

Targeted alpha particle therapy for cancer.

Trickle Microcap Conference Denver, CO

November 11, 2024

NYSE: CATX

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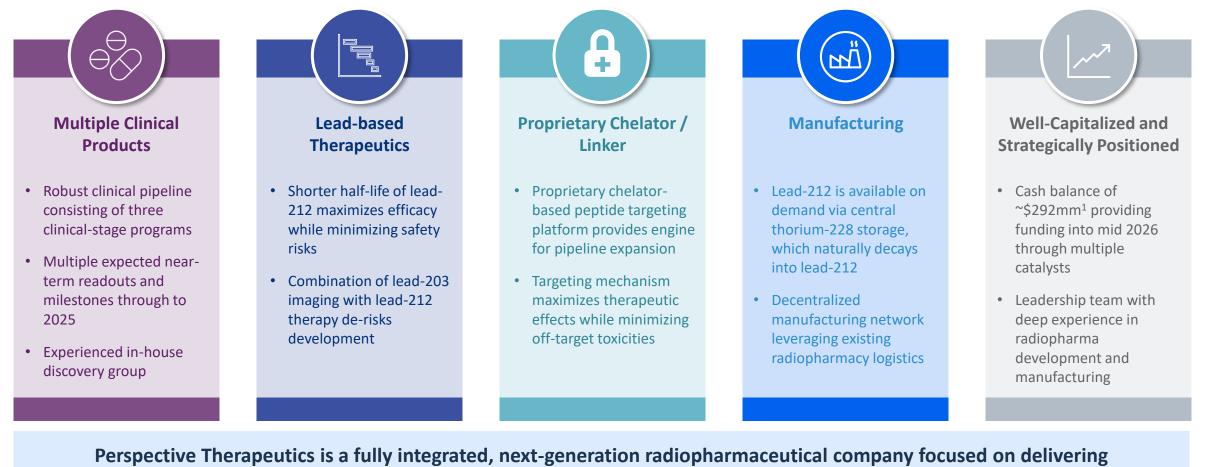
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### Developing the Next Generation of Targeted Radiopharmaceutical Therapies (RPT)

Key Differentiators Enable an Expanded Therapeutic Window and De-risked Manufacturing and Development



targeted alpha particle therapies across a broad range of cancers with high unmet need



# Deeply Experienced Management Team in RPT & Oncology Drug Development



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

H

Thijs Spoor Chief Executive Officer





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

Jonathan Hunt Chief Financial Officer





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

Markus Puhlmann, MD MBA Chief Medical Officer

| CFORGETOWN<br>UNIVERSITY<br>LMU<br>McDancugh<br>Scroot of Bisarts |                 | <b>ðSeagen</b> <sup>,</sup> |
|---|-----------------|-----------------------------|
| I MERCK   | BAYER<br>E<br>R | AMGEN                       |



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

Frances Johnson, MD Chief Innovation Officer





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

Michael Schultz, PHD Chief Science Officer





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

Amos Hedt Chief Business Strategy Officer



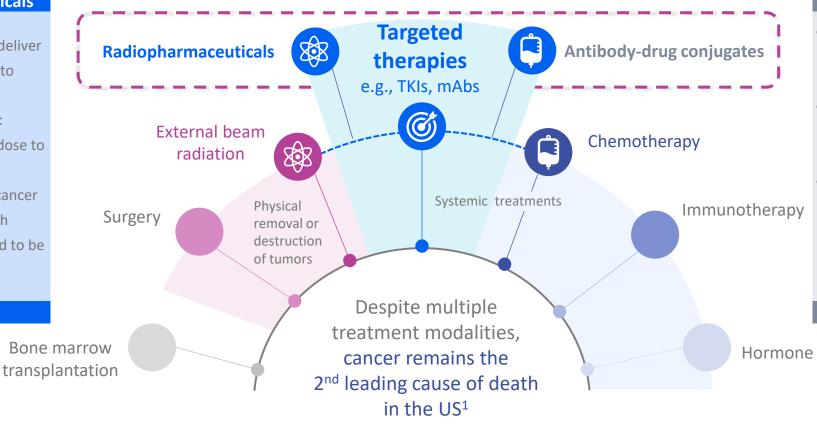


# Radiopharmaceutical Therapy Poised to Revolutionize Oncology Treatment

Technology Developments Enable Higher Potency Payloads with Cancer-Specific Targeting

#### Radiopharmaceuticals

- Targeted molecules deliver radioactive isotopes to cancer
- Therapeutic window: limited by radiation dose to healthy tissues
- The number of U.S. cancer survivors treated with radiation is estimated to be 4.2 million in 2030<sup>2</sup>



"Next Generation Therapies" combining cytotoxicity with cancer-specific targeting

#### **ADCs**

- Antibody-based targeting delivers chemotherapy to cancer
- Therapeutic window: limited by unstable linker/toxin
- The number of patients in high income countries treated with chemotherapy drugs is estimated to be 4.7 million per year in 2024<sup>3</sup>

