William Blair

Equity Research
Healthcare | Biotechnology

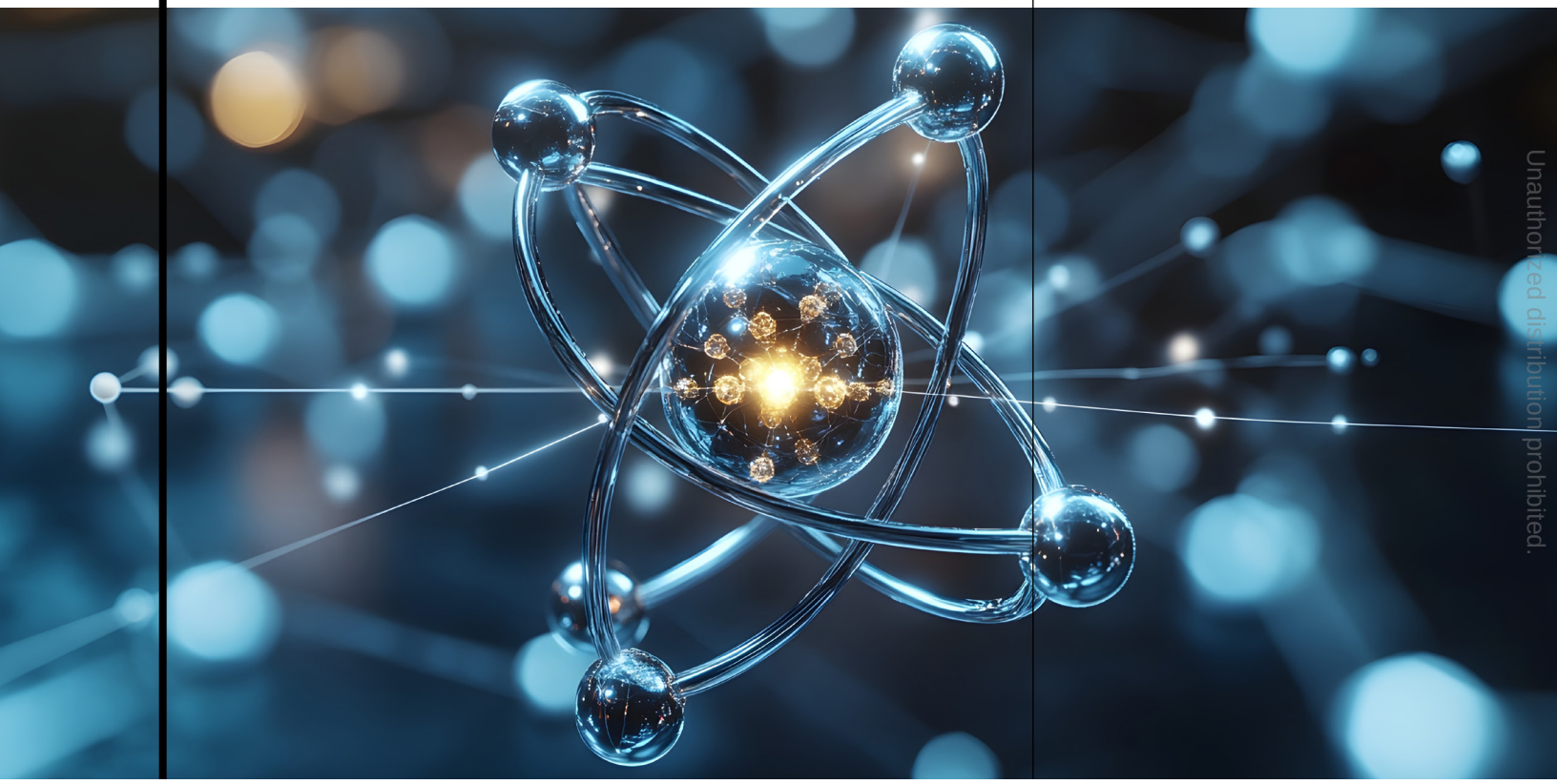
September 1, 2026
Industry Report

**Andy T. Hsieh, Ph.D.** +1 312 364 5051

**Alexandra V. Ramsey, Ph.D.** +1 312 801 7785

**Kelsey Lucerne, Ph.D.** +1 312 364 8097

# Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Fifth Edition



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# Introduction

We believe the radiopharmaceutical industry represents one of the most compelling secular growth opportunities in biotech in the next three to five years. Defying the conventional belief that it remains a niche market, we are optimistic that the recent resurgence in investor and big pharma interest that culminated in four high-profile acquisitions that closed throughout 2023 and 2024 (Point Biopharma by Eli Lilly, RayzeBio by Bristol Myers, Fusion Pharma by AstraZeneca, and Mariana Oncology by Novartis), coupled with Novartis's late-2024 increase in Pluvicto peak sales guidance (to $5 billion, from $3 billion previously), will continue to drive investment in the field. Year-to-date, over $1 billion has been raised in public financing by radiopharmaceutical companies (including the $318 million IPO of Aktis Oncology) and nearly $2 billion has been raised when also including private financing. We believe that over the next few years, the field will reach an inflection point as the therapeutics class emerges from a niche modality to become one of the centerpieces of the cancer treatment paradigm. In our view, Novartis is spearheading that effort, and in the United States, more than 880 sites are administering Pluvicto, representing year-over-year growth of nearly 40%. In addition, Pluvicto is expanding its penetration in the prostate cancer treatment paradigm following its recent approval in the metastatic hormone-sensitive setting.

As the market continues to grow, it is our aim to provide a yearly update on radiopharmaceuticals to serve as a resource for investors who would like to gain knowledge and understanding of this rapidly evolving space that has attracted a significant inflow of investment. Our first edition (see: Bioluminescence—Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals) provided an in-depth analysis of the field at large, and we refer readers to that report for a historical background on the field and fundamental nuclear chemistry concepts. In our second edition (see: Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Second Edition), we focused on elucidating the supply chain portion of the industry, given that we view this as one of the more obscure and difficult-to-understand and -visualize areas. We also provided an overview of the various medically relevant radioisotopes that are being explored for therapeutic applications, a description of current and future trends, and a comprehensive list of radiopharmaceutical companies in both the therapeutic and diagnostic fields, though we focused our discussion on the therapeutic application. In the third edition (see: Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Third Edition), we provided a brief update on the radiopharmaceutical field, including recent financing, the current company landscape, clinical updates, and targets of interest (again focusing on the therapeutic aspect of the industry).

In the fourth edition (see: Illuminating the Road Less Traveled in Biotech: Radiopharmaceuticals – Fourth Edition), we took a departure from the therapeutic landscape and focused instead on the role of diagnostics. Given that we view the PET imaging market as a promising area of growth for radiopharmaceuticals, we aimed to elucidate the evolving role of PET in the context of diagnosing Alzheimer's disease. We believe this application represents a material use-case for radiopharmaceuticals beyond oncology and provides an example of the diagnostic power of medically relevant radioisotopes.

In this current edition, we again provide a market update, focusing on financings, recent and upcoming clinical data updates, and the current landscape of radiopharmaceutical companies and related assets.

# Radiopharmaceutical Market Update

**Market Size and Trajectory**

Taking into account the increased number of potential addressable oncology indications, owing to the rise in new targets under investigation for radiopharmaceuticals, we have increased our TAM estimate (exhibit 1 and 2). Our base-case assumption is now $35 billion, up from $31 billion previously, while our bull-case assumption is now $68 billion, up from the prior $60 billion. Our bear-case assumption remains roughly the same at $4.6 billion.

**Exhibit 1**
**Radiopharmaceuticals**
**Potential Future Total Market Size of the Therapeutic Radiopharmaceuticals Industry in the United States**

| Oncology Indication | Molecular Target (Clinical) | Molecular Target (Preclinical) | Total U.S. Patients*[1] | Net Realized Price* | TAM (mil.) | Market Penetration | | | Market Size (mil.) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Bear | Base | Bull | Bear | Base | Bull |
| **Prostate** | PSMA, GRPR, hK2, STEAP2 | B7-H3, undisclosed | 314 | $180 | $56,480 | 7% | 14% | 25% | $3,954 | $7,907 | $14,120 |
| **Neuroendocrine** | SSTR(2), CXCR4 | N/A | 23 | $180 | $4,176 | 15% | 30% | 50% | $626 | $1,253 | $2,088 |
| **Breast** | GRPR, HER2, nectin-4, FAP | Neurotensin, FAP, B7-H3, undisclosed | 317 | $180 | $57,051 | 0% | 10% | 20% | $0 | $5,705 | $11,410 |
| **NSCLC** | PD-L1, GRPR, nectin-4, FAP | FAP, B7-H3, undisclosed | 193 | $180 | $34,677 | 0% | 10% | 20% | $0 | $3,468 | $6,935 |
| **Colon** | B7-H3, neurotensin, nectin-4, FAP | Undisclosed | 154 | $180 | $27,769 | 0% | 10% | 20% | $0 | $2,777 | $5,554 |
| **Melanoma** | MC1R, GD2, undisclosed | Undisclosed | 105 | $180 | $18,893 | 0% | 10% | 20% | $0 | $1,889 | $3,779 |
| **Bladder** | Nectin-4 | N/A | 85 | $180 | $15,277 | 0% | 10% | 20% | $0 | $1,528 | $3,055 |
| **Kidney** | CAIX | N/A | 81 | $180 | $14,576 | 0% | 10% | 20% | $0 | $1,458 | $2,915 |
| **NHL** | CD38, lipid rafts | N/A | 80 | $180 | $14,463 | 0% | 10% | 20% | $0 | $1,446 | $2,893 |
| **Head and neck** | FAP, NTSR1 | Undisclosed | 73 | $181 | $13,155 | 0% | 10% | 20% | $0 | $1,316 | $2,631 |
| **Pancreatic** | Integrins, FAP, undisclosed | B7-H3, neurotensin, integrins, undisclosed | 67 | $180 | $12,139 | 0% | 10% | 20% | $0 | $1,214 | $2,428 |
| **Thyroid** | FAP | N/A | 44 | $181 | $7,968 | 0% | 10% | 20% | $0 | $797 | $1,594 |
| **Liver** | GPC3 | B7-H3 | 42 | $180 | $7,603 | 0% | 10% | 20% | $0 | $760 | $1,521 |
| **Multiple Myeloma** | SSTR(2), CD38 | N/A | 36 | $180 | $6,500 | 0% | 10% | 20% | $0 | $650 | $1,300 |
| **SCLC** | SSTR(2), DLL3, GD2, B7-H3 | CCK2R, DLL3, B7-H3, undisclosed | 34 | $180 | $6,120 | 0% | 10% | 20% | $0 | $612 | $1,224 |
| **Gastric** | HER2, FAP | N/A | 30 | $180 | $5,454 | 0% | 10% | 20% | $0 | $545 | $1,091 |
| **Gastroesophageal** | HER2, FAP | N/A | 22 | $180 | $3,973 | 0% | 10% | 20% | $0 | $397 | $795 |
| **Ovarian** | FRα, FAP | Undisclosed | 21 | $180 | $3,760 | 0% | 10% | 20% | $0 | $376 | $752 |
| **Sarcoma** | FAP | NTSR1, PDGFRα | 17 | $180 | $3,132 | 0% | 10% | 20% | $0 | $313 | $626 |
| **Cervical** | Nectin-4 | N/A | 13 | $181 | $2,418 | 0% | 10% | 20% | $0 | $242 | $484 |
| **Glioblastoma** | SSTR(2), GRPR, LAT-1, CAXII | PARP | 12 | $180 | $2,142 | 0% | 10% | 20% | $0 | $214 | $428 |
| **Mesothelioma** | FAP | Undisclosed | 3 | $181 | $543 | 0% | 10% | 20% | $0 | $54 | $109 |
| **Neuroblastoma** | SSTR(2) | N/A | 1 | $180 | $135 | 0% | 10% | 20% | $0 | $14 | $27 |
| | | | | | **Total Addressable Market (mil.)** | | | | **$4,600** | **$35,000** | **$67,800** |

