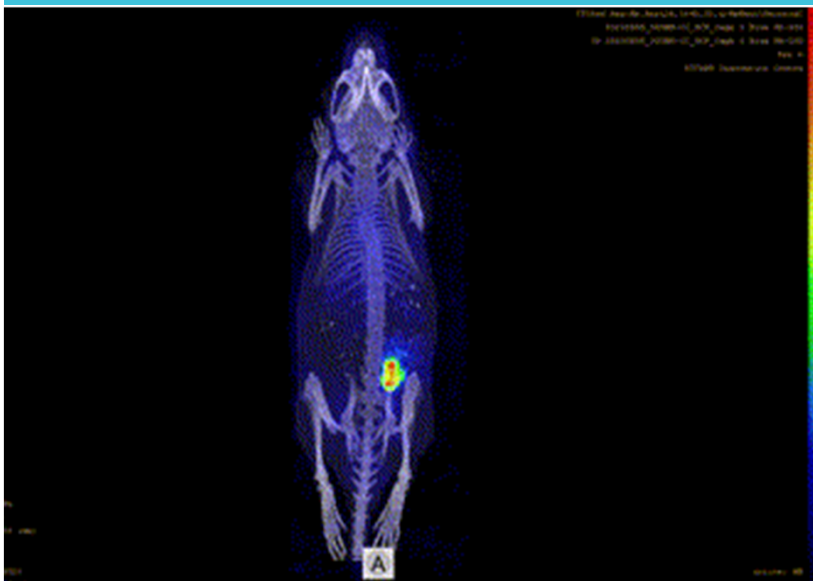
mAb Kinetics⁶



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

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

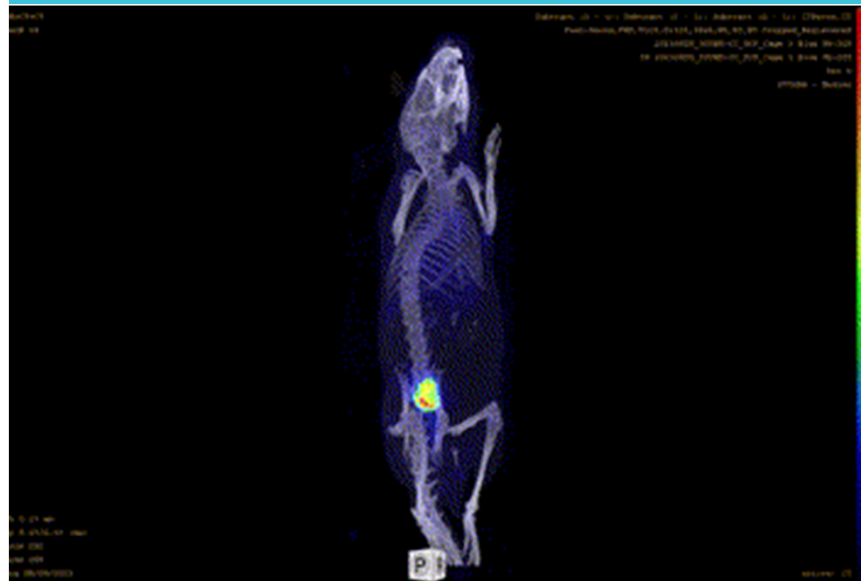
48 hours post- injection



Observations

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

120 hours post- injection



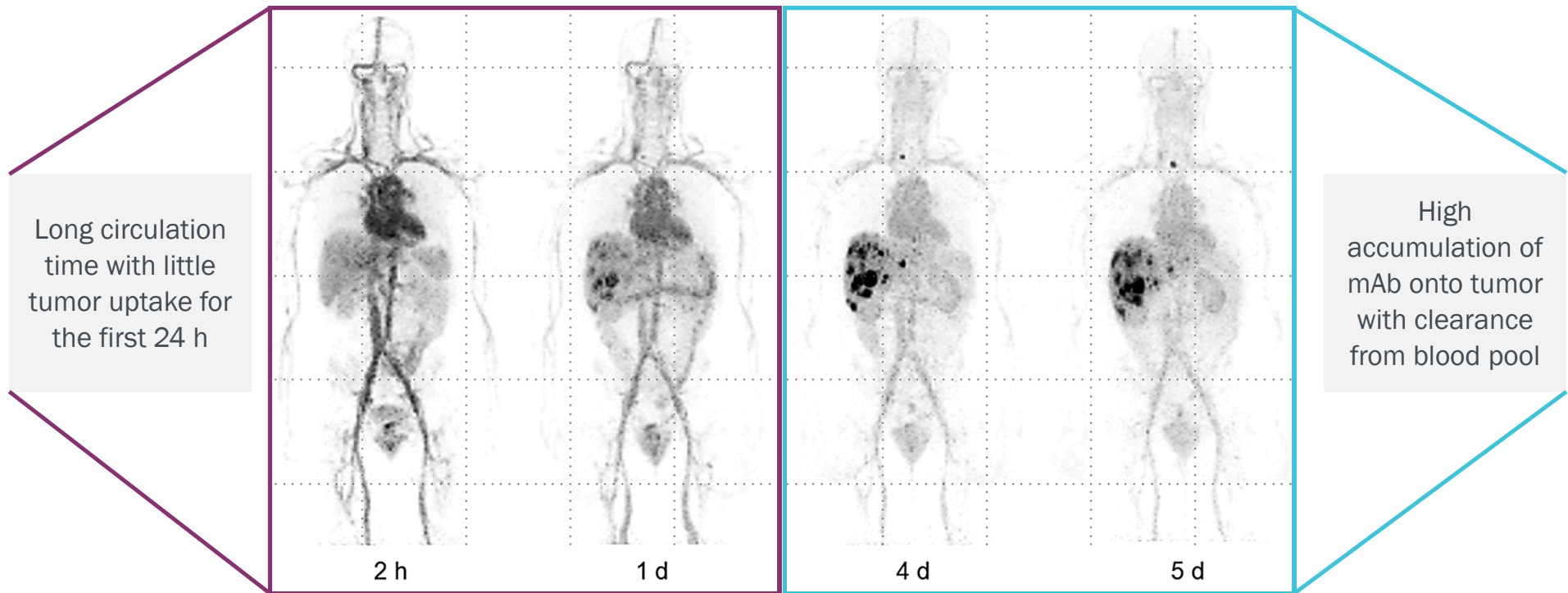
Question?

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

Biokinetic Properties of mAbs are Ideal for Accumulation on Target

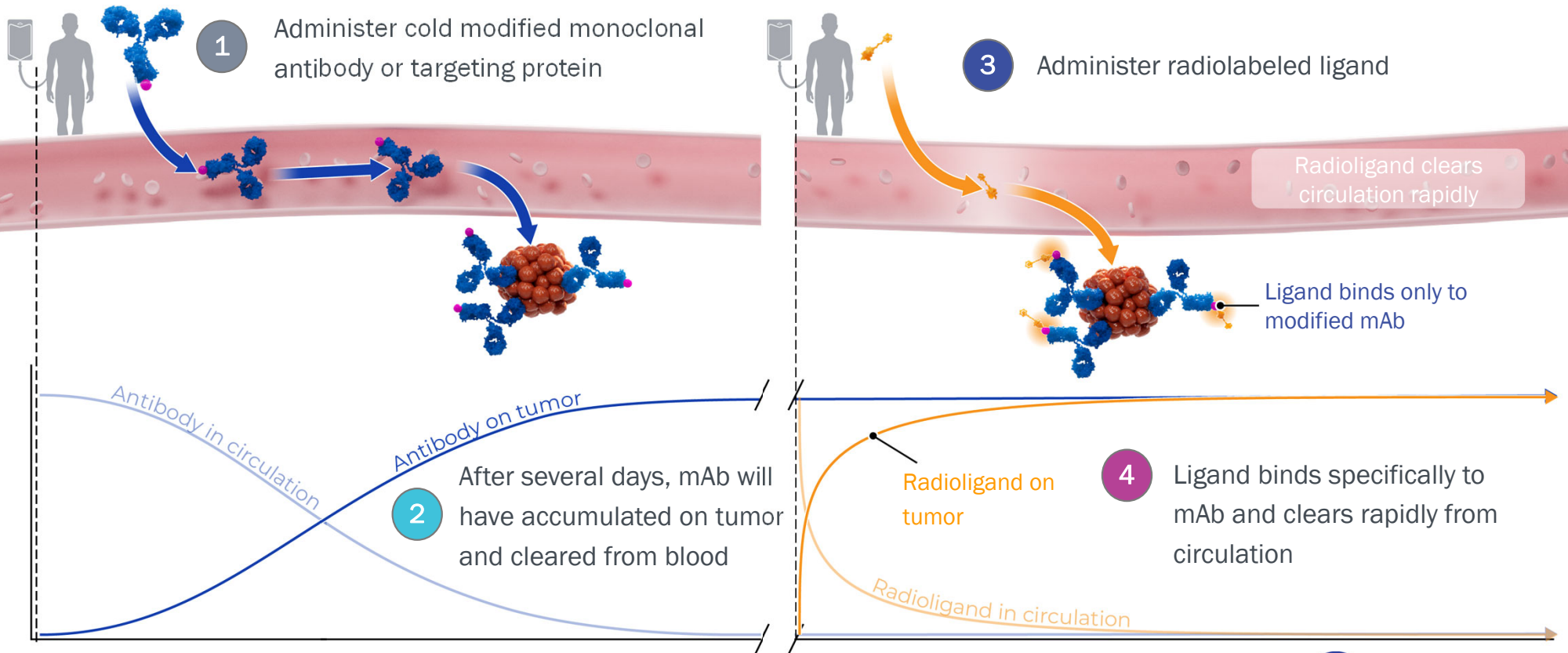
Representative imaging across longer time frame demonstrates clearance and uptake kinetics