Hormone therapy



### Radiopharmaceuticals are a Pillar of Oncology Treatment

Unique Mechanism of Action Offers Pan-Cancer Opportunities

Molecularly Targeted Radiation

Optimized Patient Selection

Monotherapy Activity and Combination Synergies

**Outpatient Friendly** 

Unique Business Opportunity 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** 

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** 

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

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** 

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** 

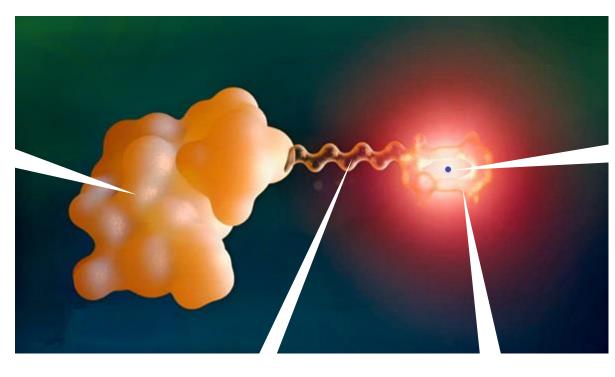


### Perspective's Radiopharmaceutical Optimization Process

Unique Payload Delivery Technology Offers Pan-Cancer Opportunities

#### **Targeting Peptide**

Engineered for cancer specific receptors to ensure highly directed uptake



#### Isotope

<sup>203</sup>Pb for SPECT imaging or

<sup>212</sup>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



# **Delivering Momentum Across Solid Tumor Programs**

Platform for consistent generation and development of new assets

| Program         | Target      | Tumor<br>Types                | Nominate<br>Candidate | IND<br>Filing         | Initiate<br>Cohort 1 | Enrolled<br>Cohort 2 | Preliminary<br>Update                        | RP2D <sup>2</sup><br>Status                                      | Key future milestones & expected timelines  |
|-----------------|-------------|-------------------------------|-----------------------|-----------------------|----------------------|----------------------|--|--|---|
| VMT-α-NET       | SSTR2       | Neuro-<br>endocrine<br>Tumors |                       |                       |                      |                      | (Investigator led<br>research <sup>1</sup> ) | Update to timing<br>expected late 2024                           | <u>Cohorts 1&amp;2</u><br>Initial results: 2H 2024<br>Duration of results: 2025<br><u>Cohort 3:</u><br>Pending FDA interaction                                    |
| VMT01/<br>VMT02 | MC1R        | Metastatic<br>Melanoma        |                       |                       |                      |                      | Expected<br>2H 2024                          | ICI combo<br>study with<br>nivolumab<br>results expected<br>2025 | <u>Cohorts 1&amp;2</u><br>Initial results: 2H 2024<br>Duration of results: 2025<br><u>Combination cohorts</u><br>Initial dosing: 2H 2024<br>Initial results: 2025 |
| PSV359          | FAΡ-α       | Multiple<br>solid tumors      |                       | Expected<br>late 2024 | Expected<br>2025     |                      |  |  |   |
| Various         | PSMA        | Prostate                      | From a set o d        |                       |                      |                      |  |  |   |
| Discovery       | Undisclosed | Breast                        | Expected<br>late 2024 |                       |                      |                      |  |  |   |
| Programs        | Undisclosed | Lung                          |                       |                       |                      |                      |  |  |   |

<sup>1</sup>Investigator led research in India in patients with neuroendocrine tumor and medullary thyroid carcinomas.



 $^{2}$  RP2D = recommended Phase 2 dose; ICI = immune check point inhibitor.

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

Alpha Particles Provide Numerous Benefits Over Currently Used Beta Particle Radiotherapies

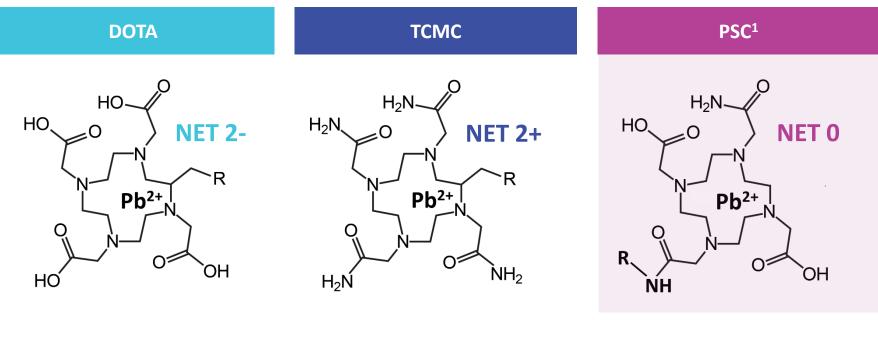
- With a much higher atomic mass, alpha (α) particles generate more energy and travel a shorter distance compared to beta (β) particles, making them more cytotoxic, while reducing their off-targeting effects on healthy tissue
- Alpha radiation causes direct lethal double-stranded DNA breaks, vs indirect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

|                          | Lead ( <sup>212</sup> Pb) | lodine ( <sup>131</sup> l) | Lutetium ( <sup>177</sup> Lu) | Actinium ( <sup>225</sup> Ac) | Implication <sup>1</sup> |
|--------------------------|---------------------------|----------------------------|-------------------------------|-------------------------------|--------------------------|
| 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 <sup>212/203</sup>Pb