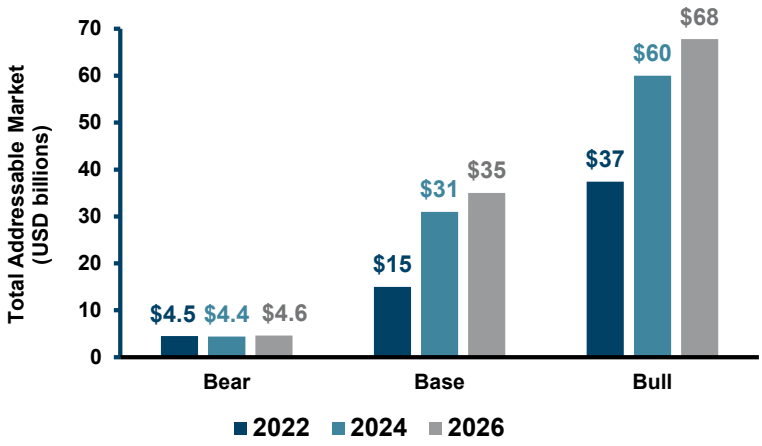
*Patient numbers and price in thousands.

[1]Total U.S. patient numbers are based on yearly incidence.

AML=Acute myeloid leukemia. CAIX=Carbonic anhydrase 9. CCK2R=Cholecystokinin 2 receptor. CAXII=Carbonic anhydrase 12. CXCR4=Chemokine receptor type 4. DLL3=Delta-like ligand 3. FAP=Fibroblast activation protein. FRα=Folate-receptor alpha. GRPR=Gastrin releasing peptide receptor. HER2=Human epidermal growth factor receptor 2. hK2=Human kallikrein-2. IGF-1R=insulin-like growth factor 1 receptor. LAT-1=L-type amino acid transporter 1. MC1R=Melanocortin 1 receptor. NHL=Non-Hodgkin lymphoma. NSCLC=Non–small-cell lung cancer. NTSR1=Neurotensin receptor 1. PARP=Poly (ADP-ribose) polymerase. PDGFRα=Platelet-derived growth factor receptor alpha. PSMA=Prostate-specific membrane antigen. SCLC=Small-cell lung cancer. SSTR=somatostatin receptor.

Sources: The Human Protein Atlas; NIH Surveillance, Epidemiology, and End Results (SEER) Program; William Blair Equity Research

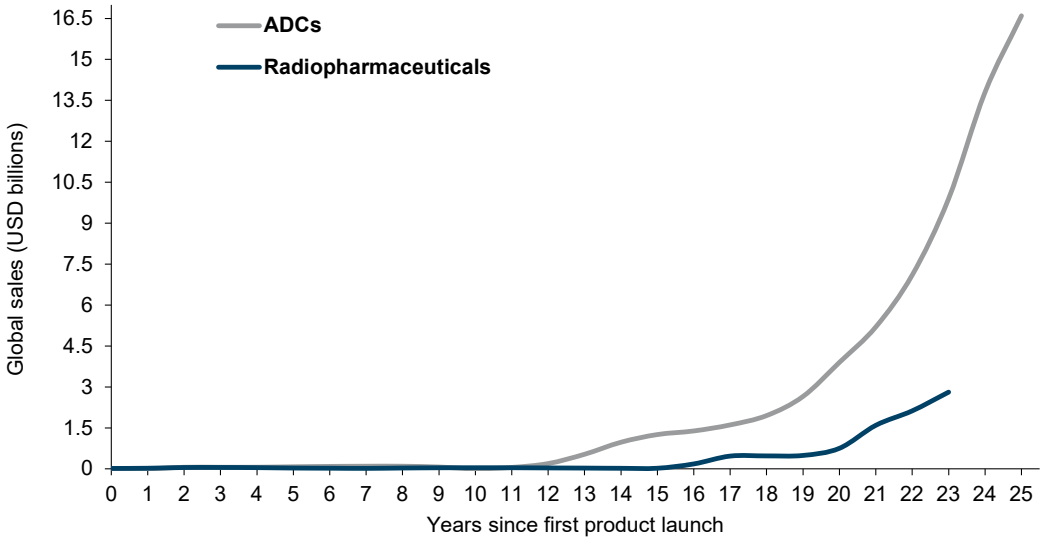
**Exhibit 2**
**Radiopharmaceuticals**
**Comparison of Changes in U.S. Total Addressable Market Estimates for the Radiopharmaceuticals Industry**




Source: William Blair Equity Research

We also conducted an analysis (exhibit 3) of sales for radiopharmaceuticals since the first launch of the modality (Zevalin in 2022) compared to sales of ADCs since the first ADC was launched (Mylotarg in 2000). Given that we view ADCs as an analogous asset to radiopharmaceuticals (essentially replacing the radioisotope with a chemotherapy toxin), our aim was to assess the progress of the radiopharmaceuticals launch trajectory. Similar to ADCs, a notable increase in radiopharmaceuticals sales was not seen until at least a decade after their launch. However, by comparing the trajectories of the two modalities, we believe that radiopharmaceuticals are nearing an inflection point as Pluvicto continues to penetrate deeper into prostate cancer and new therapies are likely to be approved.

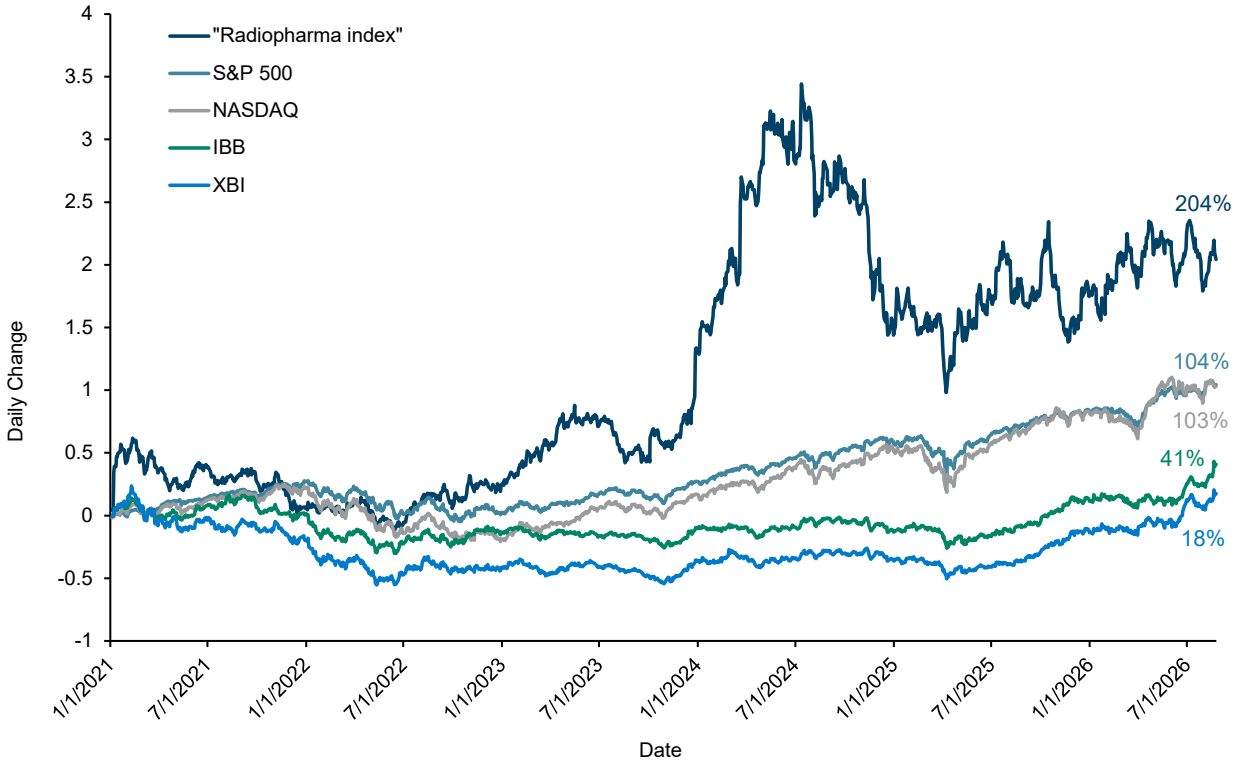
**Exhibit 3**
**Radiopharmaceuticals**
**Sales Trajectory of Radiopharmaceuticals Compared to ADCs Since Initial Launch (Through 2025)**




Sources: Evaluate Pharma, company reports, and William Blair Equity Research

To gauge the performance of radiopharmaceuticals companies, we generated a hypothetical "radiopharma index" and compared it over the past five years to the performance of the S&P 500, Nasdaq, IBB, and XBI. As shown in exhibit 4, investing in our hypothetical index would have provided a return of roughly 200% from early 2021, compared with a return of about 100% for the S&P 500 and Nasdaq or roughly 40% and 20% for the IBB and XBI, respectively. In this case, the "radiopharma index" includes Aktis Oncology, Telix Pharmaceuticals, Lantheus, Actinium Pharmaceuticals, Australia-based Clarity Pharmaceuticals and Radiopharm Theranostics, and previously acquired Fusion, Point, and RayzeBio.