Patient with HER2 positive esophagogastric adenocarcinoma metastatic to liver, imaged with [^{89}Zr]trastuzumab¹



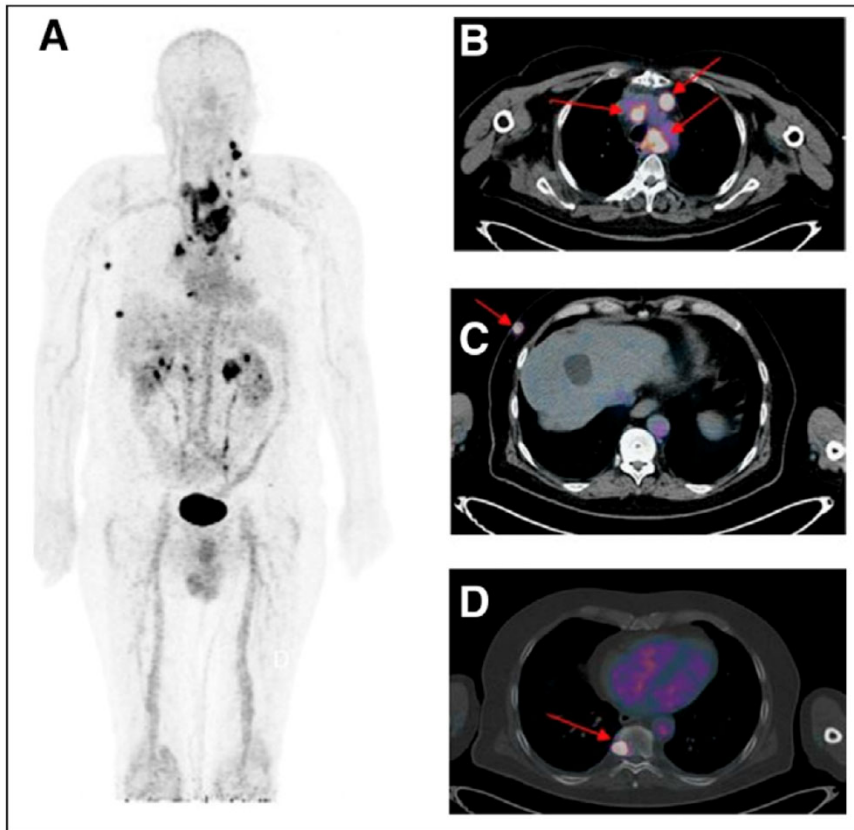
Pre-Targeting Platform Background

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



Promise of Pre-Targeted Approach – Clinical Data

^{68}Ga -IMP288 – Images ≥ 24 hours following Anti-CEA Bispecific mAb¹



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

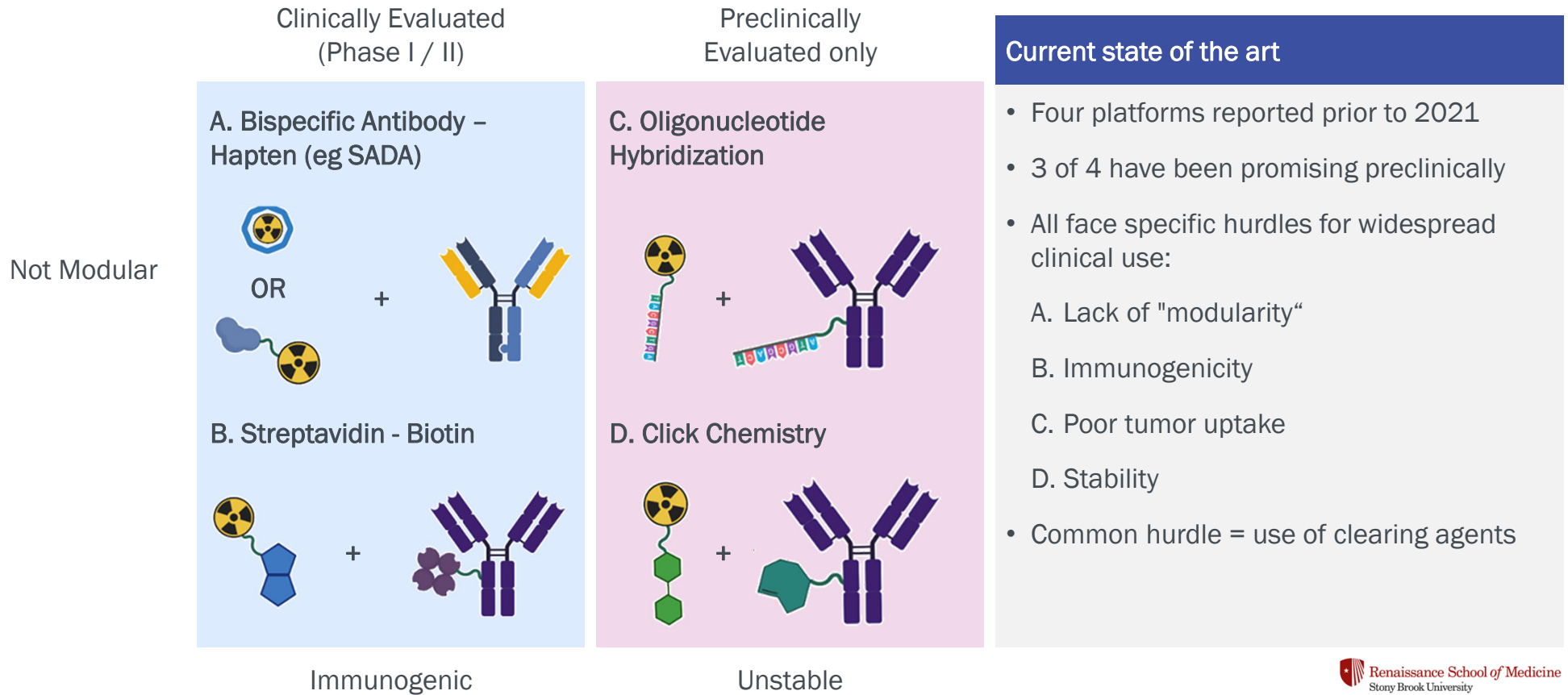
Maximum-intensity-projection (MIP) image (A) showed several pathological lesions

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”

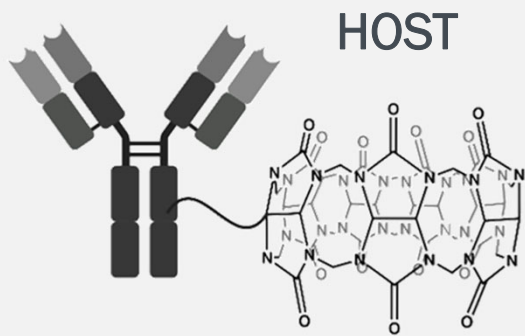
State of the Art in Pre-Targeting for Radiopharmaceuticals

Review of current state of the art technology platforms



Perspective Pre-Targeting Platform: Host - Guest Chemistry

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



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

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

+

An ideal pretargeting agent:

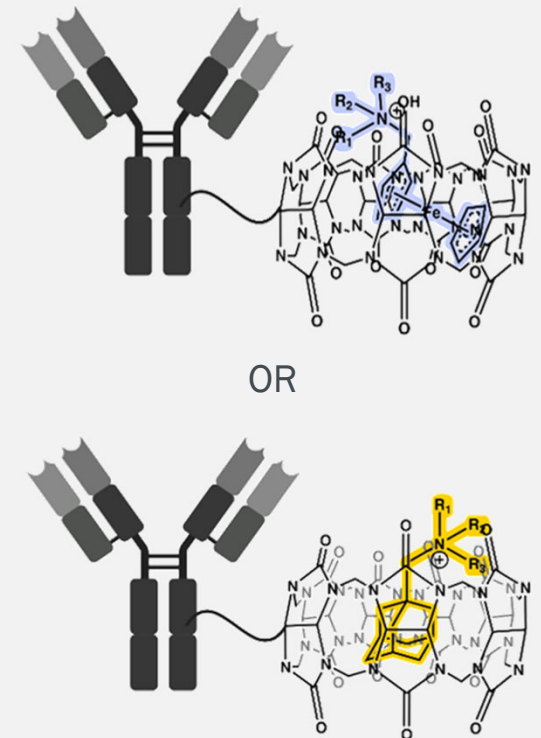
High *in vivo* stability

Modular

Non-toxic

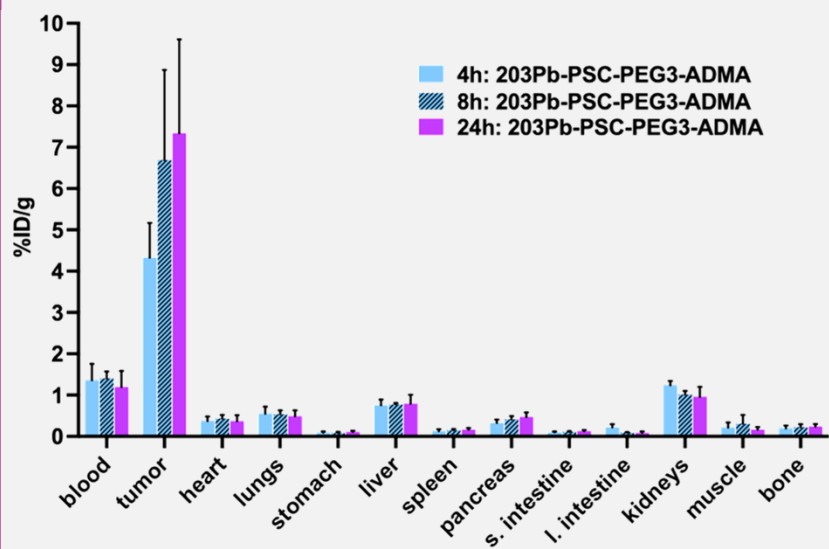
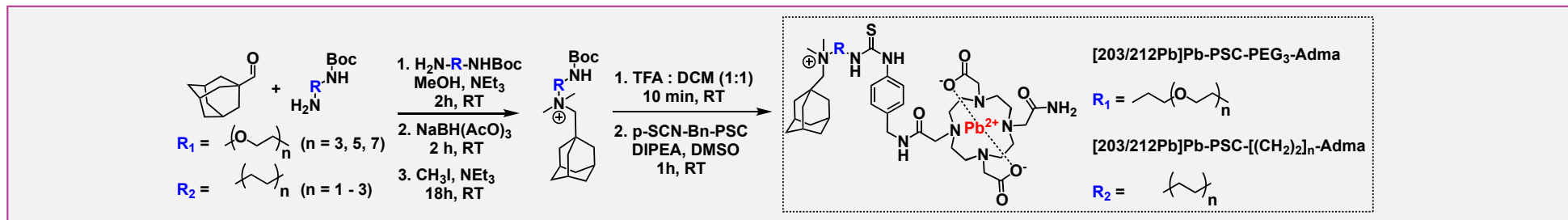
Non-immunogenic

No need for a clearing agent



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

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



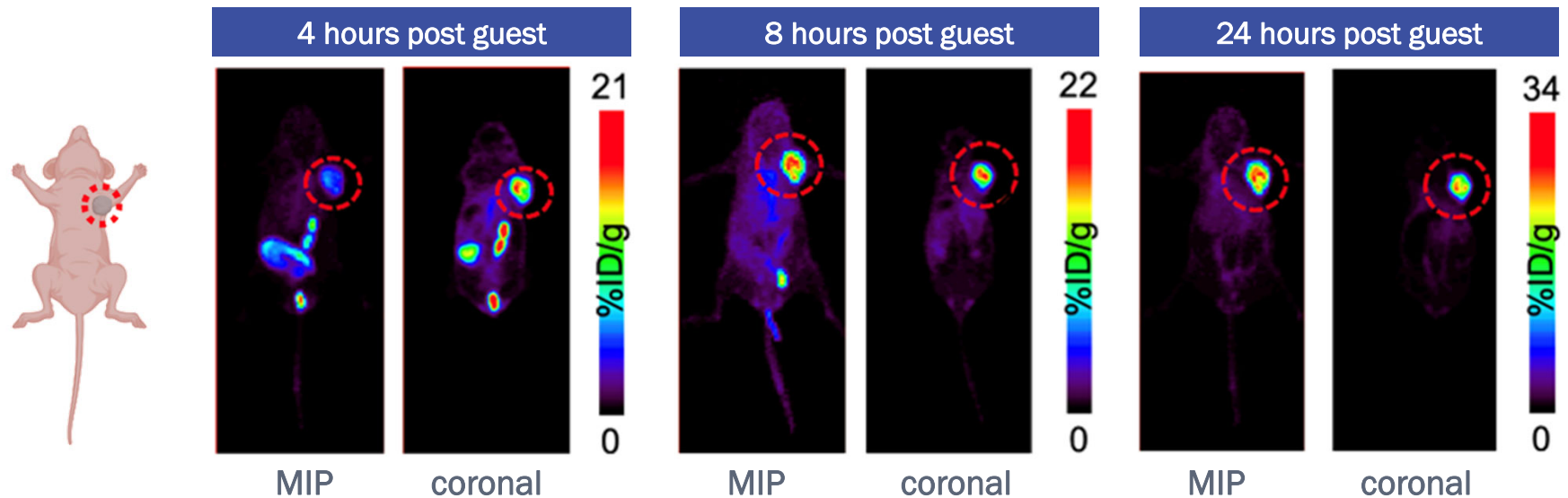
First in vivo Experiment: Observations

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

Representative images of ligand during optimization process

- Host is a mAb targeting Carcinoembryonic Antigen (CEA)
- Guest is an adamantane-PEG3-NOTA labeled with ^{64}Cu
- 72 h lag time post Host administration



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

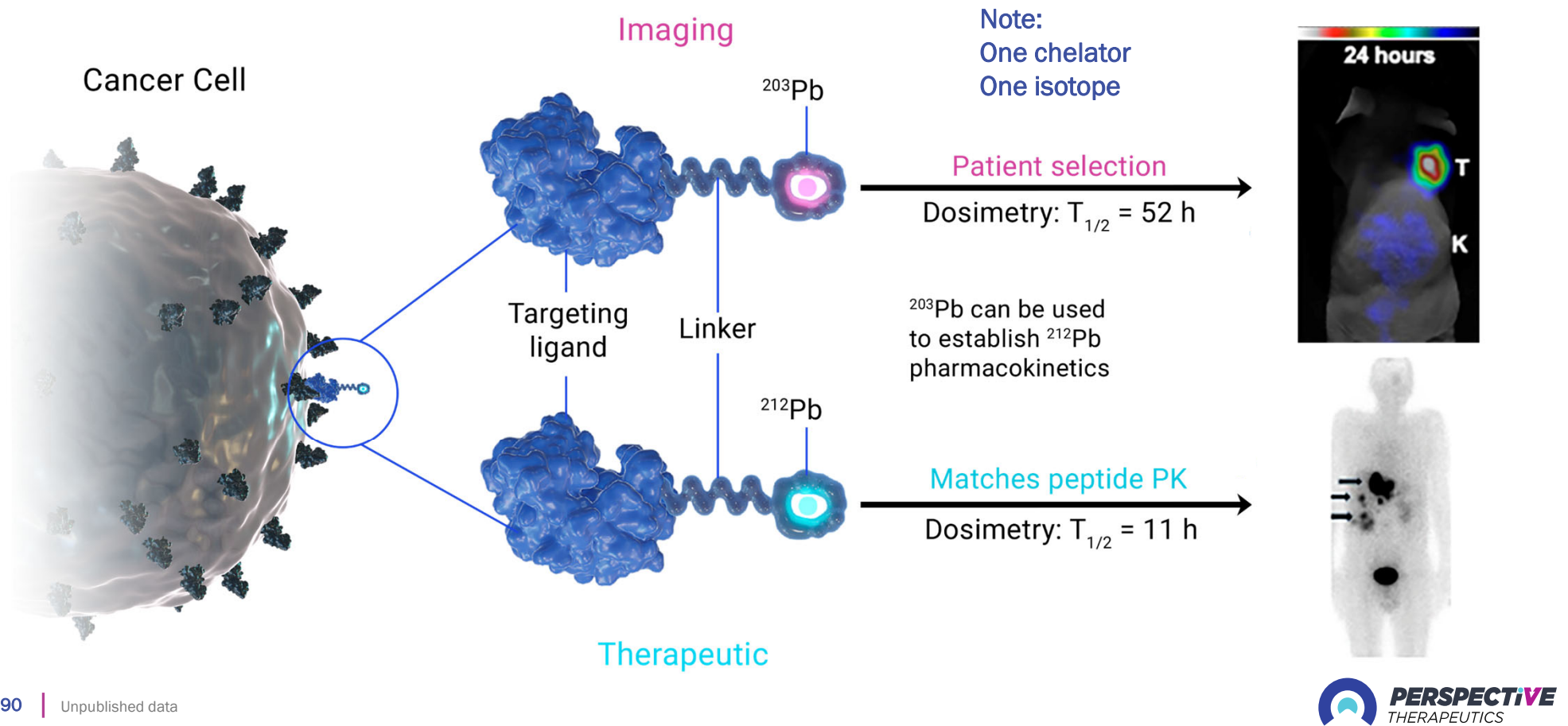
Perspective’s pre-targeting platform has the potential to transform a large range of existing molecules and targets into “radio-ADCs” with superior efficacy and reduced toxicity