Perspective's Enabling Technology for Pb-based Radiopharmaceuticals



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 <sup>212</sup>Bi alpha-emitting daughter up to 36%<sup>2</sup>

Commercially Available

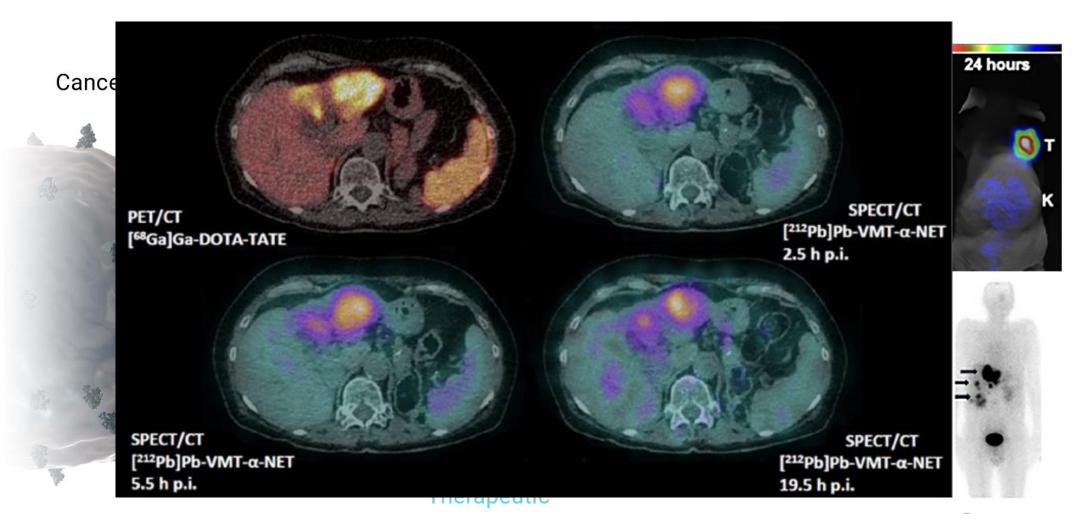
**Perspective's Chelator** 

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



### Today's Theranostic Approach: One Target, One Molecule, One Chelator, One Isotope

Example: SSTR2 peptide chelated to <sup>203</sup>Pb for imaging; <sup>212</sup>Pb for therapy







# Neuroendocrine Tumors: VMT- $\alpha$ -NET

Targeting the somatostatin receptor to treat rare neuroendocrinetype cancers



### Neuroendocrine Tumors: VMT- $\alpha$ -NET

#### Targeting the Somatostatin Receptor to Treat Neuroendocrine and Other Cancers

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- $\alpha$ -NET will potentially expand into this population as well as PRRT naïve patients

#### **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

- Small cell lung cancer
- Breast cancer
- Meningioma
- Nasopharyngeal carcinoma
- Thyroid cancer
- Merkel cell carcinoma
- Neuroblastoma



# Perspective's Platform Demonstrates Superior Therapeutic Window: VMT- $\alpha$ -NET

In House Discovery Capabilities Deliver Differentiated Molecules

#### Key Takeaways vs Generic Compounds

#### Preclinical Studies: Decreased Off-Target Toxicity, **Increased Tumor Uptake and Retention**

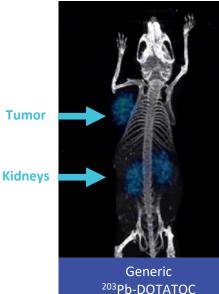


SSTR2 tumor model demonstrates superiority of VMT- $\alpha$ -NET to generic compounds



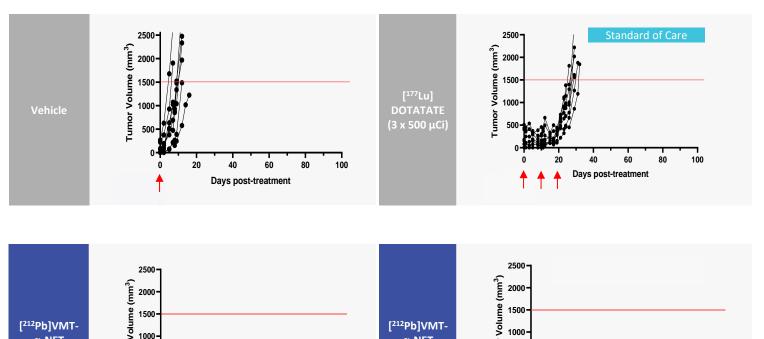
8-fold improved tumor uptake with decreased kidney retention