**Exhibit 4**
**Radiopharmaceuticals**
**Hypothetical "Radiopharma Index" and Performance Benchmarked to Standard Indices and Biotech-Specific Indices**



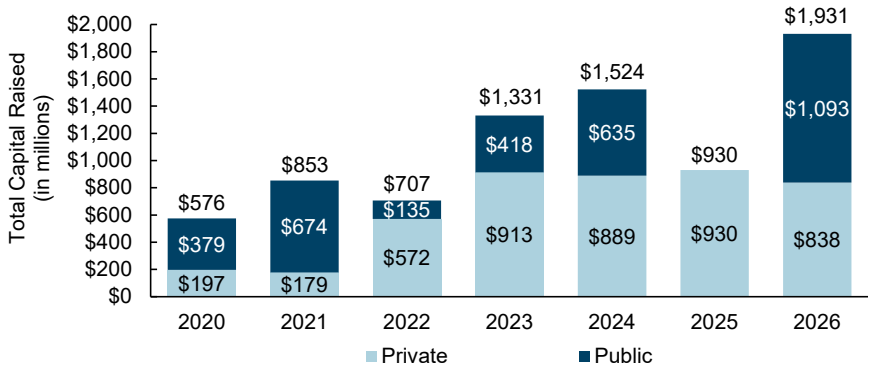

Index includes Aktis Oncology, Telix Pharmaceuticals, Lantheus, Actinium Pharmaceuticals, Australia-based Clarity Pharmaceuticals and Radiopharm Theranostics, and previously acquired Fusion, Point, and RayzeBio.
Source: William Blair Equity Research

## Recent Financings in the Sector

Public funding was significant in 2020 and 2021, owing to several IPOs in the space, but in 2023, 2024, and 2025, the majority of funding was from the private sector. Last year, radiopharmaceutical companies raised roughly $930 billion, centered on private funding (exhibit 5). So far in 2026 we have witnessed a rise in public funding, including what we view as a highly successful IPO from Aktis Oncology (described in more detail below). Overall, when considering both public and private investments, 2026 already marks the strongest year in financing since at least 2020 from a total amount raised perspective. This strong funding scene, in our view, demonstrates the sincere interest in and potential of radiopharmaceutical companies in both the near and long term. We would also be remiss to not mention the significant M&A activity that underscored 2023 and 2024.

In our view, the lack of more recent M&A activity is driven by a scarcity of companies focused on the manufacturing and supply chain aspect of the industry, which arguably drove three of the four acquisitions that occurred in 2023 and 2024.

**Exhibit 5**
**Radiopharmaceuticals**
**Private and Public Capital Raised by Radiopharmaceutical Companies, 2020-2026**




Sources: Company reports and BioCentury Inc.

The public debut of Aktis Oncology in early 2026 marked the first radiopharmaceutical IPO since 2023. The public offering was upsized, and gross proceeds were roughly $365 million, including a $100 million investment from Eli Lilly. Aktis is currently trading above its $18 per share IPO price, signaling enthusiasm for the radiopharmaceutical modality, in our view. Aktis's pipeline is built around actinium-225, and the company has developed a class of targeting moiety called miniproteins that aim to bridge favorable characteristics of small molecules or peptides with larger antibody formats. The lead program targets nectin-4, which is a commercially validated target owing to the success of Padcev; Phase Ib dose-escalation data is expected in the first quarter of 2027.

Within private funding, we highlight AdvanCell's $315 million oversubscribed and upsized series D financing from July. We believe the highly successful round of funding from top investors is a testament to AdvanCell's strategy and clinical data (discussed in more detail later in this report) and to the potential of lead-212 as a therapeutic radioisotope. An overview of the radiopharmaceutical financings completed thus far in 2026 is shown in exhibit 6.

**Exhibit 6**
**Radiopharmaceuticals**
**Financing in the Radiopharmaceuticals Sector During 2026**

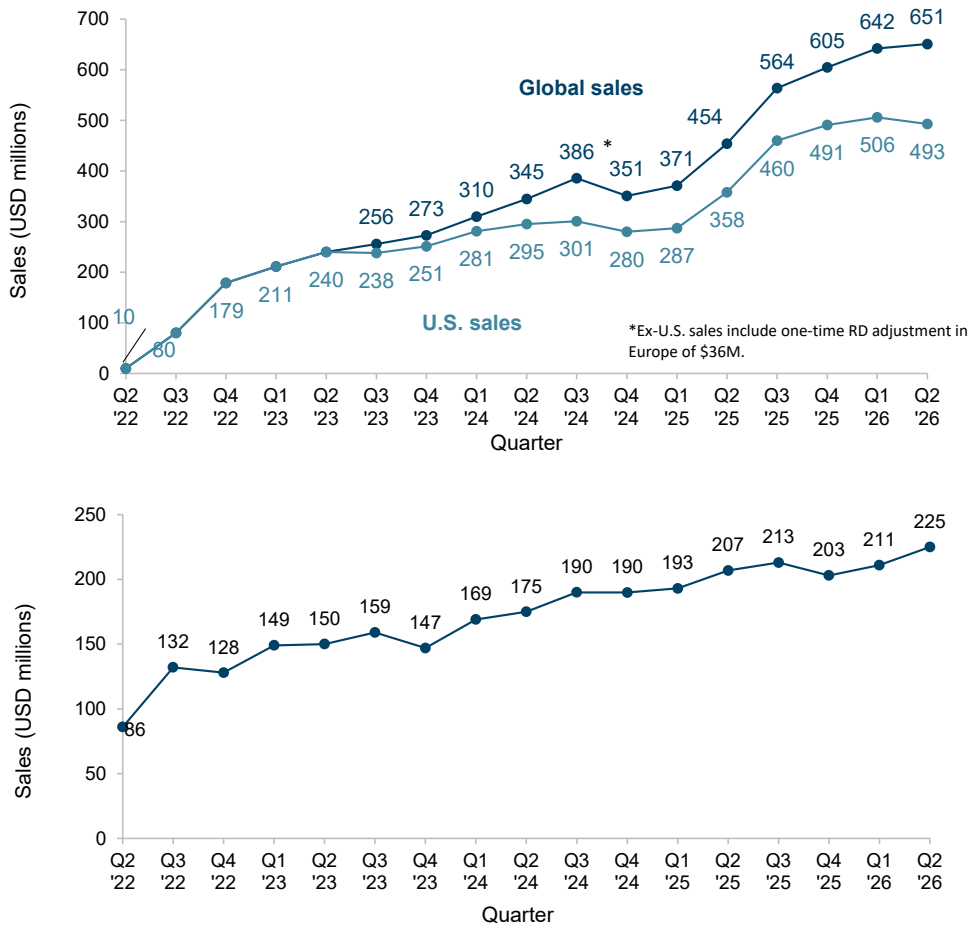
| Company | Series/Type | Amount (mil.) | Date | Investors |
|---|---|---|---|---|
| **Ratio Therapeutics** | Series C | $70 | July 31, 2026 | Duquesne Family Office, Bristol Myers Squibb, Catalio Capital Management, Eli Lilly and Company, and Wasatch Group |
| **AdvanCell** | Series D | $315 | July 15, 2026 | Ally Bridge, Alpha Wave, Bain Capital Life Sciences, Fidelity, T. Rowe Price, Eventide Asset Management, Velocity Capital |
| **Orano Med** | Debt | $143 | July 1, 2026 | The European Investment Bank |
| **Nuclidium** | Series B | $130 | May 27, 2026 | Kurma Growth Opportunities Fund, Angelini Ventures, Aurea, Wellington Partners, Neva SGR, DeepTech & Climate Fonds, Bayern Kapital, Vives Partners, NRW.BANK |
| **Full-Life Technologies** | Series D / debt | $150 ($109 / $41) | May 19, 2026 | SK Biopharmaceuticals, Chengwei Capital, HSG, Junson Capital, Plaisance, Sky9 Capital, Yunion |
| **Ionetix** | Go-public transaction | >$30 | April 21, 2026 | Network 1 Financial Securities (placement agent), consulted by Intuitive Ventures Partners |
| **Telix** | Convertible bonds | $600 | April 15, 2026 | NA |
| **Perspective Therapeutics** | Public equity | $175 | February 2, 2026 | Commodore Capital, TCGX, Spruce Street Capital, Surveyor Capital, Affinity Asset Advisors, HBM Healthcare Investments, Ally Bridge Group |
| **Aktis Oncology** | IPO | $318 | January 8, 2026 | Eli Lilly ($100M), among others |

Sources: BioCentury Inc. and company reports

## Commercial Highlights

In March 2025, the FDA approved Pluvicto in the pre-taxane setting of mCRPC, based on the Phase III PSMAfore trial. As seen in exhibit 7, this corresponded with a notable increase in sales for Pluvicto. Novartis management disclosed on its fourth quarter 2025 earnings call that it had reached 16% share in the pre-taxane setting, and based on the second quarter of 2026, the pre-taxane setting was driving 70% of new patient starts. The National Comprehensive Cancer Network (NCCN) recently removed androgen receptor pathway inhibitor (ARPI) sequencing recommendations in mCRPC from its guidelines, which management speculated has increased use of Pluvicto in the post-ARPI setting. Global sales during the second quarter of 2026 alone reached $651 million, marking a 43% year-over-year increase. The label for Pluvicto expanded again on July 31, 2026, with approval in metastatic hormone-sensitive prostate cancer (mHSPC), based on the Phase III PSMAddition study. Meanwhile, Lutathera sales remain steady to slightly increasing.