Appendix: Prostate Cancer Program – Financials

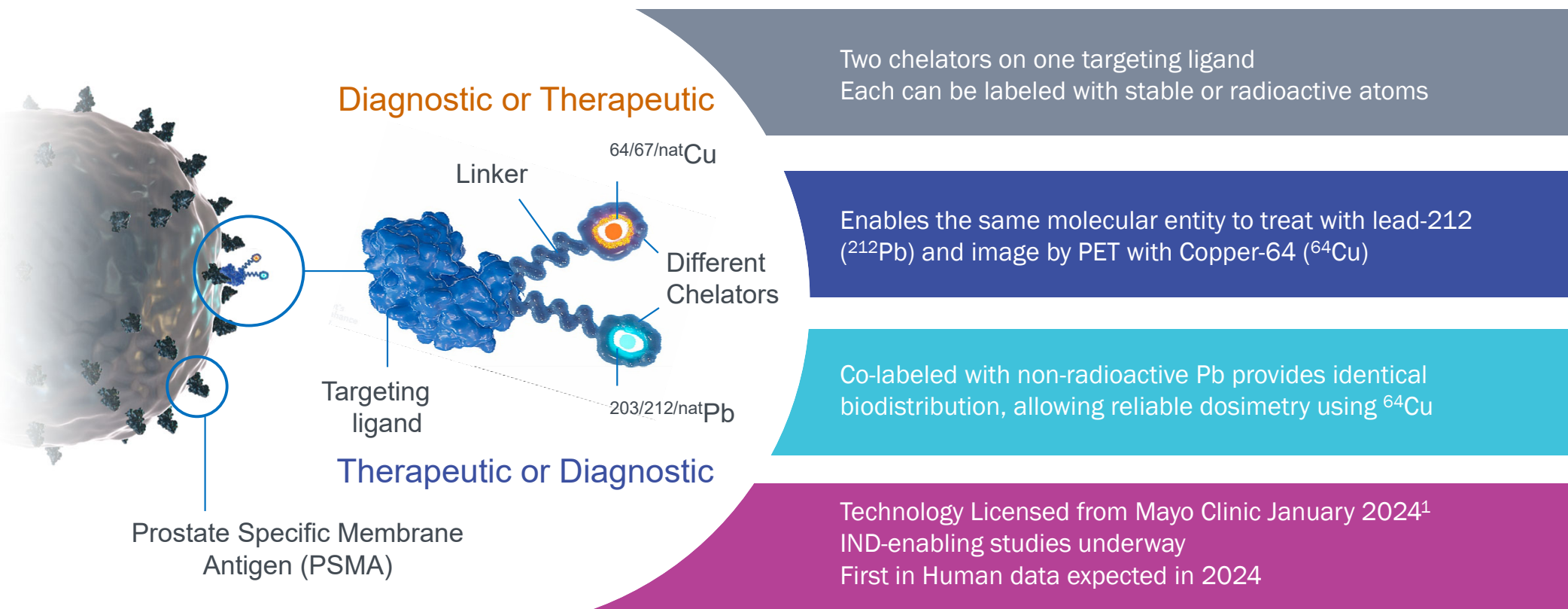
Typical Theranostic Approach : One Molecule, One Chelator, One Isotope

Separate But Chemically Identical Molecules Labeled with Either ^{203}Pb or ^{212}Pb for Imaging and Treatment, Respectively



PSV401 Doublet^{1,2}: One Molecule, Two Chelators, Four Possible Isotopes

One Molecule Labelled with Two Elements at Once, with Isotope Selection Determining Diagnostic or Therapeutic



PSV401 Has Potential to be “Best-In-Class” Prostate Cancer Targeted Alpha Therapy

Current Standard of Care with Beta-Based Radiopharmaceutical Therapy (RPT) Still Requires Improvement

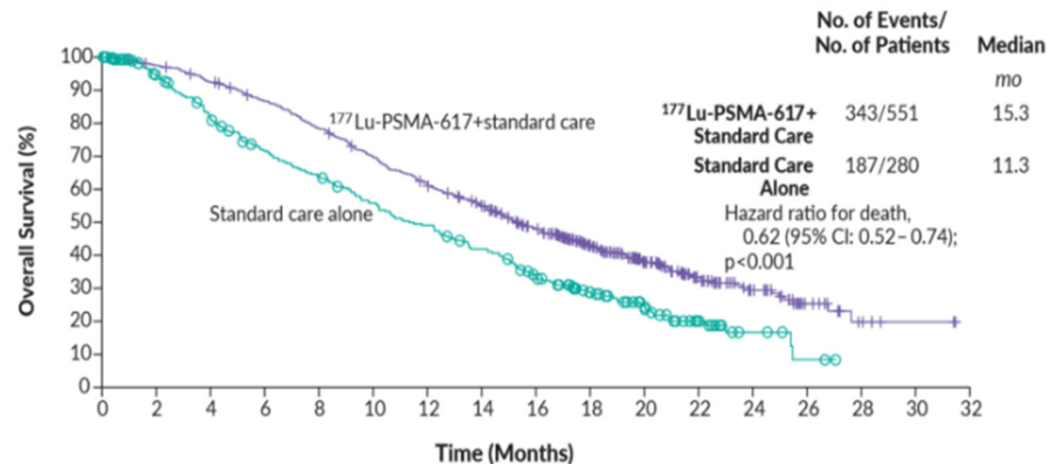
Significant Unmet Need:

- ~288K new diagnoses annually in the US¹
- ~3.3M+ men living with this diagnosis in the US¹
- ~35K deaths annually in the US¹

Market Opportunity:

- Projected to be \$27.5 billion+ in 2032²
- Existing radiopharmaceutical treatment PLUVICTO® (Novartis) has an overall response rate (ORR) of 30%, and an overall survival (OS) benefit of 4 months³
- PLUVICTO® expected to reach sales (\$1B plus) in only 2nd year on market⁴

VISION Study: Overall survival⁵



- Treatment depends on the stage of tumor. Typical approaches include surgery, radiation, chemotherapy and androgen-deprivation therapy
- Broad acknowledgment that targeted alpha therapies are needed to improve care⁶
- **Salivary gland toxicity (xerostomia) is a common adverse side effect of PSMA targeted RPT (≈ 40%) and negatively impacts quality of life⁷**

PSV401: Preclinical ⁶⁴Cu PET Imaging Data Showing Tumor Uptake

Rapid Tumor Uptake and Effective Renal Clearance with Radioactive Imaging Isotope¹

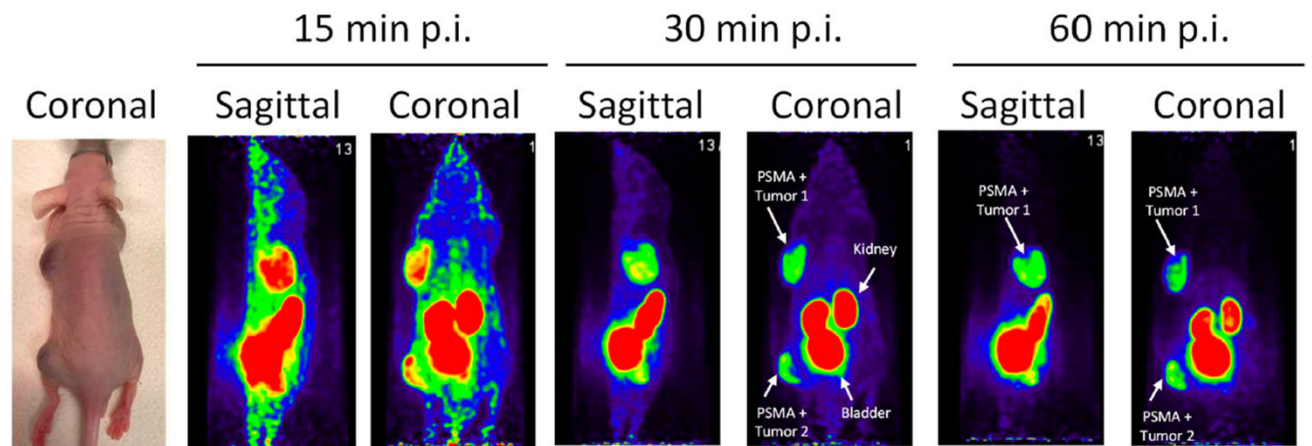
Key Takeaways



PSMA+ LNCaP tumor model suggests [⁶⁴Cu]PSV401 targets tumor rapidly – suitable for diagnostic or treatment monitoring