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



α-NET

(4 x 30 μCi)

umor



Days post-treatment

Drug Administered

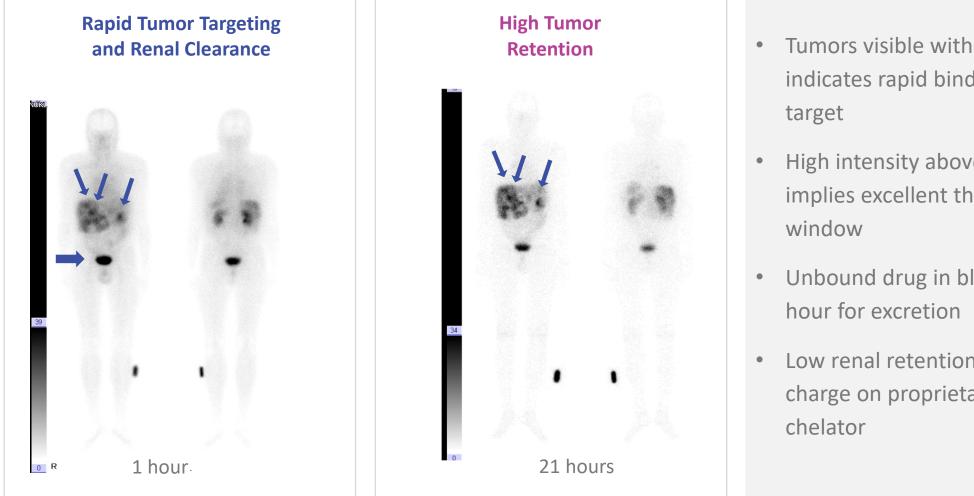
Days post-treatment

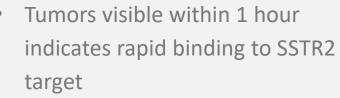
1000

α-NET

(1 x 120 µCi)

# <sup>203</sup>Pb SPECT Imaging Reveals Favorable VMT- $\alpha$ -NET Properties<sup>1</sup>



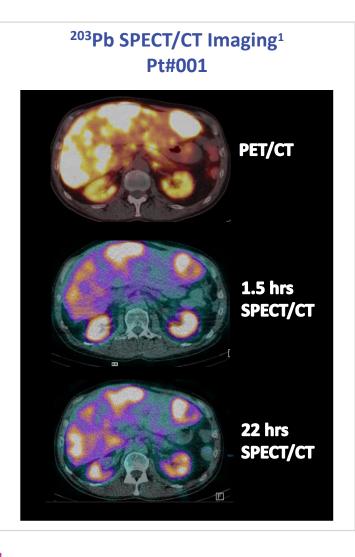


- High intensity above background implies excellent therapeutic
- Unbound drug in bladder within 1
- Low renal retention due to neutral charge on proprietary Pb-specific

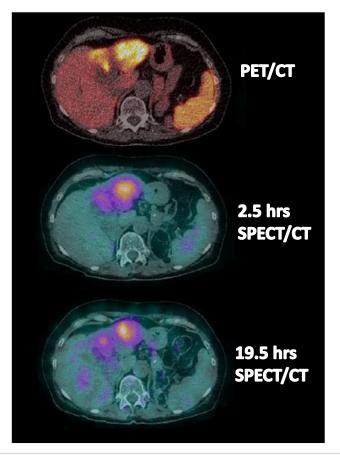


# <sup>212</sup>Pb SPECT/CT Imaging Confirms VMT-α-NET Tumor Uptake

Diagnostic and Therapeutic Show Same Uptake and Retention Characteristics



#### <sup>212</sup>Pb SPECT/CT Imaging<sup>2</sup> Pt#009



- Both <sup>203</sup>Pb and <sup>212</sup>Pb can be imaged directly using SPECT
- SPECT/CT shows very rapid tumor uptake and retention of [<sup>212</sup>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



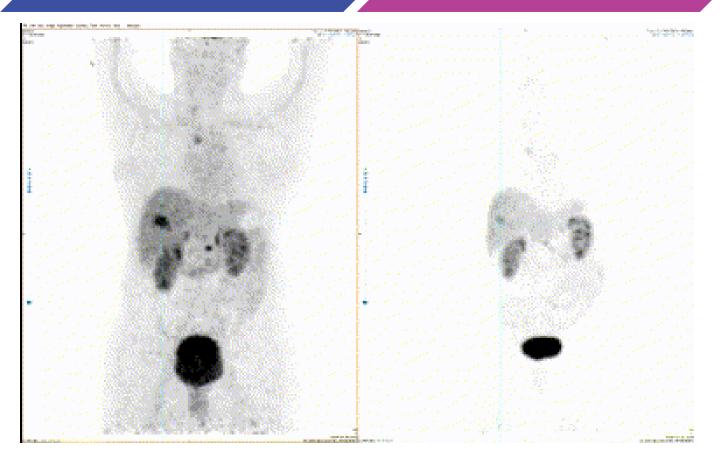
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# Significant Response After Single Dose of [<sup>212</sup>Pb]VMT- $\alpha$ -NET

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

Tumor Before Treatment

Tumor After 1 Dose



- <sup>68</sup>Ga-DOTA-NOC PET
  images at base line and
  post 1st dose of
  [<sup>212</sup>Pb]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