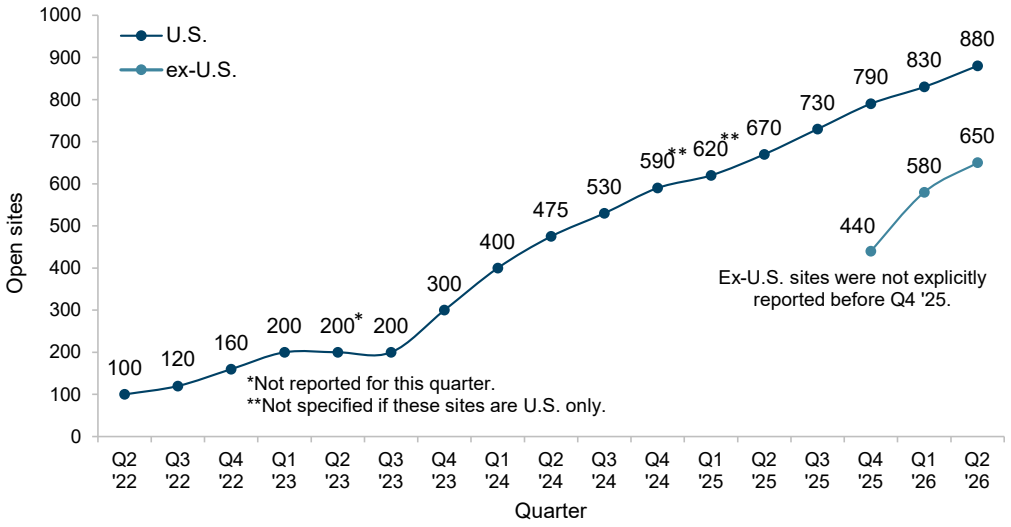
**Exhibit 7**
**Radiopharmaceuticals**
**Sales of Pluvicto (Top) and Lutathera (Bottom) by Quarter**




Sources: Novartis company reports and William Blair Equity Research

According to Novartis management, the mHSPC setting could increase the eligible patient population by 75%, and the company believes that Pluvicto will be rapidly adopted in this setting given that two-thirds of mHSPC patients attend clinics that already use Pluvicto. Novartis previously disclosed that Pluvicto is on track to exceed $5 billion in peak sales (increased in late 2024 from the $2 billion peak potential from the post-chemotherapy VISION population). Given the $651 million in quarterly sales from VISION/PSMAfore alone and the estimated 75% increase from PSMAddition, we agree that $5 billion peak sales is well within reach and could even be an underestimate since it does not include the oligometastatic setting (Phase III PSMA-DC trial). In accordance with Pluvicto's success to date, the number of clinical sites administering Pluvicto has been increasing rapidly, in both the United States and ex-U.S. territories (exhibit 8).

**Exhibit 8**
**Radiopharmaceuticals**
**Number of Open Clinical Sites Administering Pluvicto**




Sources: Novartis company reports and William Blair Equity Research

Novartis's conviction in Pluvicto and the radiopharmaceutical modality as a whole is underscored by its investment in manufacturing facilities. In April 2025, Novartis disclosed a $23 billion investment to expand U.S.-based manufacturing. This includes building two new facilities in Florida and Texas dedicated to manufacturing radioligand therapies and expanding the three existing radioligand therapy facilities in Indiana, New Jersey, and California. The 10,000-square-foot site in Carlsbad, California, is the newest completed site, having come online in November 2025. The new facility in Winter Park, Florida, is expected to encompass 35,000 square feet and open by 2029. The Texas site, to be in the Dallas–Fort Worth area, is expected to be even larger at 46,000 square feet and is slated to be operational in 2028. Characteristics of Novartis's five manufacturing sites for radiopharmaceuticals are summarized in exhibit 9. Based on commentary from Novartis, we expect the facilities to support not only existing products (Pluvicto and Lutathera), but also the company's next wave of radiopharmaceutical therapies.

**Exhibit 9**
**Radiopharmaceuticals**
**Novartis's Radioligand Therapy (RLT) Manufacturing-Dedicated Facilities in the United States**

| Site Location | City | Size (square feet) | Initial Operation | Region Serviced | Primary Role |
|---|---|---|---|---|---|
| **New Jersey** | Millburn | Not disclosed[1] | 2023 | U.S. broadly[2] | Initial U.S. site; Isotope production |
| **Indiana** | Indianapolis | 70,000[3] | 2024 | U.S. broadly | Flagship site; First-of-its-kind RLT automation; Isotope production |
| **California** | Carlsbad | 10,000 | 2025 | Western U.S., Alaska, Hawaii | Increase capacity; Regional manufacturing |
| **Florida** | Winter Park | 35,000 | 2029 | Southeast U.S. | Increase capacity; Regional manufacturing |
| **Texas** | Denton (Dallas–Fort Worth) | 46,000 | 2028 | Southern U.S. | Increase capacity; Regional manufacturing |

[1]Initial size was 70,000 square feet, but there are plans to roughly double the size by adding a roughly 80,000-square-foot building. Exact timing of expansion completion is uncertain but could occur this year based on estimates from 2024.

[2]May have some kind of regional focus on Northeast.

[3]The size has not been disclosed in detail, but it has been described as small scale and, according to a former unit head at Novartis, is roughly the size of "two one-story single houses."

Source: Novartis reports

## Regulatory Impediments

Despite the clinical and regulatory success of Pluvicto and Lutathera, there have been a number of complete response letters (CRLs) in the industry, along with several other regulatory hurdles, in recent years. These include both therapeutic and diagnostic candidates. Deficiencies in CMC and third-party manufacturing are commonly cited, which we believe could be a testament to the complexities of radionuclide production, supply chain logistics, and radiation control requirements. At this time, we do not know whether these manufacturing deficiencies were concentrated in a small number of CDMOs or attributable to the agency's inability to inspect manufacturing facilities on time due to recent reduction-in-force initiatives. We provide a summary of CRLs and other regulatory impediments in exhibit 10.

Despite the setbacks, we highlight a recent approval on the diagnostic side. In mid-August of this year, Tauklarify (previously known as MK-6240) was approved for imaging Alzheimer's disease. The agent targets tau neurofibrillary tangles and incorporates fluroine-18. For more information on this agent and PET imaging of Alzheimer's disease, please refer to the fourth edition of our radiopharmaceuticals report linked to earlier in the report.

**Exhibit 10**
**Radiopharmaceuticals**
**Summary of Complete Response Letters (CRLs) and Other Regulatory Impediments in the Radiopharmaceuticals Industry**

| Asset | Company | Original PDUFA | Outcome | Rationale | Current Status |
|---|---|---|---|---|---|
| $^{177}$Lu-edotreotide (ITM-11) | ITM | August 28, 2026 | CRL[1] | CMC and third-party manufacturing deficiencies | Plans to resubmit |
| $^{68}$Ga-edotreotide (Octevy) | Lantheus | March 29, 2026 | Delay, followed by CRL | Further review of manufacturing-related information needed / unresolved third-party manufacturing concerns | Working to address concerns |
| $^{89}$Zr-DFO-girentuximab (Zircaix) | Telix | August 27, 2025 | CRL[2] | CMC and third-party manufacturing deficiencies; requested bridging study to demonstrate formulation comparability | Resubmission expected in 2026 |
| $^{18}$F-floretyrosine (Pixclara) | Telix | April 26, 2025 | CRL[3] | Additional confirmatory clinical evidence requested given single-center nature and borderline diagnostic performance | Resubmitted with September 11, 2026, PDUFA |
| $^{131}$I-apamistamab (Iomab-B) | Actinium Pharmaceuticals | NA | BLA not accepted | Additional head-to-head randomized trial demonstrated overall survival requested | Seeking partner |
| $^{177}$Lu-dotatate (Lutathera) | Novartis | December 28, 2016 | CRL | Pivotal trial data not complete; requested subgroup analysis, safety update, and addressing of any CMC concerns | Resubmitted and approved on January 26, 2018 |

[1]https://download.open.fda.gov/crl/CRL_NDA218705_20260807.pdf
[2]https://download.open.fda.gov/crl/CRL_BLA761401_20260410.pdf
[3]https://download.open.fda.gov/crl/CRL_NDA218592_20250425.pdf
Sources: Company websites and the U.S. FDA

# Private and Public Companies in the Industry

Taking a broader view, the entrance of new companies into the radiopharmaceuticals industry has been occurring at a rapid pace. According to our research, there are almost 50 therapeutic radiopharmaceuticals companies across both the public (exhibit 11) and private (exhibit 12) sectors (though we note that a few are not radiopharmaceutical pure-plays), with the number increasing on a regular basis. There are also nearly 20 companies operating in the diagnostic space (exhibit 13), with many companies spanning both therapeutics and diagnostics. The programs encompass a range of study phases, from discovery to Phase III, and are investigating a variety of radionuclides, targets, and indications, although we note the large concentration in the PSMA target and prostate cancer indication.