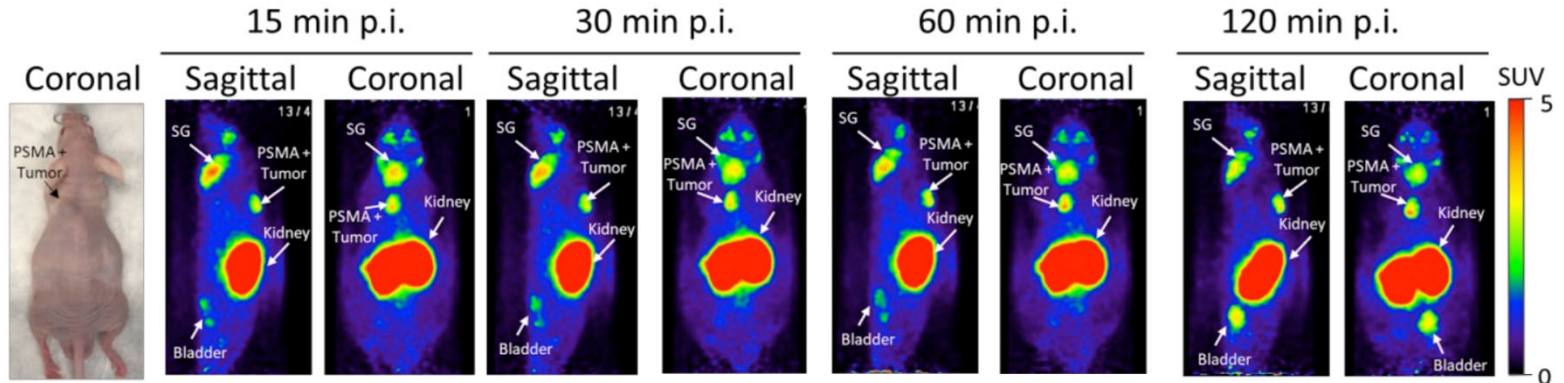
Imaging product also indicates effective renal clearance and no other dose-limiting organs, essential for targeted alpha particle therapy



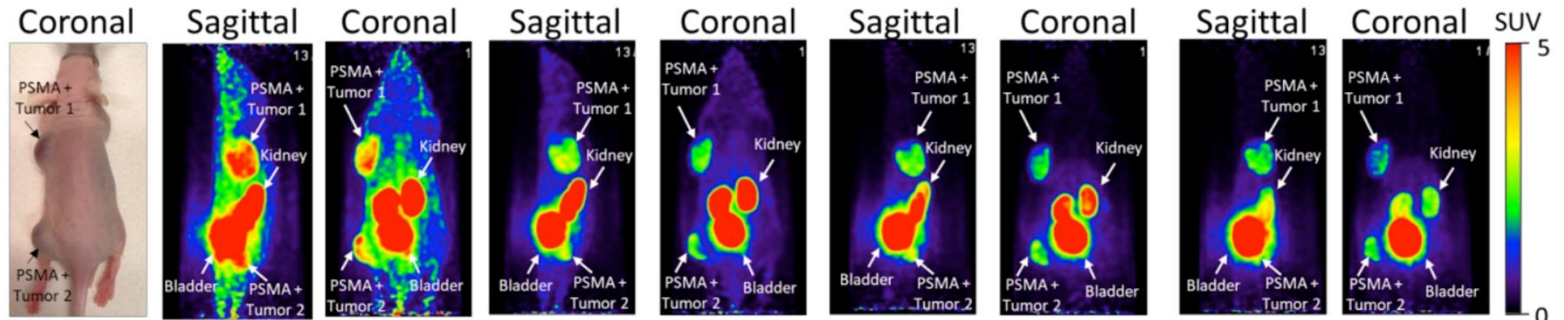
PSV401: Preclinical Comparison to Industry Standard¹

[⁶⁴Cu]PSV401 Compares Favorably to FDA-Approved Imaging Agent [⁶⁸Ga]PSMA-11 (ILLUCCIX[®], Telix)²

[⁶⁸Ga]PSMA-11



[⁶⁴Cu]PSV401

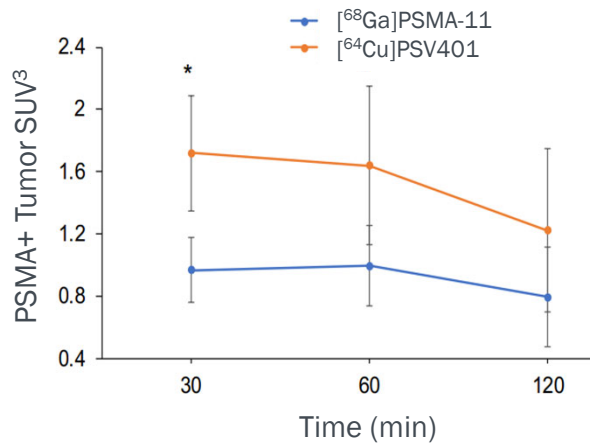


Note absence of salivary gland (SG) uptake with PSV401

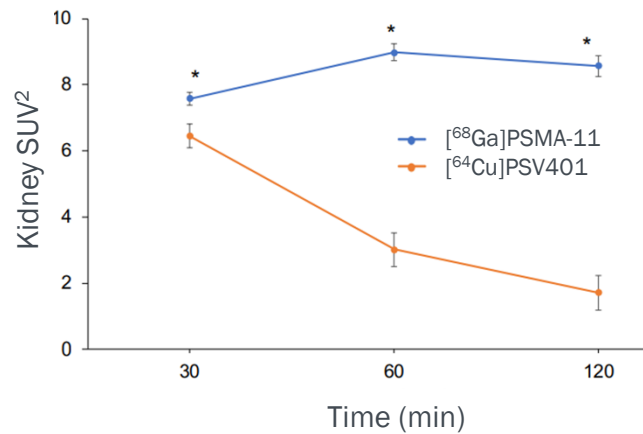
PSV401: Preclinical Comparison to Industry Standard

[⁶⁴Cu]PSV401 Significantly¹ Improved Uptake/Clearance Compared to [⁶⁸Ga]PSMA-11²

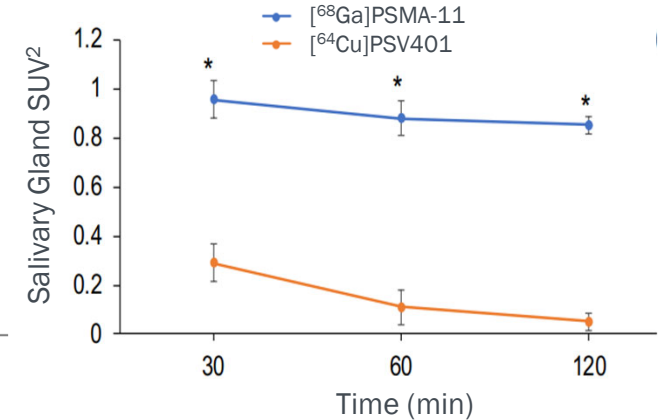
Tumor Retention



Kidney Retention



Salivary Gland Retention



Key Differentiation to Competitors

- Higher tumor accumulation/retention
- Significantly lower salivary gland uptake and retention
- Significantly lower kidney accumulation and retention

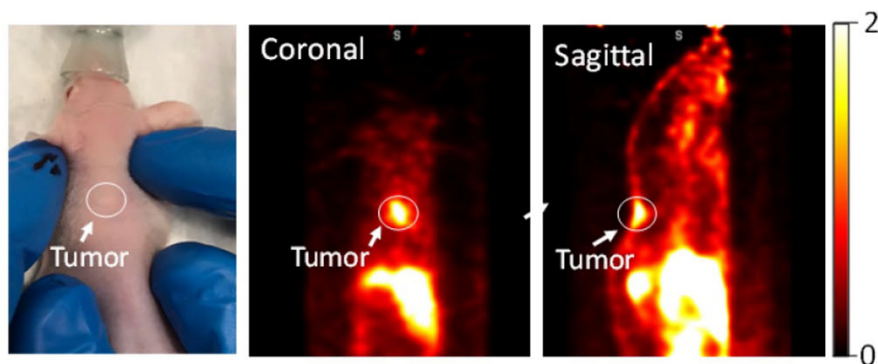
Larger therapeutic window
(greater efficacy and reduced toxicity)

Preclinical [^{212}Pb]PSV401 Therapy

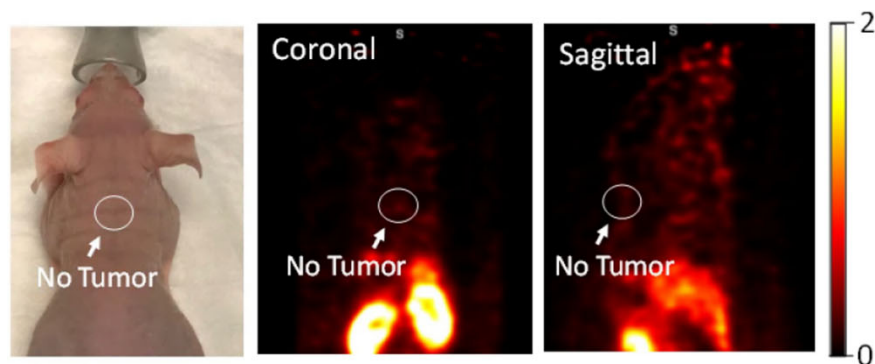
Preliminary [^{212}Pb]PSV401 Data Shows Potential to Effectively Kill Tumors ¹