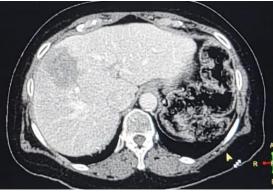
Metastatic NET Pancreas with Adrenal Crisis

#### Tumor Before Treatment

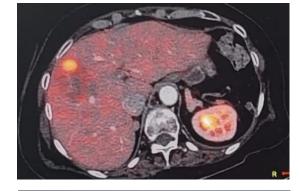
#### Tumor After 1 Dose

#### Tumor After 3 Doses

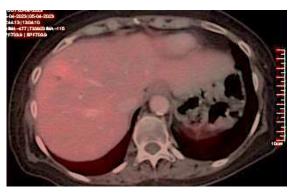




(S.ACTH)<sup>1</sup>- 790 pg/ml









S.ACTH – 96 pg/ml



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

| Primary Objective:   | To determine the MTD/MFD of [212PB   | Imaging:  |  | FDA approved SSTR2 PET/CT  |  |   |  |
|--|--|---|--|--|--|---|--|
| Population:  | Unresectable or metastatic SSTR2-pc<br><b>PRRT naïve</b> ( <i>"First line"</i> ) | Therapeutic Dose:<br>Estimated Time to Primary<br>Completion: |  | <ul><li>2.5–10 mCi dose escalation with fixed dosing every 8 weeks for up to 4 cycles</li><li>~18 months</li></ul> |  |   |  |
| Design Methodology:  | Bayesian mTPI2 based on iterative to monitoring                                  | oxicity probability   | Dosimetry:   |  | To be assessed during screening for cohorts 1 & 2 using 5-7 mCi $[^{203}Pb]VMT-\alpha-NET$ |   |  |
|  | Escalation phase   |   |  | Cohort 4<br>[ <sup>212</sup> Pb]VMT-α-NET  | Dose   | Expansion phase   |  |
|  | Recruited<br>Cohort 2  | Cohort 3<br>[ <sup>212</sup> Pb]VMT-α·<br>n = 3 - 8 / 7.5 r   | -NET   | n = 3 – 8 / 10 mCi x   | Phase 2  | Expansion Cohort<br>[ <sup>212</sup> Pb]VMT-α-NET<br>RP2D mCi x 4 |  |
| Recruitment Complete<br>Cohort 1<br>[ <sup>212</sup> Pb]VMT-α-NET<br>n = 2 / 2.5 mCi x 4 | [ <sup>212</sup> Pb]VMT-α-NET  |   | tion possible for Cohort 2 – 4<br>ing for intermediate doses |  | Recommended  | Expansion into non-NET<br>indications (eg SCLC)<br>also possible  |  |





# Pan Cancer Target: PSV359

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



### Pan Cancer Program: PSV359

#### Novel Peptide Targeting Fibroblast Activation Protein alpha (FAP-a)

Fibroblast Activation Protein alpha (FAP-a) is expressed in the tumor stoma of many epithelial cancers and on the cell surface of other tumor types

IND-enabling preclinical studies complete IND for US Therapeutic Dose Escalation Trial under preparation

Preclinical data indicates superiority of therapeutic effect vs other FAP-targeted therapeutics

First-in-human imaging with [<sup>203</sup>Pb]PSV359 in multiple tumor types indicates rapid uptake, tumor retention and fast clearance of and [<sup>68</sup>Ga]VMT02

#### Potential [<sup>212</sup>Pb]PSV359 indications:

#### FAP Expression on Tumor Stroma

- Non-Small Cell Lung Cancer
- Pancreatic
- Hepatocellular Carcinoma
- Colorectal Cancer
- Breast Cancer
- Ovarian Cancer
- Others