**Exhibit 11**
**Radiopharmaceuticals**
**Public U.S. Companies Operating in Therapeutics Within the Radiopharmaceuticals Industry**

| Company | Ticker | Location | Asset | Radionuclide | Targets | Targeting moiety | Indication | Phase |
|---|---|---|---|---|---|---|---|---|
| Actinium | ATNM | New York | Iomab-B | I-131 | CD45 | Antibody | BMC for AML | Seeking partner |
| | | | Actimab-A | Ac-225 | CD33 | Antibody | R/R fit AML | Seeking collaborator |
| | | | | | | | Frontline AML | Phase I |
| | | | | | | | Refractory MDS | Phase I |
| | | | | | | | Other AML/MDS indications | Preclinical |
| | | | | | | | Solid tumor resistance | Preclinical |
| | | | ATNM-400 | Ac-225 | Not disclosed | Antibody | mCRPC, NSCLC, BC | Phase I |
| | | | Iomab-ACT | I-131 | CD45 | Antibody | Cell conditioning | Phase I |
| Aktis | AKTS | Boston, MA | AKY-1189 | Ac-225 | Nectin-4 | Miniprotein | Bladder, breast, other solid tumors | Phase Ib |
| | | | AKY-2519 | Ac-225 | B7-H3 | Miniprotein | Prostate cancer | Phase Ib |
| | | | | | | | Lung, colorectal, other solid tumors | Preclinical |
| Bristol Myers Squibb | BMY | New Jersey | RYZ101 | Ac-225 | SSTR2 | Peptide | NETs | Phase III ACTION-1 |
| | | | | | | | SCLC | Phase Ib |
| | | | | | | | HR+/HER2- breast cancer | Phase I TRACY-1 |
| | | | RYZ401 | Ac-225 | SSTR2 | Peptide | SSTR+ solid tumors | Phase I |
| | | | RYZ801 | Ac-225 | GPC3 | Macrocyclic peptide | HCC | Phase I |
| | | | OncoACP3 | Ac-225 | ACP3 | SM | Prostate cancer | Preclinical |
| Cellectar | CLRB | New Jersey | Iopofosine | I-131 | Lipid rafts | Phospholipid | Waldenstrom macroglobulinemia | Pivotal |
| | | | | | | | B-cell malignancies, multiple myeloma | Phase II |
| | | | | | | | pHGG | Phase Ib |
| | | | | | | | Mycosis fungoides | Unknown status |
| | | | CLR 125 | I-125 | Lipid rafts | Phospholipid | TNBC | Phase I |
| | | | CLR 225 | Ac-225 | Lipid rafts | Phospholipid | Solid tumors | Planned Phase I |
| Eli Lilly | LLY | Indianapolis, IN | PNT2003 | Lu-177 | SSTR | Peptide | NETs | Tentative approval |
| | | | PNT2001 | Ac-225 | PSMA | Ligand | Prostate cancer | Phase I ACCEL[1] |
| | | | PNT6555 | Ac-225 | FAP | SM | Solid tumors | Status unknown |
| | | | LY4257496 | Lu-177 | GRPR (antagonist) | Peptide | Advanced cancer | Phase Ia/b OMINRAY |
| | | | LY4337713 | Lu-177 | FAP | SM | FAP-positive solid tumors | Phase Ia/Ib FiREBOLT |
| Immunome | IMNM | Bothell, WA | IM-3050 | Lu-177 | FAP | SM | Solid tumors | Phase I |
| Lantheus[2] | LNTH | Bedford, MA | LNTH-2402 | Lu-177 | GRPR | Peptide | Prostate cancer | Preclinical |
| | | | LNTH-2403 | Lu-177 | LRRC15 | Antibody | Osteosarcoma | Phase I |
| | | | LNTH-2404 | Not disclosed | TROP2 | Nanobody | Solid tumors | Preclinical |
| | | | LNTH-2503 | Lu-177 | CCK2R | Peptide | SCLC | Phase I |
| | | | LNTH-2505 | Lu-177 | Not disclosed | Not disclosed | Glioblastoma | Preclinical |
| | | | LNTH-2507 | Lu-177 | Not disclosed | Not disclosed | PDAC | Preclinical |
| | | | LNTH-2509 | Lu-177 | Not disclosed | Not disclosed | Lobular breast cancer | Preclinical |
| Perspective Therapeutics | CATX | Richland, WA | $^{212}$Pb-VMT-α-NET | Pb-212 | SSTR2 | Peptide | NETs | Phase I/IIa |
| | | | | | | | Meningioma | Phase I/IIa |
| | | | VMT01 | Pb-212 | MC1R | Peptide | Melanoma | Phase I/IIa |
| | | | PSV359 | Pb-212 | FAP | Peptide | Solid tumors | Phase I/IIa |
| | | | PSV594 | Pb-212 | CCK2R | Peptide | Solid tumors | Preclinical |

ACP3=Acid phosphatase 3. AML=Acute myeloid leukemia. BC=Breast cancer. BMC=Bone marrow conditioning. CCK2R=Cholecystokinin 2 receptor. CD=Cluster of differentiation. FAP=Fibroblast activation protein. GPC3=Glypican-3. GRPR=Gastrin-releasing peptide receptor. HCC=Hepatocellular carcinoma. pHGG=Pediatric high-grade gliomas. LRRC15=Leucine-rich repeat containing 15. MC1R=Melanocortin 1 receptor. mCRPC=Metastatic castration-resistant prostate cancer. MDS=Myelodysplastic syndrome. NETs=Neuroendocrine tumors. NSCLC=Non-small-cell lung cancer. PDAC=Pancreatic ductal adenocarcinoma. PSMA=Prostate-specific membrane antigen. R/R=Relapsed/refractory. SCLC=Small-cell lung cancer. SSTR=Somatostatin receptor. TNBC=Triple-negative breast cancer.

[1]Trial is still active on clinicaltrials.gov but has not been recently updated is not listed on Lilly's clinical trial site.

[2]Given the proposed acquisition with Curium, we have limited visibility into recent pipeline development progress for Lantheus and its future plans.

Sources: Company reports and William Blair Equity Research

**Exhibit 11 (Continued)**
**Radiopharmaceuticals**
**Public International Companies Operating in Therapeutics Within the Radiopharmaceuticals Industry**

| Company | Ticker | Location | Asset | Radionuclide | Targets | Targeting moiety | Indication | Phase |
|---|---|---|---|---|---|---|---|---|
| AstraZeneca | AZN | United Kingdom | Zadavotide guraxetan | Ac-225 | PSMA | Ligand | mCRPC | Phase III VECTRA-01 |
| | | | AZD2284 | Ac-255 | STEAP2 | Antibody | mCRPC | Phase I |
| Bayer | BAYRY | Germany | Pelivotide mopaxetan | Ac-225 | PSMA | Antibody | mCRPC | Phase I PAnTHA |
| | | | BAY 3547926 | Ac-225 | GPC3 | Antibody | HCC | Phase I BANTAM-01 |
| Bicycle Therapeutics | BCYC | United Kingdom | BT1702 | Pb-212 | MT1-MMP | Bi-cyclic peptide | Solid tumors | IND-enabling |
| | | | N/A | Not disclosed | EphA2 | Bi-cyclic peptide | Solid tumors | Preclinical |
| Clarity | CU6-AU | Sydney | $^{67}$Cu-SAR-bisPSMA | Cu-67 | PSMA | Ligand | Prostate cancer | Phase I/IIa SECuRE |
| | | | $^{67}$Cu-SAR-Bombesin | Cu-67 | GRPR | Ligand | Prostate cancer | Phase I/IIa COMBAT (terminated) |
| | | | $^{67}$Cu-SARTATE | Cu-67 | SSTR2 | Peptide | Neuroblastoma | Phase I/II CL04 (terminated) |
| Janssen | JNJ | Belgium | JNJ-69086420 | Ac-225 | hK2 | Antibody | Advanced prostate cancer | Phase I |
| Novartis | NVS | Switzerland | Pluvicto | Lu-177 | PSMA | SM | mCRPC | Approved |
| | | | | | | | mCRPC (pre chemo) | Approved |
| | | | | | | | mHSPC | Approved |
| | | | | | | | Oligometastatic prostate cancer | Phase III PSMA-DC |
| | | | Lutathera | Lu-177 | SSTR | Peptide | Second-line+ NETs | Approved |
| | | | | | | | Frontline NETs (G2/G3) | Phase III NETTER-2 |
| | | | | | | | Frontline NETs (G1/G2) | Phase III NETTER-3 |
| | | | | | | | ES-SCLC | Phase II |
| | | | | | | | Glioblastoma | Phase II |
| | | | AAA817 | Ac-225 | PSMA | Ligand | post-Pluvicto mCRPC | Phase III |
| | | | AAA603 (177Lu-NeoB) | Lu-177 | GRPR | Ligand | Multiple solid tumors | Phase I NeoRay complete[1] |
| | | | | | | | Breast cancer | Phase I/II[1] |
| | | | | | | | Glioblastoma | Phase I[1] |
| | | | $^{177}$Lu-FAP-2286 | Lu-177 | FAP | Cyclic peptide | Advanced solid tumors | Phase I/II LuMIERE |
| | | | AAA802 (225Ac-PSMA-R2) | Ac-225 | PSMA | Ligand | Prostate cancer | Phase I/II SatisfACtion[1] |
| | | | 177Lu-NNS309 | Lu-177 | FAP | Peptide | Solid tumors | Phase I |
| | | | $^{177}$Lu-DMJ155 | Lu-177 | HER2 | Ligand | Solid tumors | Phase I |
| | | | $^{225}$Ac-ETN029 | Ac-225 | DLL3 | Ligand | Solid tumors | Phase I |
| Pentixapharm | PTP.F | Germany | PT-002 (PentixaTher) | Lu-177, Y-90 | CXCR4 | Peptide | CNS lymphoma | Phase I/II |
| | | | | | | | Acute Myeloid leukemia | Phase I/II IST |
| | | | GT-008 | Ac-225 | CD24 | Antibody | Solid female cancers | Preclinical |
| Philogen | PHIL.MI | Italy | OncoFAP-23 | Lu-177 | FAP | SM | FAP+ solid tumors | Phase I TheraTri |
| Radiopharm Theranostics | RAD.AX | Melbourne | RV01 | Lu-177 | B7H3 | Antibody | Solid tumors | Phase I/IIa BetaBart |
| | | | RAD204 | Lu-177 | PD-L1 | Nanobody | Solid tumors | Phase I |
| | | | RAD202 | Lu-177 | HER2 | Nanobody | Solid tumors | Phase I |
| | | | RAD402 | Tb-161 | KLK3 | Antibody | Advanced prostate cancer | Phase I |
| Roche | RHHBY | Switzerland | $^{212}$Pb-CEA-PRIT (with Orano Med) | Pb-212 | CEA | Antibody[2] | Metastatic CRC | Phase I |
| StarPharma | SPHRY | | DEP HER2 | Lu-177 | HER2 | Nanobody[3] | HER2-expressing cancers | Entering Phase I |
| Telix | TLX | Melbourne | TLX591 | Lu-177 | PSMA | Antibody | mCRPC | Phase III ProstACT |
| | | | TLX250 | Lu-177 | CAIX | Antibody | Relapsed ccRCC | Phase II/III LUTEON |
| | | | | | | | 1L ccRCC | Phase Ib/II STARLITE-1 |
| | | | TLX101 | I-131 | LAT-1 | SM | Recurrent glioblastoma | Phase III IPAX BrIGHT |
| | | | | | | | 1L glioblastoma | Phase I IPAX-2 |
| | | | TLX597 | Lu-177 | PSMA | SM | mHSPC | Phase IIa OPTIMAL-E |
| | | | TLX66 | Y-90 | CD66 | Antibody | BMC/rare diseases | Phase II |
| | | | TLX592 | Ac-225 | PSMA | Antibody | Prostate cancer | Phase I AlphaPRO initiating 2026 |
| | | | TLX090 | SM-153 | N/A | SM | Bone metastases | Phase I SOLACE |
| | | | TLX252 | Ac-225 | CAIX | Antibody | Kidney/other cancers | Phase I ALPHIX initiating 2026 |
| | | | TLX400 | Lu-177 | FAP | SM | Pan-cancer | Phase I initiating 2026 |
| | | | TLX300 | Undisclosed | PDGFRα | Antibody | Soft tissue sarcoma | Phase I |
| | | | TLX102 | At-211 | LAT-1 | SM | Recurrent glioblastoma | Phase I initiating 2026 |