- All imaging performed with [^{64}Cu]PSV401 microPET
- Treatment of PSMA+ prostate cancer xenograft with [^{212}Pb]PSV401 reduced tumor size 38% in 3 days and complete response after 9 days
- Additional preclinical work underway

2 Days Prior to [^{212}Pb]PSV401



18 Days Post [^{212}Pb]PSV401 Dose

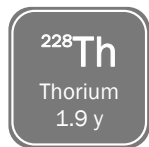




Appendix: Manufacturing, Production and Characteristics of ^{212}Pb -labeled Therapeutics

Isotope Decay Chain Dictates Supply, Purification, Manufacturing & Logistics

Naturally Occurring Isotope Decay – No Irradiation Processes Required



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



- Multiple global suppliers including natural decay
- 2 year half-life allows stockpiling



Chemical Separation:
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 storage



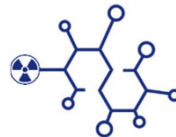
Chemical Separation from ^{224}Ra :
Isotope used for manufacturing
finished product



- Regional finished product manufacturing
- Leverages existing networks for logistics



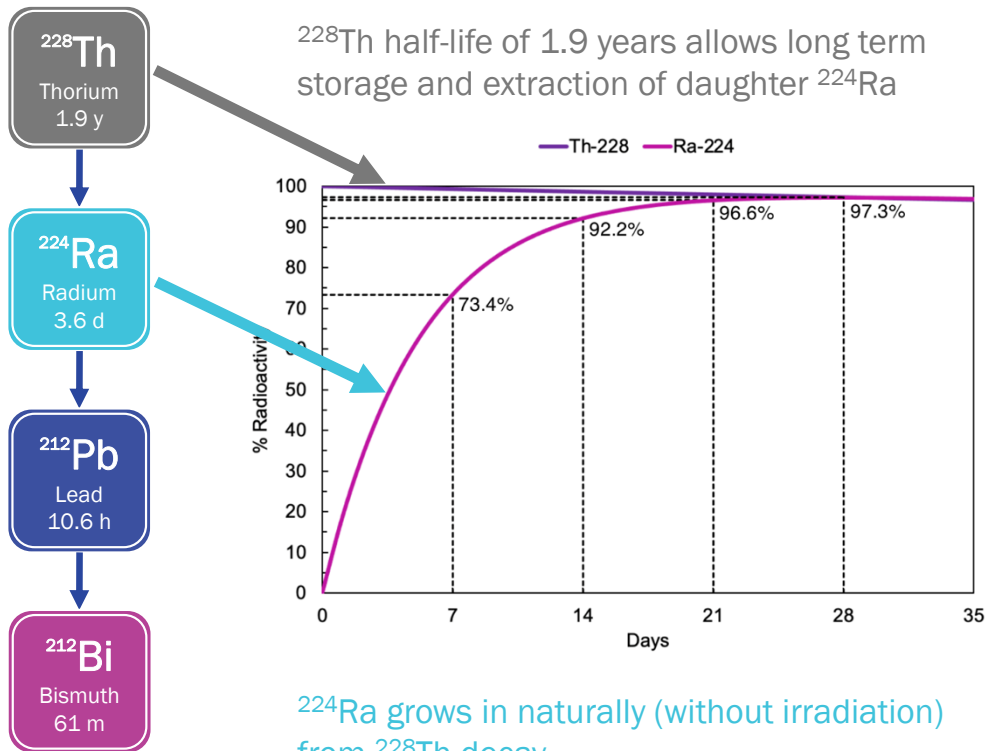
High dose-rate alpha-emitting
therapeutic isotope



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

Parent Isotope Source

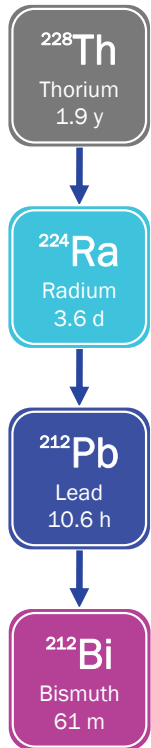
Key Isotopes for Supply: ^{228}Th and ^{224}Ra



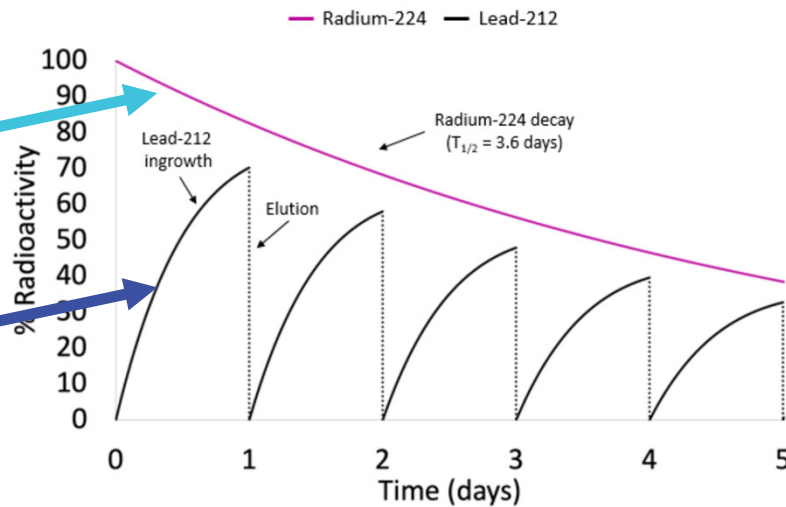
- Perspective currently has a 10 year supply agreement with US Department of Energy
- Produced as a waste by-product from isotope ^{223}Ra (Xofigo) manufacture
- Irradiation to produce very large quantities (100s of Ci) in a high-flux reactor can be performed every 6-12 months in a single batch, or as needed
- 2-year half-life allows stockpiling and de-risks the supply chain
- 8+ suppliers identified across the globe

Flexible and Scalable Isotope Supply

^{224}Ra enables Regional Manufacturing Hubs

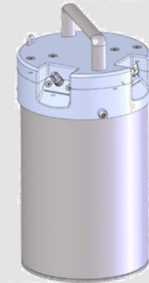


^{224}Ra half-life of 3.6 days allows weekly shipments to regional manufacturing sites






^{212}Pb grows in naturally (without irradiation) from ^{224}Ra decay

- Perspective's proprietary VMT- α -GEN enables shipping of isotope and purification of ^{212}Pb in one package, simplifying supply
- VMT- α -GEN generator technology scales for commercial production
- Extremely pure isotope allows straightforward production process
- Regional manufacturing sites will not require licenses for any long-lived isotopes, reducing costs and waste concerns
- Other ^{212}Pb production processes are possible



^{212}Pb is Plentiful, Storable, Scalable & Suitable for Distributed Logistics

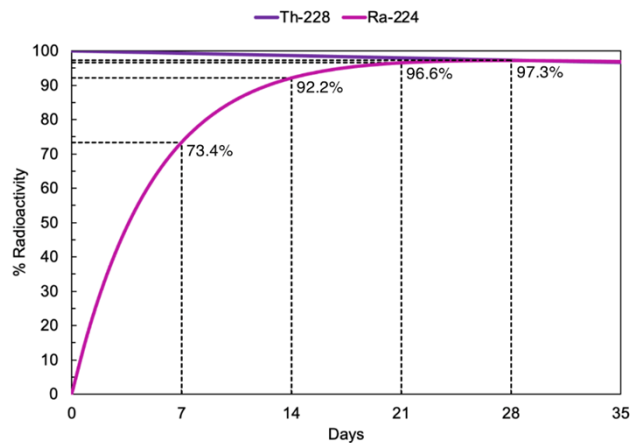
The supply chain is lower-risk and more robust than other therapeutic isotopes

Isotope Source	Isotope Purification	Product Manufacturing
 <p>Naturally occurring in mining waste Also produced in industrial nuclear processes Can be made on demand if needed</p>	 <p>Parent isotope Thorium-228 can be stored (2 yr half-life) ^{212}Pb purified from ^{228}Th or ^{224}Ra source in simple separation step</p>	 <p>VMT-α-GEN ^{212}Pb generator technology scales for commercial production Extremely pure isotope allows straight forward manufacturing process</p>
<p>All other therapeutic isotopes require capital-intensive infrastructure manufacturing processes (irradiation)</p>	<p>VMT-α-GEN enables shipping of isotope and purification of ^{212}Pb in one package</p>	<p>10.5 hr half life of ^{212}Pb allows for robust regional distribution of finished radiopharmaceuticals</p>