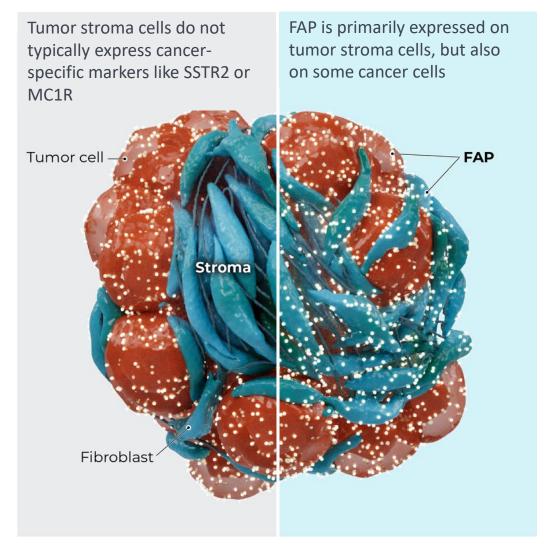
#### FAP Expression on Tumor Cells

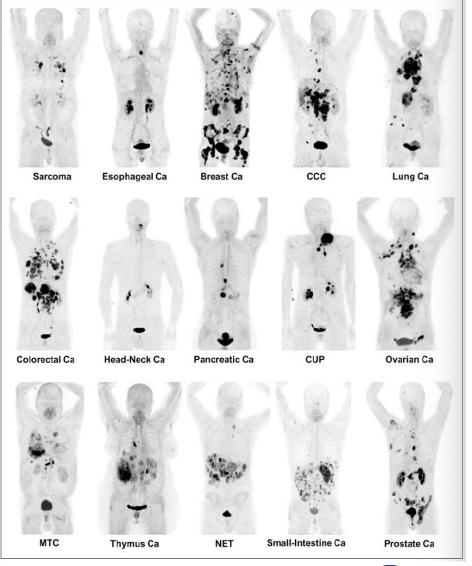
- Sarcoma
- Mesothelioma
- Others



## Pan Cancer Program: PSV359

Fibroblast Activation Protein alpha ("FAP") is a Pan Cancer Target



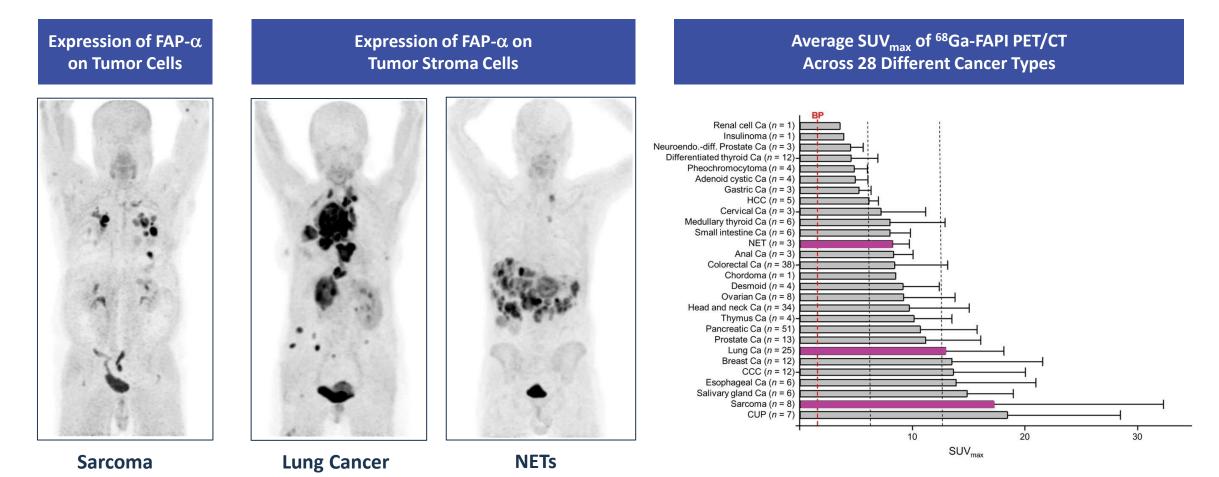


Kratochwil et al., JNM, 2019



## Fibroblast Activation Protein Shows High Uptake Across a Range of Tumor Types<sup>1</sup>

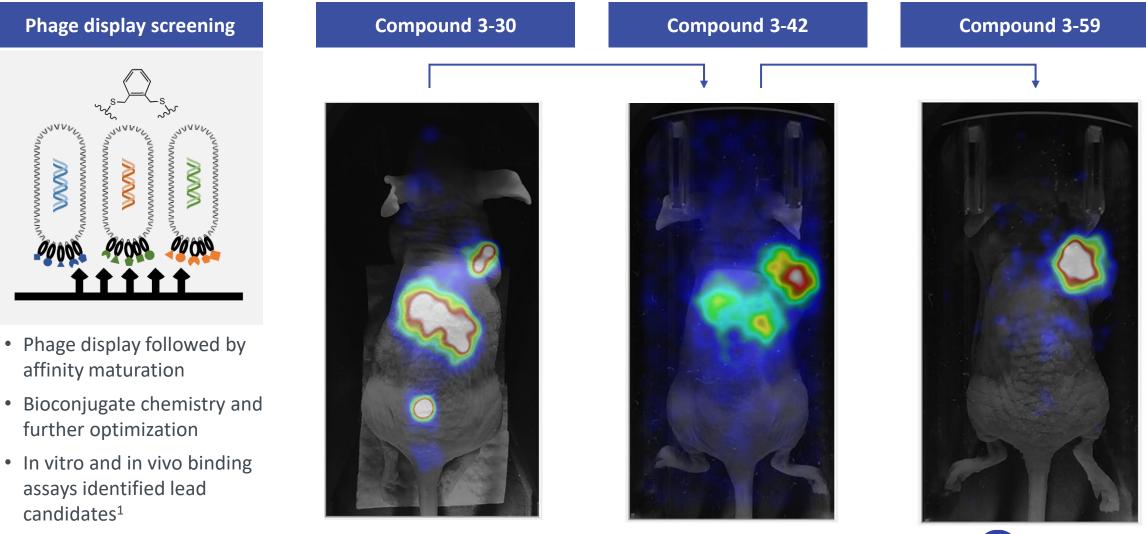
Multiple Imaging Products in Development Such as <sup>68</sup>Ga-FAPi, But Significant Therapeutic Opportunity Remains