CAIX=Carbonic anhydrase IX. ccRCC=Clear-cell renal cell carcinoma. CD=Cluster of differentiation. CEA=Carcinoembryonic antigen. CRC=Colorectal cancer. CSCR4=C-X-C motif chemokine receptor 4. DLL3=Delta-like ligand 3. EphA2=Ephrin type-A receptor 2. ES-SCLC=Extensive stage small-cell lung cancer. FAP=Fibroblast activation protein. GPC3=Glypican-3. GRPR=Gastrin releasing peptide receptor. HCC=Hepatocellular carcinoma. hK2=Human kallikrein 2. KLK3=kallikrein-related peptidase 3. LAT-1=L-type amino acid transporter 1. mCRPC=Metastatic castration-resistant prostate cancer. mHSPC=Metastatic hormone-sensitive prostate cancer. MT1-MMP=Membrane-type 1 matrix metalloproteinase. NETs=Neuroendocrine tumors. PDGFRα=Platelet-derived growth factor receptor alpha. PSMA=Prostate-specific membrane antigen. SM=Small molecule. SSTR=Somatostatin receptor. STEAP2=Six-transmembrane epithelial antigen of the prostate 2.

[1]Still listed on clinicaltrials.gov but not included in Novartis's second-quarter 2026 earnings presentation.
[2]Pre-targeted radio immunotherapy approach.
[3]Incorporates a dendrimer scaffold for conjugating the nanobody and lutetium and controlling overall molecular weight.

Sources: Company reports and William Blair Equity Research

**Exhibit 12**
**Radiopharmaceuticals**
**Private U.S. and Canadian Companies Operating in Therapeutics Within the Radiopharmaceuticals Industry**

| Company | Location | Asset | Radionuclide | Targets | Targeting moiety | Indication | Phase |
|---|---|---|---|---|---|---|---|
| Alpha9 Theranostics | Vancouver | A9-0631 | Lu-177 | GRPR | Ligand | Breast, prostate, CRC | Phase I/Ib |
| | | A9-0642 | Ac-225 | GRPR | Ligand | Breast, prostate, CRC | Phase I/Ib |
| | | A9-0941 | Ac-225 | Undisclosed | Ligand | PDAC, HNSCC | Preclinical |
| | | A9-0731 | Lu-177 | CCK2R | Ligand | SCLC, NETs | Preclinical |
| | | A9-0741 | Ac-225 | CCK2R | Ligand | SCLC, NETs | Preclinical |
| Asta Bio | Boston, MA | Undisclosed | At-211 | Undisclosed | Single-domain antibody | Solid tumors | Preclinical |
| Cancer Targeted Technology | Washington | CTT1403[1] | Lu-177 | PSMA | Ligand | mCRPC | Phase I trial completed 2023 |
| Convergent Therapeutics | Cambridge, MA | CONOV1-α | Ac-225 | PSMA | Antibody (J591) | mCRPC | Phase II CONVERGE-01 |
| | | | | | | Progressive mCRPC | Phase I/II |
| | | | | | | Non-prostate cancer | IND enabling |
| dGenThera | Durham, NC | DGT-77 | At-211 | Undisclosed transporter | SM | Breast cancer | Preclinical |
| | | DGT-207 | At-211 | Undisclosed receptor | Bioligand | Undisclosed | Preclinical |
| Fuzionaire Theranostics | Woodlands, TX | FTX-426 | Lu-177 | GRPR | Ligand | Prostate and breast cancer | First-in-human |
| | | N/A | Tb-161 | Not disclosed | Ligand | Not disclosed | Lead optimization |
| | | N/A | Pb-212 | Not disclosed | Ligand | Not disclosed | Discovery |
| Grafton Therapeutics | New York | SMTR-001 to SMTR-005[2] | Not disclosed | SSTR2/SSTR5 | Ligand | Not disclosed | Preclinical |
| Monopar | Wilmette, IL | MNPR-101-Lu | Lu-177 | uPAR | Antibody | Advanced solid cancers | Phase Ia |
| | | MNPR-101-Ac | Ac-225 | uPAR | Antibody | Advanced solid cancers | Late preclinical |
| NAYA Therapeutics | Miami, FL | NY-703 | At-211 | GPC3 | Antibody fragment | HCC | Early clinical (China) |
| | | NY-738 | At-211 | CD38 | Antibody fragment | Multiple myeloma | Early clinical |
| RadioMedix | Houston, TX | RMX-GPC3-VH | Pb-212 | GPC3 | Vect-Horus vectors | HCC | Preclinical |
| | | RMX-PSMA | Pb-212 | PSMA | Not disclosed | Prostate cancer | Preclinical |
| | | RMX-VH | Pb-212 | LDLR | Vect-Horus vectors | GBM, PDAC | Preclinical |
| Radionetics | California | N/A | Alpha and beta | GPCR | SM | Solid cancers | Preclinical |
| Ratio Therapeutics | Boston, MA | [Ac-225]-RTX-2358 | Ac-225 | FAP | SM | Advanced sarcoma | Phase I/II ATLAS |
| | | N/A | Lu-177 | FAP | SM | Solid tumors | Phase I[3] |
| | | N/A | Not disclosed | SSTR2 | SM | NETs | Preclinical |
| | | N/A | Not disclosed | GRPR/GRPR+FAP | SM | Solid tumors | Preclinical |
| Trevarex | Philly, PA | AlphaPARP | At-211 | PARP | SM | Ovarian cancer | Preclinical |
| Z-Alpha | San Diego, CA | PMI21 | At-211 | PSMA | Not disclosed | Prostate cancer | IND-enabling[4] |
| | | PMI31 | At-211 | FAP | Not disclosed | Not disclosed | Not disclosed |
| | | PMI41 | At-211 | CAIX | Not disclosed | Not disclosed | Not disclosed |

CAIX=Carbonic anhydrase 9. CCK2R=Cholecystokinin B receptor. CRC=Colorectal cancer. FAP=Fibroblast activation protein. GBM=Glioblastoma. GPC3=Glypican-3. GPCR=G-protein coupled receptor. GRPR=Gastrin-releasing peptide receptor. HCC=Hepatocellular carcinoma. HNSCC=Head and neck squamous cell carcinoma. LDLR=Low-density lipoprotein receptor. mCRPC=Metastatic castration-resistant prostate cancer. NETs=Neuroendocrine tumors. PARP=Poly(ADP-ribose) polymerase. PDAC=Pancreatic ductal adenocarcinoma. PSMA=Prostate-specific membrane antigen. SCLC=Small-cell lung cancer. SM=Small molecule. SSTR=Somatostatin receptor. uPAR=Urokinase-type plasminogen activator receptor.

[1]Asset available for licensing.
[2]The company has mentioned designing and synthesizing these five agonists but unclear which, if any, are being advanced.
[3]Compassionate use/investigator-initiated trial.
[4]Exact development status of PMI21, along with remaining pipeline assets, is not certain.