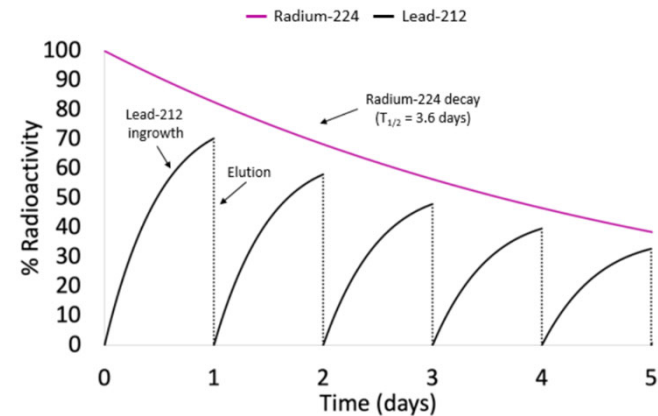
Parent Isotope Source

Key Isotopes for Supply: Th-228 and Ra-224

- Storage of thorium-228 (half-life of 1.9 years) allows for “on-demand” purification of Ra-224 and Pb-212
- Multiple purification/production methods for Th-228 with different starting materials and processes, including Ra-228 generators (half-life 5.7 years)
- Ra-224 (half-life 3.6 days) allows for continental shipping of material to network of finished product manufacturing sites (CDMOs)
- A weekly supply of Ra-224 can be purified daily to produce batches of Pb-212



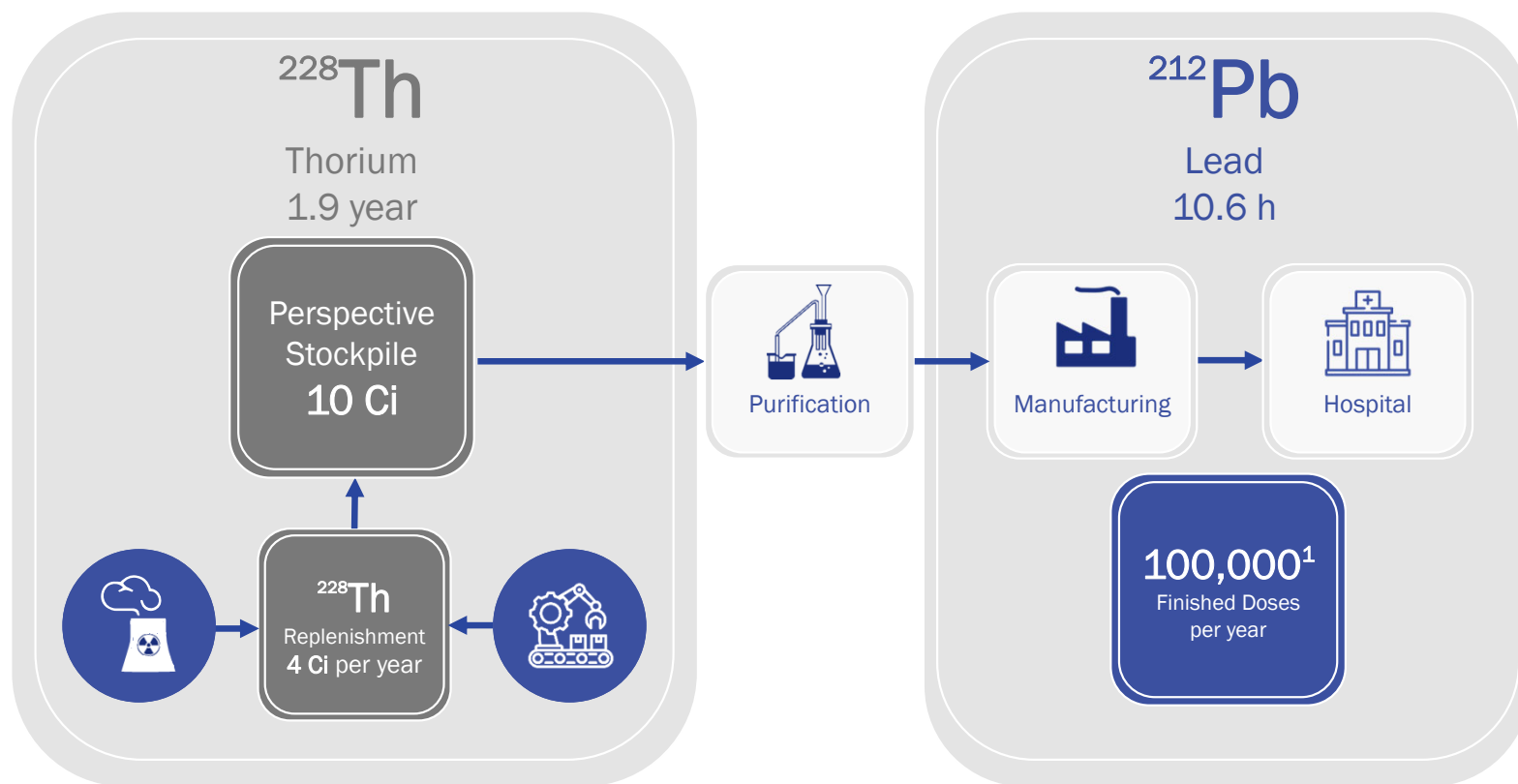
Ra-224 grows in naturally (without irradiation) from a Th-228 “source”



Pb-212 grows in naturally (without irradiation) from a Ra-224 “source”

^{212}Pb Dose Modeling from Parent Isotope

Replenishable ^{228}Th stockpile ensures supply of commercial quantities of ^{212}Pb for finished dose manufacture¹



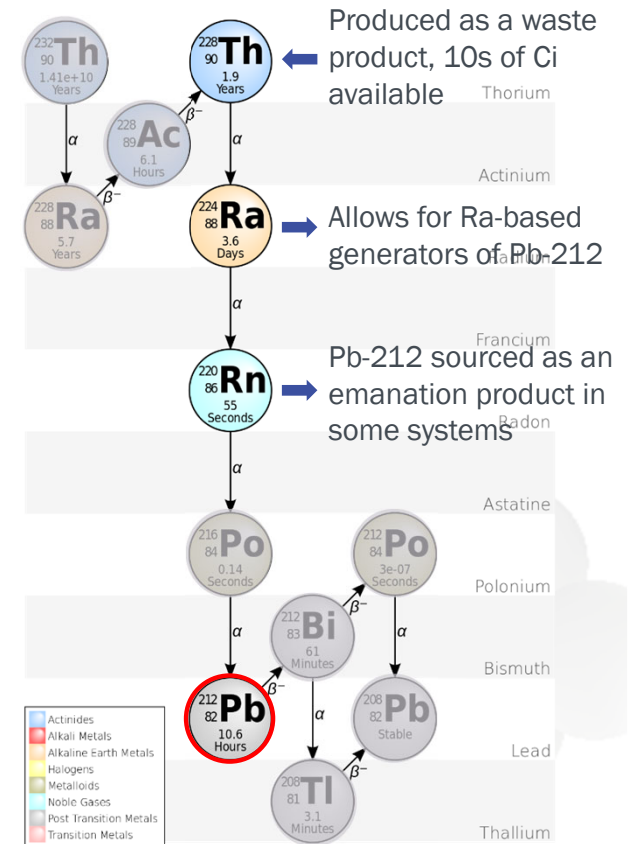
Parent Isotope Supply

Large quantities of precursor Th-228 available

- Thorium-228 is available as a natural isotope but is also produced as a waste product from the nuclear fuel cycle, and as a result of production of therapeutic isotope Ra-223 (marketed as Xofigo, Bayer)
- Both Ac-227 (the parent isotope of Ra-223) and Th-228 are created when DOE's ORNL irradiates radium-226 in the High Flux Isotope Reactor.¹
- The DOE therefore has 10s of curies of Th-228 available in a highly purified form
- Perspective Therapeutics estimates that such current quantities would suffice for approximately 150,000+ patient doses per year
- Perspective has a long-term supply agreement with the DOE for supply of Th-228

The availability of parent isotope in large quantities significantly de-risks supply of Pb-212 as a therapeutic isotope. In addition, it provides methodological flexibility for Pb-212, as there are many processes available for large-scale purification.

Natural decay,
no input
needed



Pb-212 Isotope Purification

Multiple purification paths to Pb-212 available

Small scale

- Similar in size to Ga-68 generators
- Useful for preclinical R&D and clinical trials
- Nimble, portable supply available for either local or regional production
- Typically chromatography column based
- Using Ra-224 as parent
- Shelf life approx. 1-2 weeks
- 1-2 doses per batch per day

Examples:

- DOE
- VMT- α -GEN



Medium scale

- “Desktop” generators
- Useful for clinical trials & limited commercial production
- Non-portable, fixed location within hot cell in local production facility
- Gas-phase separation of the Rn-220
- Shelf life approx. 1 year
- 1-3 doses per batch per day

Examples:

- Advancell, others



Commercial scale

- Hot cell-sized generators
- For commercial production
- Non-portable, fixed location within hot cell in regional production facility
- Either chromatography or gas-phase separation using Th-228 source
- Permanent installation, topped up with Th-228 approx every 3 to 6 mo
- Questions about scalability and licensing

Examples:

- Multiple In development



The production of Pb-212 is inherently scalable to demand, flexible due to different purification schemes and cost-effective due to existing isotope availability. This contrasts with other alpha-emitting isotopes which require large infrastructure to produce and purify.