# Fibroblast Activation Protein-targeted Novel Compound Development

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

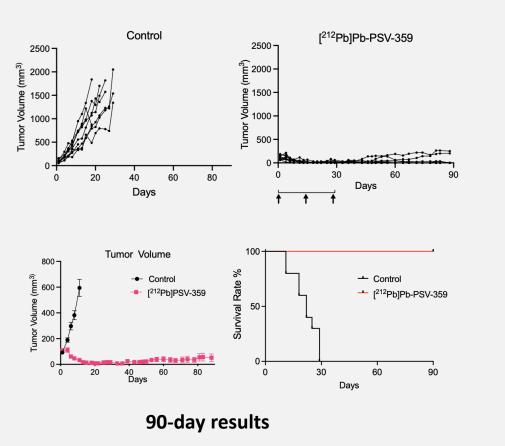




# [<sup>212</sup>Pb]PSV359 Demonstrates Preclinical Efficacy in Human Fibrosarcoma Model

Compares favorably against other therapeutic products in development<sup>2</sup>

#### Preclinical [<sup>212</sup>Pb]PSV359 Targeted Alpha Therapy<sup>1</sup>



hFAP-HT1080 Fibrosarcoma Model – Expressing hFAP-a

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<sup>1</sup> · Aileen Hoehne<sup>1</sup> · Anne Bredenbeck<sup>1</sup> · Anne Schumann<sup>1</sup> · Minh Nguyen<sup>2</sup> · Eberhard Schneider<sup>1</sup> ·