Sources: Company reports and William Blair Equity Research

**Exhibit 12 (Continued)**
**Radiopharmaceuticals**
**Private International Companies Operating in Therapeutics Within the Radiopharmaceuticals Industry**

| Company | Location | Asset | Radionuclide | Targets | Targeting moiety | Indication | Phase |
|---|---|---|---|---|---|---|---|
| AdvanCell | Sydney | ADVC001 | Pb-212 | PSMA | Ligand | mCRPC | Phase I/II TheraPb |
| | | ADVC002 | Pb-212 | Not disclosed | Ligand[1] | Melanoma | Development candidate |
| | | ADVC003 | Pb-212 | Not disclosed | Ligand[1] | Ovarian, breast, lung | Lead optimization |
| | | ADVC004 | Pb-212 | Not disclosed | Ligand[1] | Lung, prostate, head and neck, other | Lead optimization |
| | | ADVC005 | Pb-212 | Not disclosed | Ligand[1] | Lung, pancreatic | Lead generation |
| | | ADVC006 | Pb-212 | Not disclosed | Ligand[1] | RCC, ovarian | Lead generation |
| Affibody | Sweden | ABY-271 | Lu-177 | HER2 | Engineered protein | Breast, GEA, other cancers | First-in-human |
| | | ABY-071 | Lu-177 | B7-H3 | Engineered protein | TNBC, pancreatic, SCLC, NSCLC | Preclinical |
| Alpha Fusion | Japan | af-001 | At-211 | Sodium iodide symporter | SM | Thyroid cancer | Phase I |
| | | af-002 | At-211 | PSMA | SM | Prostate cancer | Phase I |
| | | af-003 | At-211 | LAT1 | SM | Pan-cancer | IND-enabling |
| | | Undisclosed | At-211 | Undisclosed | Peptide | Undisclosed | Screening |
| | | Undisclosed | At-211 | Undisclosed | SM | Undisclosed | Screening |
| ArtBio | Norway | AB001 | Pb-212 | PSMA | Small molecule | mCRPC | Phase I |
| | | ABD | Pb-212 | Not disclosed | Not disclosed | TNBC, HNSCC, others | Preclinical |
| | | ABA | Pb-212 | Not disclosed | Small molecule | NSCLC, pancreatic, others | Preclinical |
| | | ABC | Pb-212 | Not disclosed | Small molecule[1] | Multiple solid tumors | Discovery |
| Atonco | France | ATO-101 | At-211 | CAIX | Antibody[2] | Bladder cancer | Phase I (IST) |
| Blue Earth Therapeutics | UK | $^{177}$Lu-rhPSMA-10.1 | Lu-177 | PSMA | Radiohybrid ligand | Prostate cancer | Phase I/II |
| | | $^{225}$Ac-rhPSMA-10.1 | Ac-225 | PSMA | Radiohybrid ligand | Prostate cancer | Preclinical |
| Curium | UK | Lu-177-PSMA-I&T | Lu-177 | PSMA | Ligand | mCRPC | Phase III ECLIPSE |
| Full-Life Technologies | Shanghai, China | FL-020 | Ac-225 | PSMA | Ligand | Prostate cancer | Phase I ProTACT |
| | | FL-091 | Not disclosed | NTSR1 | Ligand | GI cancers, SCCHN | First-in-human |
| | | FL-031 | Not disclosed | SSTR | Ligand | NETs, SCLC, breast | First-in-human |
| | | FL-802 | Not disclosed | B7-H3 | Ligand | SCLC, CRC | First-in-human |
| | | FL-261 | Not disclosed | c-MET | Ligand | NSCLC, gastric, CRC | First-in-human |

CAIX=Carbonic anhydrase 9. CRC=Colorectal cancer. GEA=Gastroesophageal adenocarcinoma. GI=Gastrointestinal. HNSCC=Head and neck squamous cell carcinoma. LAT1=L-type amino acid transporter 1. mCRPC=Metastatic castration-resistant prostate cancer. NETs=Neuroendocrine tumors. NSCLC=Non-small-cell lung cancer. NTSR1=Neurotensin receptor 1. PSMA=Prostate-specific membrane antigen. RCC=Renal cell carcinoma. SCCHN=Squamous cell carcinoma of the head and neck. SCLC=Small-cell lung cancer. SM=Small molecule. SSTR=Somatostatin receptor. TNBC=Triple-negative breast cancer.

[1]Not specifically disclosed.
[2]Administered intravesically.
Sources: Company reports and William Blair Equity Research

**Exhibit 12 (Continued)**
**Radiopharmaceuticals**
**Private International Companies Operating in Therapeutics Within the Radiopharmaceuticals Industry**

| Company | Location | Asset | Radionuclide | Targets | Targeting moiety | Indication | Phase |
|---|---|---|---|---|---|---|---|
| GlyTherix | Sydney, Australia | $^{177}$Lu-Miltuximab | Lu-177 | GPC-1 | Antibody | Not disclosed | Planning Phase Ib |
| ITM | Germany | ITM-11 | Lu-177 | SSTR | Peptide | GEP-NETs (grade 1 and 2) | Recent CRL |
| | | | | | | GEP-NETs (grade 2 and 3) | Phase III COMPOSE |
| | | | | | | Lung NETs | Phase III LEVEL |
| | | | | | | Pediatric SSTR-positive tumors | Phase I KinLET |
| | | ITM-91 | Lu-177 | CAIX | Ligand | ccRCC, CAIX-positive tumors | Phase I |
| | | ITM-31 | Lu-177 | CAXII | Ligand | Glioblastoma | Phase I |
| | | ITM-23 | Tb-161 | PSMA | Ligand | Prostate | Phase I |
| | | ITM-63 | Tb-161 | SSTR | Ligand (antagonist) | SSTR-positive tumors | Phase I |
| | | ITM-22 | Ac-225 | PSMA | Ligand | Prostate | Preclinical |
| | | ITM-51 | Lu-177 | FRα | Ligand | Ovarian cancer | Preclinical |
| Molecular Partners | Switzerland | MP0712 | Pb-212 | DLL3 | DARPin | SCLC and NECs | Phase I/IIa (with Orano Med) |
| | | MP0726 | Pb-212 | Mesothelin | DARPin | Ovarian cancer | FIH initiating 2026 |
| Nuclidium | Switzerland | NU101 | Cu-67 | PSMA | Ligand | mCRPC | Entering Phase I |
| | | NU201 | Cu-67 | SSTR | Peptide | HR+/HER2- breast cancer | Preclinical |
| Orano Med | France | AlphaMedix (with RadioMedix) | Pb-212 | SSTR | Peptide | NETs | Phase II ALPHAMEDIX02 |
| | | $^{212}$Pb-GRPR | Pb-212 | GRPR | Ligand | Breast and prostate cancer, glioblastoma | Phase I |
| | | $^{212}$Pb-PSMA | Pb-212 | PSMA | Ligand | Prostate cancer | Pre-IND |
| PeptiDream | Japan | PD-32766 | Ac-225 | CAIX | Macrocyclic peptide ligand | Renal cell carcinoma | Phase I |
| | | PD-29875 | Ac-225 | Claudin18.2 | Macrocyclic peptide ligand | Gastric cancer | IND-enabling |
| | | N/A | Ac-225, Lu-177 | Cadherin 3 | Macrocyclic peptide ligand | HNSCC | IND-enabling |

CAIX=Carbonic anhydrase 9. CAXII=Carbonic anhydrase 12. ccRCC=Clear cell renal cell carcinoma. CEA=carcinoembryonic antigen. CRL=Complete response letter. DARPin=Designed ankyrin repeat proteins. DLL3=Delta-like ligand 3. FAP=Fibroblast activation protein. FIH=First in-human. FRα=Folate receptor alpha. GEP=Gastroenteropancreatic. GPC-1=Glypican-1. GRPR=Gastrin-releasing peptide receptor. HNSCC=Head and neck squamous cell carcinoma. mCRPC=Metastatic castration-resistant prostate cancer. NECs=Neuroendocrine carcinomas. NETs=Neuroendocrine tumors. PSMA=Prostate-specific membrane antigen. SCLC=Small-cell lung cancer. SSTR=Somatostatin receptor.

[1]Pre-targeted radio immunotherapy approach.
Sources: Company reports and William Blair Equity Research

**Exhibit 13**
**Radiopharmaceuticals**
**Public Companies Operating in Diagnostics Within the Radiopharmaceuticals Industry**

