203{}^{\text{Pb}}/212{}^{\text{Pb}} \text{ Image-guided alpha-particle therapy for cancer. Progress and Metrology Challenges}

February 2024

NYSE: CATX
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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 develops patent-protected best-in-class intellectual property**
**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 Response
- 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
Management Team
Deep Experience in Radiopharmaceuticals and Oncology Drug Development

Thijs Spoor
Chief Executive Officer
20+ years of expertise in biotechnology companies; public and private companies; oncology and nuclear pharmacy

Markus Puhlmann, MD MBA
Chief Medical Officer
20+ years of oncology drug development across all phases, experience coordinating multiple regulatory filings

Michael Schultz, PhD
Co-Founder and Chief Science Officer
20+ years industry and research experience in radiopharmaceuticals; inventor of Perspective radiopharmaceutical 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
Co-Founder and Chief Innovation Officer
20+ years in clinical trials execution, managing academic research programs, and start-up of CareDx, Inc.

Amos Hedt
Chief Business Strategy Officer
20+ years of expertise in early-stage pharmaceutical and biotech drug development; 10+ years in radiopharmaceuticals
# Platform Expansion Engine

Two Lead Programs in Clinic and Broad Proprietary Pipeline

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Discovery</th>
<th>Human Clinical Imaging</th>
<th>First in Human Therapy</th>
<th>Phase 1/2</th>
<th>Phase 3</th>
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<tbody>
<tr>
<td>VMT-α-NET</td>
<td>Neuroendocrine cancer</td>
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<td></td>
<td>Pheochromocytomas, paragangliomas</td>
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<td>Small cell lung cancer</td>
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<td>VMT01</td>
<td>Melanoma (MC1R)</td>
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<tr>
<td>VMT02 (PET agent)</td>
<td>Melanoma (imaging of MC1R)</td>
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<td>Program 3 (Novel peptide)</td>
<td>Multiple solid tumors</td>
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<tr>
<td>PSV401 (Radio-hybrid)</td>
<td>Prostate (PSMA imaging &amp; therapy)</td>
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<td>Program 5 (Novel peptide)</td>
<td>Prostate, Breast</td>
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<td>Other Programs</td>
<td>Solid and hematological tumors</td>
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Lead-212 ($^{212}$Pb): The Optimal Therapeutic Isotope

Alpha Particles Provide Numerous Benefits Over Currently Used Beta Particle Radiotherapies

- With a much higher atomic mass, alpha ($\alpha$) particles generate more energy and travel a shorter distance compared to beta ($\beta$) 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 ($\beta$) radiation.
- Cell death expected – NO resistance.
- Greater therapeutic efficacy expected to improve outcomes with better safety.

<table>
<thead>
<tr>
<th></th>
<th>Lead ($^{212}$Pb)</th>
<th>Iodine ($^{131}$I)</th>
<th>Lutetium ($^{177}$Lu)</th>
<th>Actinium ($^{225}$Ac)</th>
<th>Implication $^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emission Profile</td>
<td>Alpha</td>
<td>Beta</td>
<td>Beta</td>
<td>Alpha</td>
<td>Potent</td>
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<tr>
<td>Half Life</td>
<td>0.46 days</td>
<td>8 days</td>
<td>6.7 days</td>
<td>10 days</td>
<td>High dose-rate</td>
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<td>Off Target Toxicity Risk</td>
<td>Low</td>
<td>Very high</td>
<td>Low</td>
<td>High</td>
<td>Best</td>
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<td>Supply</td>
<td>High</td>
<td>High</td>
<td>Low</td>
<td>Low</td>
<td>Abundant</td>
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<tr>
<td>Cost of Production</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>High margin</td>
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</table>

$^1$Company estimates and assumptions based on current literature and known physical constants.
Pb-based Theranostics Enable Both Diagnosis and Targeted Treatment of Cancer

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

- **Imaging**
  - Dosimetry: $T_{1/2} = 52\text{ h}$

- **Therapeutic**
  - Dosimetry: $T_{1/2} = 11\text{ h}$

$^{203}\text{Pb}$ can be used to establish $^{212}\text{Pb}$ pharmacokinetics

Cancer Cell

Targeting ligand

Linker

$^{203}\text{Pb}$

$^{212}\text{Pb}$

Patient selection
Neuroendocrine Tumors: VMT-α-NET

Targeting the somatostatin receptor to treat rare neuroendocrine-type cancers
VMT-α-NET Currently in Phase1/2a Studies: Key Facts

Targeting somatostatin receptor type 2 (SSTR2) for the imaging and treatment of neuroendocrine tumors

Initiated first-in-human imaging (2021) & therapy (2022) under compassionate use

Fast Track Designation for first line therapy received October 2022
Therapeutic Trial in first line setting currently recruiting under open IND

US Phase 1 prospective dosimetry study in PRRT refractory patients recruiting at the University of Iowa
VMT-α-NET Shows Significant Improvement vs Standard of Care in Preclinical Models

Superior Efficacy with Single Dose or Multiple Administrations

[212Pb]VMT-α-NET (1 x 120 µCi)

[177Lu]DOTATATE (3 x 500 µCi)

[212Pb]VMT-α-NET (4 x 30 µCi)
Rapid Tumor Targeting and Renal Clearance

High Tumor Retention

- 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

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

Muller et al., Clin. Nucl. Med. 2023
$^{212}$Pb SPECT/CT Imaging Confirms VMT-α-NET Tumor Uptake

Diagnostic and Therapeutic Show Same Uptake and Retention Characteristics

- 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
Almost Complete Response After 3 Doses of $[^{212}\text{Pb}]\text{VMT-} \alpha\text{-NET}$

Metastatic NET Pancreas with Adrenal Crisis – PET/CT

(S.ACTH)$^1$ – 790 pg/ml

S.ACTH – 96 pg/ml
### 212Pb is Plentiful, Storable, Scalable & Suitable for Distributed Logistics

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

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

Where the drug goes = where the alpha particle is deposited

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

\(^1\)Mirzadeh et al., Radiochimica Acta, 1993
225Ac Isotope Decay Chain and Potential for Off-Target Toxicity

Alpha-particle emission imparts sufficient “recoil” energy to break chemical bonds.
Summary

Thank you!

- Cancer targeted alpha-particle radionuclide therapy for cancer emerging as a potent approach to cancer treatment
- $^{212}\text{Pb}$ has ideal properties for cancer therapy
- Imaging of $^{203}\text{Pb}$ and $^{212}\text{Pb}$ are powerful tools for radiopharmaceutical development and patient care
- Decay series of alpha-particle emitters has presented a measurement challenge to the metrology community