^{212}Pb Supply via Reusable Desktop Isotope Generator



VMT- α -GEN

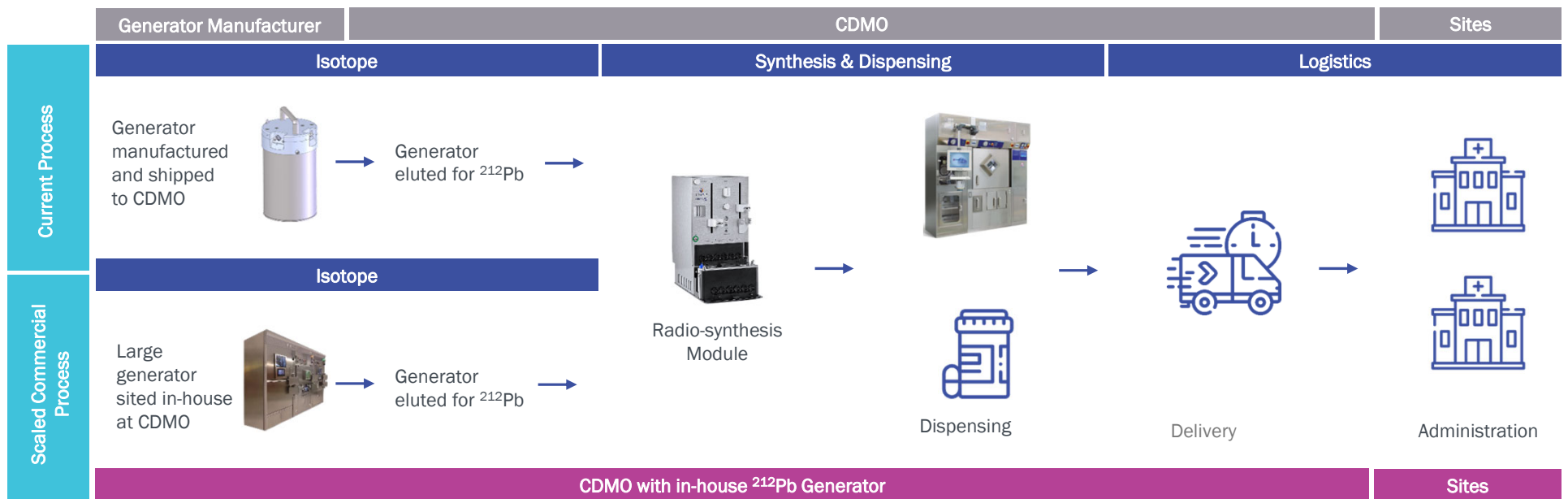
- Extensive feedstock from nuclear and mining waste material
- Long-term supply contract secured with US DOE
- On demand daily doses
 - Auto-regenerates overnight
 - ~1 week shelf life

Small, Elegant ^{212}Pb Isotope Generator

- Integrated lead shielded containment
- Simple inlet and outlet ports
- Radioactive feedstock for nearly 300 generators fits in a small vial

Scalable Manufacturing and Distribution Logistics

Perspective's plan to flexibly scale manufacturing to commercial levels (100,000+ doses per year)



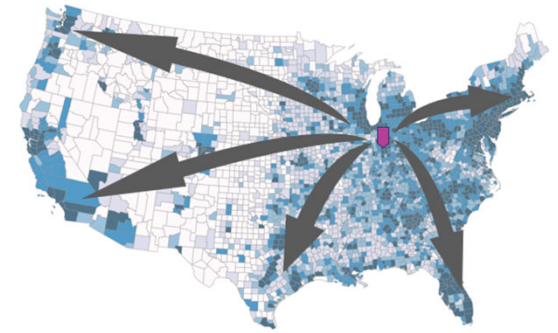
- Commercial supply will require the use of an isotope production system of larger scale than the current $^{224}\text{Ra}/^{212}\text{Pb}$ generators
- The current isotope separation process remains highly scalable with larger activity levels
- Regional CDMOs will have capabilities to expand capacity as needed as more ^{212}Pb products come on-line

Centralized vs Distributed Network Production

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

Single centralized manufacturing facility

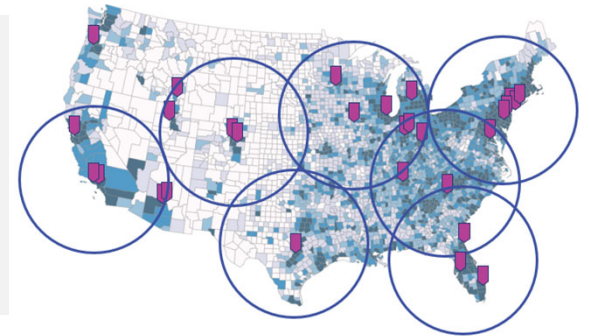
- Suitable for longer half-life isotopes (eg ^{177}Lu , ^{131}I , ^{225}Ac , ^{67}Cu)
- Allows for national/international production
- Shipping of finished product typically requires air and road transport
- **Single point of failure** (eg Novartis' PLUVICTO[®] production issues)



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

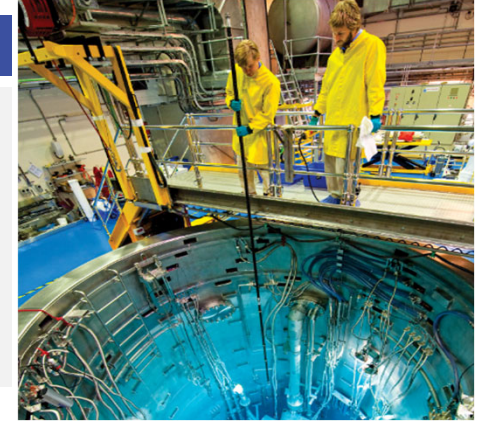


Isotope: Availability and Scalability at Clinical Development Stages

Isotope Production methods

Large, centralized capital-intensive infrastructure such as reactors, cyclotrons, LINACs etc.

- Suitable for longer half-life isotopes (eg. Lu-177, I-131, Ac-225, Cu-64/67, Pb-203 etc.)
- Allows for national/international production, shipping of finished product
- Somewhat vulnerable as redundancy can be expensive
- Large capital investment required (subsidized by government currently)



Vs.

Generator-based supply that can be deployed locally or regionally (Portable or in-house permanent installation)

- Suitable for shorter half-life isotopes with appropriate decay schemes (eg. Tc-99m, Pb-212, Ga-68)
- Requires multiple manufacturing sites across a network & local/regional finished product
- Allows for flexibility and redundancy, improving reliability of patient dose supply

Can be scaled for multi-dose manufacture at regional CDMOs with permanent in-house Pb-212 generator: Perspective's approach for commercialization



Isotope and Finished Product Landscape: Commercial Supply

	Centralized Isotope and Manufacturing - Competitors	Cost	Pb-212-labeled Commercial Perspective Products
Parent Isotope Source	<ul style="list-style-type: none"> Lu-177: Ytterbium-176 is expensive. Limited supply from Russian sources. Purification is a cumbersome process Ac-225: Limited access to parent supplies such as Ra-226, U-233 	High-mid vs Low	<ul style="list-style-type: none"> Th-228 available in very plentiful, pure supply Allows for stockpiling of precursor parent isotope
Isotope Production Method	<ul style="list-style-type: none"> Multiple production methods available, some lead to contaminants Typically requires dedicated nuclear reactors or large accelerators 	High-mid vs Low	<ul style="list-style-type: none"> No need for irradiation – Th-228 decays to Ra-224 and Pb-212
Purification of Isotope	<ul style="list-style-type: none"> Extremely large hot cells required for initial separation Can be off site at third parties in dedicated facilities 	High vs Mid	<ul style="list-style-type: none"> Occurs on-site prior to finished product within existing CDMO facilities (commercial)
Isotope Shipping	<ul style="list-style-type: none"> Isotope frequently shipped to site for finished product manufacture 	Mid vs Low	<ul style="list-style-type: none"> Parent isotope at site already (commercial)
Finished Product Manufacturing	<ul style="list-style-type: none"> Typically centralized at one large site 	Similar (1 \$\$\$ site vs multiple \$)	<ul style="list-style-type: none"> Distributed network of scalable regional manufacturing sites
Logistics	<ul style="list-style-type: none"> Distributed nationally 	Similar	<ul style="list-style-type: none"> Distributed by regional facilities
Summary	Long supply chains, higher 3 rd Party risk, complex processing, less redundancy, more labor and capital intensive, less environmentally friendly, not scalable to demand	Higher up front for centralized approach, but similar costs post finished product	Short supply chains, vertical integration of activities, simple processing, greater redundancy, less capital intensive, more environmentally friendly, scalable to demand