#### Summary Table

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

#### 40-day results

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

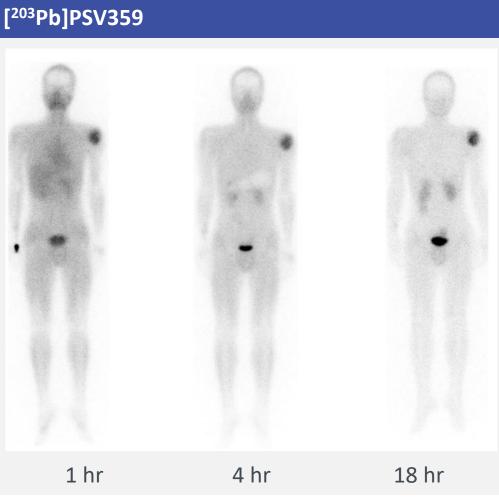


# FIH Imaging of [<sup>203</sup>Pb]PSV359 in Different Types of Cancers

Patient 1 Chondroblastic Osteosarcoma



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



#### [<sup>203</sup>Pb]PSV359 SPECT/CT

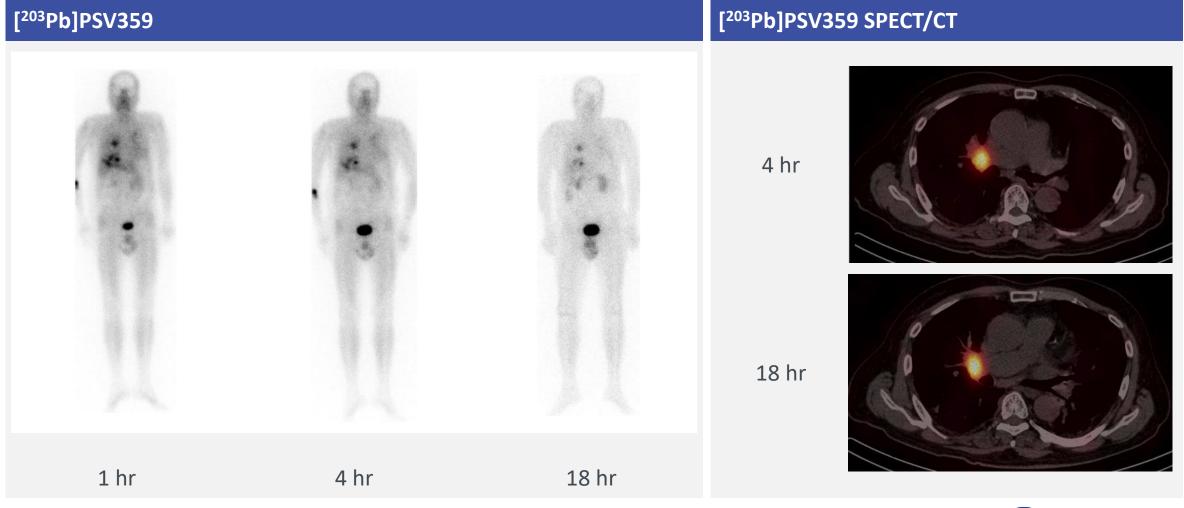


#### Lesion in head of left humerus



# FIH Imaging of [<sup>203</sup>Pb]PSV359 in Different Types of Cancers

Patient 2 Neuroendocrine Tumor

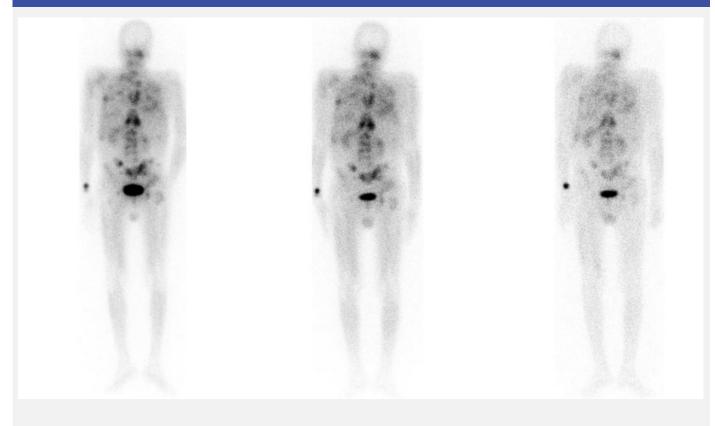




# FIH Imaging of [<sup>203</sup>Pb]PSV359 in Different Types of Cancers

Patient 3 Lung Adenocarcinoma

### [<sup>203</sup>Pb]PSV359

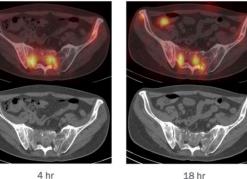


4 hr

18 hr

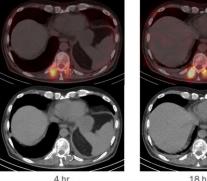
[<sup>203</sup>Pb]PSV359 SPECT/CT

#### Lytic lesion in sacrum



2011

Lytic lesion in thoracic vertebra







1 hr

### Summary – PSV359 FAP- $\alpha$ Program

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

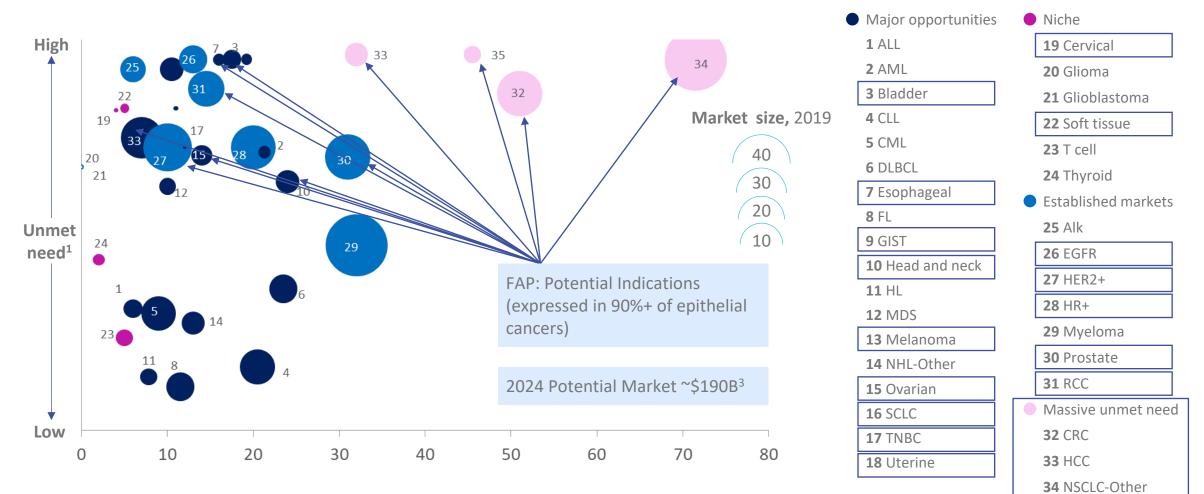
- FAP- $\alpha$  is a pan-cancer target that is highly expressed in many cancers
- Perspective's in-house discovery team has developed an optimized peptide with potential best-in-class characteristics as demonstrated in preclinical models
- First in human clinical SPECT/CT imaging suggests the tumor 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





### Fibroblast Activated Protein $\alpha$ is a Pan Cancer Target with Significant Market Potential

Tumor types with large patient populations and high unmet need



**35** Pancreatic

HERAPEUTICS

#### Patient size,<sup>2</sup> thousands

<sup>1</sup>Unmet need defined as one- minus five-year survival rate (overall for heme, metastatic for solid). <sup>2</sup> Patient size calculated as annual incidence for heme, and larger of mortality and metastatic incidence for solid.

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

# **Centralized vs Distributed Network Production**

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

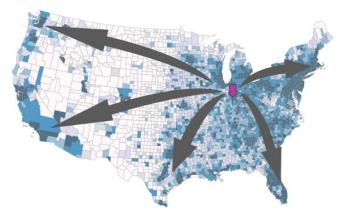
#### Single centralized manufacturing facility

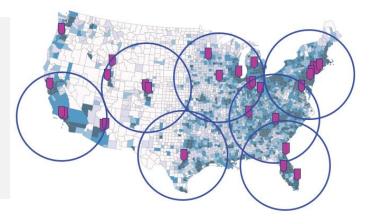
facilities

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



- Suitable for shorter half-life isotopes (eg <sup>212</sup>Pb, <sup>211</sup>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







# Thank you!

# **Questions?**