| Company | Asset | Radionuclide | Targets | Indication | Phase |
|---|---|---|---|---|---|
| Bicycle Therapeutics | N/A | Ga-68 | EphA2 | Solid tumors | IND-enabling |
| | N/A | Ga-68 | MT1-MMP | Solid tumors | IND-enabling |
| Clarity | $^{64}$Cu-SARTATE | Cu-64 | SSTR2 | NETs | Phase II DISCO complete |
| | $^{64}$Cu-SAR-bisPSMA | Cu-64 | PSMA | High-risk prostate cancer | Phase III CLARIFY |
| | | | | Recurrent prostate cancer | Phase I/II COBRA complete |
| | | | | mCRPC | Phase I/II SECuRE |
| | $^{64}$Cu-SAR-Bombesin | Cu-64 | GRPR | Recurrent prostate cancer | Phase II SABRE complete |
| Eli Lilly | Tauvid | F-18 | Tau | Alzheimer's disease | Commercialized |
| | Amyvid | F-18 | Amyloid beta | Alzheimer's disease | Commercialized |
| Lantheus[1] | Pylarify | F-18 | PSMA | Prostate cancer | Commercialized |
| | Tauklarify | F-18 | Tau | Alzheimer's disease | Approved |
| | Octevy/LNTH-2501 | Ga-68 | SSTR | NETs | Resubmission in progress |
| | NAV-4694 | F-18 | Amyloid beta | Alzheimer's disease | Phase III |
| | LNTH-2515 | F-18 | Amyloid | Cardiac amyloidosis | Phase III |
| | LNTH-2620 | F-18 | Tau | Alzheimer's disease | Phase III |
| | LNTH-2401 | Ga-68 | GRPR | Prostate cancer | Phase II |
| | LNTH-2513 | F-18 | GPIIb-IIIa | Thromboembolism | Phase II |
| | LNTH-2503 | Ga-68 | CCK2R | SCLC | Phase I |
| | LNTH-1363S | Cu-64 | FAP | Tumor/fibrosis assessment | Phase I |
| | LNTH-2511 | F-18 | MAO-B | Neuroinflammation | Phase I |
| | LNTH-2205 | Ga-68 | Undisclosed | Glioblastoma | Preclinical |
| | LNTH-2507 | Ga-68 | Undisclosed | Pancreatic cancer | Preclinical |
| | LNTH-2509 | Ga-68 | Undisclosed | Lobular breast cancer | Preclinical |
| Novartis | Netspot | Ga-68 | SSTR | NETs | Commercialized |
| | Locametz | Ga-68 | PSMA | Prostate cancer | Commercialized |
| | CTT1057 | F-18 | PSMA | Newly diagnosed high-risk prostate cancer | Phase II/III complete |
| | | | | Biochemical recurrent prostate cancer | Phase III complete |
| Pentixapharm | PT-001 (PentixaFor) | Ga-68 | CXCR4 | Hypertension – primary aldosteronism | Phase III ready |
| | PT-003 | F-18 | CXCR4 | Cardiovascular, endocrine, and oncology | Preclinical |
| Philogen | OncoFAP | Ga-68 | FAP | Solid tumors | Phase I FAPrimo complete |
| | OncoACP3 | Ga-68 | ACP3 | Prostate cancer | Phase I complete |
| | OncoCAIX | Ga-68 | CAIX | CAIX-positive cancer | Phase I complete |
| | OncoFAP-GlyPro-MMAE | Not disclosed | FAP | Solid tumors | Preclinical |
| Perspective Therapeutics | $^{203}$Pb-VMT-α-NET | Pb-203 | SSTR | NETs | Phase I[2] |
| | VMT01 | Pb-203 | MC1R | Melanoma | Phase I[2] |
| | VMT02 | Ga-68 | MC1R | Melanoma | Phase I[2] |
| | PSV377 | Pb-203 | FAP | Solid tumors | Phase I[2] |
| | PSV507 | Not disclosed | CCK2R | Solid tumors | Initial imaging[2] |
| Telix | Illuccix/Gozellix | Ga-68 | PSMA | Prostate cancer | Commercialized |
| | Scintimun | Tc-99m | CEA | Suspected osteomyelitis | Commercialized |
| | TLX599-CDx | Tc-99m | PSMA | Prostate cancer | Noble registry |
| | Zircaix | Zr-89 | CAIX | Kidney cancer | BLA resubmission in progress |
| | Pixclara | F-18 | LAT-1 | Brain cancer | September 11 PDUFA |
| | TLX300-CDx | Zr-89 | PDGFRα | Soft tissue sarcoma | Phase I ZOLAR |

ACP3=Acid phosphatase 3. CAIX=Carbonic anhydrase IX. CCK2R=Cholecystokinin B receptor. CEA=Carcinoembryonic antigen. CXCR4=C-X-C chemokine receptor type 4. EphA2=Ephrin type-A receptor 2. FAP=Fibroblast activation protein. GRPR=Gastrin releasing peptide receptor. LAT-1=L-type amino acid transporter 1. MC1R=Mitochondrial complex 1 receptor. mCRPC=Metastatic castration-resistant prostate cancer. MOA-B=Monoamine oxidase B. MT1-MMP=Membrane-type 1 matrix metalloproteinase. NETs=Neuroendocrine tumors. PDGFRα=Platelet derived growth factor receptor alpha. PD-L1=Programmed death-ligand 1. PSMA=Prostate-specific membrane antigen. SSTR=Somatostatin receptor. SCLC=Small-cell lung cancer.

[1]Given the proposed acquisition with Curium, we have limited visibility into recent pipeline development progress for Lantheus and its future plans.

[2]Unsure of exact development stage and to what extent this asset is being developed.

**Exhibit 13 (Continued)**
**Radiopharmaceuticals**
**Private Companies Operating in Diagnostics Within the Radiopharmaceuticals Industry**

| Company | Asset | Radionuclide | Targets | Indication | Phase |
|---|---|---|---|---|---|
| Alpha-9 | A9-6217 | Ga-68 | GRPR | Breast, prostate, colorectal | Phase I/Ib |
| | A9-0922 | Ga-68 | Undisclosed | PDAC, HNSCC | Discovery |
| | A9-0721 | Ga-68 | CCK2R | SCLC, neuroendocrine | Discovery |
| Blue Earth Diagnostics | Posluma | F-18 | PSMA | Prostate cancer | Commercialized |
| | | | | Non-prostate cancer | Phase I/II |
| | BED003 | Ga-68 | FAP | CRC, gastric, PDAC, breast, ovarian | Phase II |
| | FPyQCP | F-18 | FAP | CRC, gastric, PDAC, breast, ovarian | Phase I/II |
| Curium | Detectnet | Cu-64 | SSTR | NETs | Commercialized |
| | IASOglio | F-18 | LAT1 | Gliomas | Commercialized in Poland and France |
| | Cu-64-PSMA-I&T | Cu-64 | PSMA | Intermediate-/high-/very-high- risk prostate cancer | Phase III SOLAR-Stage |
| | | | | Biochemical recurrent prostate cancer | Phase III SOLAR-Recur completed |
| Fuzionaire Theranostics | FTX-426 | F-18 | GRPR | Prostate and breast cancer | First-in-human |
| | N/A | F-18 | Undisclosed | Not disclosed | Lead optimization |
| | N/A | F-18 | Undisclosed | Not disclosed | Discovery |
| ImaginAb | $^{89}$Zr-Df-Crefmirlimab | Zr-89 | CD8 | Melanoma, Merkel cell, renal cell, and NSCLC | Phase II iPREDICT (current status unknown) |
| | | | | Inclusion body myositis | Phase I |
| | $^{89}$Zr-Df-IAB41M2C | Zr-89 | CD4 | Oncology and autoimmune diseases | Preclinical |
| ITM | TOCscan | Ga-68 | SSTR | NETs | Commercialized[1] |
| | ITM-94 | Ga-68 | CAIX | Clear cell renal cell carcinoma | Phase I |
| | ITM-64 | Ga-68 | SSTR (antagonist) | SSTR-positive tumors | Phase I |
| | ITM-74 | Ga-68 | FAP | Oncology, fibrosis, inflammation | Phase I (compassionate use) |
| Monopar Therapeutics | MNPR-101 | Zr-89 | uPAR | Advanced solid cancers | Phase I |
| Nuclidium | NU101 | Cu-61 | PSMA | mCRPC | Entering Phase II |
| | NU201 | Cu-61 | SSTR | NETs | Phase II |
| RadioMedix | DetectNET | Cu-64 | SSTR | NETs | Commercialized |
| | PSMA-11 | Ga-68 | PSMA | Prostate cancer | Approved |
| | RMX-VH | Pb-203 | LDLR | GBM, PDAC | Phase II |
| Radiopharm Theranostics | RAD101 | F-18 | Fatty acid synthetase | Brain metastases | Phase IIb complete |
| | RAD301 | Ga-68 | αVβ6 integrin | Pancreatic/NSCLC | Phase I |

ACP3=Acid phosphatase 3. CAIX=Carbonic anhydrase IX. CCK2R=Cholecystokinin B receptor. CD=Cluster of differentiation. CRC=Colorectal cancer. FAP=Fibroblast activation protein. GBM=Glioblastoma. GRPR=Gastrin releasing peptide receptor. HNSCC=Head and neck squamous cell carcinoma. LAT1=L-type amino acid transporter 1. LDLR=Low density lipoprotein receptor. mCRPC=Metastatic castration-resistant prostate cancer. NSCLC=Non–small-cell lung cancer. NETs=Neuroendocrine tumors. PDAC=Pancreatic ductal adenocarcinoma. PSMA=Prostate-specific membrane antigen. SCLC=Small-cell lung cancer. SSTR=Somatostatin receptor. uPAR=Urokinase-type plasminogen activator receptor.

[1]Curium also has marketing authorization in certain countries, including France, Austria, and Germany.

Sources: Company reports and William Blair Equity Research

A notable development in both the public and private spaces is the roughly $8 billion proposed acquisition of Lantheus (public) by Curium (private), which is expected to close in the first half of 2027. We view Lantheus's U.S.-centric radiodiagnostics business as complementary to Curium's theranostic portfolio. Radiopharmaceutical supply chain is complex and requires impeccable logistics management due to the just-in-time manufacturing model. We are therefore encouraged that the merger could enable an expanded global manufacturing and commercial footprint.

In terms of targeting moieties, both larger antibody formats and small-molecule/peptide ligands are being investigated, although we recognize the consensus in the field that antibodies could impose unique challenges. Specifically, in many cases, employing antibodies requires administration of nonradiolabeled antibodies before administration of the radiopharmaceutical. Infusion with non-radiolabeled antibody has a long record in the field of radiopharmaceuticals, starting with Zevalin and Bexxar, and continuing with some versions of J591, though not all antibody-based

moieties require pre-targeting (including Telix's TLX591). Overall, companies are continuing to explore both types of targeting moieties, and some companies investigating antibody-based therapies are working to more precisely tune the specific characteristics and properties of the antibody portion.

There is also a belief in the field that the half-life of the isotope should roughly match the circulating time of the therapy so that the radiopharmaceutical is not excreted before being taken up in the tumor and having the opportunity to emit cancer-cell-killing radiation. Thus, there could theoretically be opportunities for both types of targeting moieties depending on the chosen isotope. However, we highlight that at the 2024 SNMMI annual meeting, stakeholders engaged in an animated debate over potential safety concerns associated with antibody-based radiopharmaceuticals when combined with actinium-225 (specifically, in the Phase I trial of JNJ-69086420, which employs an antibody targeting human kallikrein 2, four patients died from treatment-related adverse events). In our view, this supports the growing consensus in the field that full antibody modalities may have a limited use-case (especially when combined with actinium-225), even though antibodies have been the modality of choice historically.

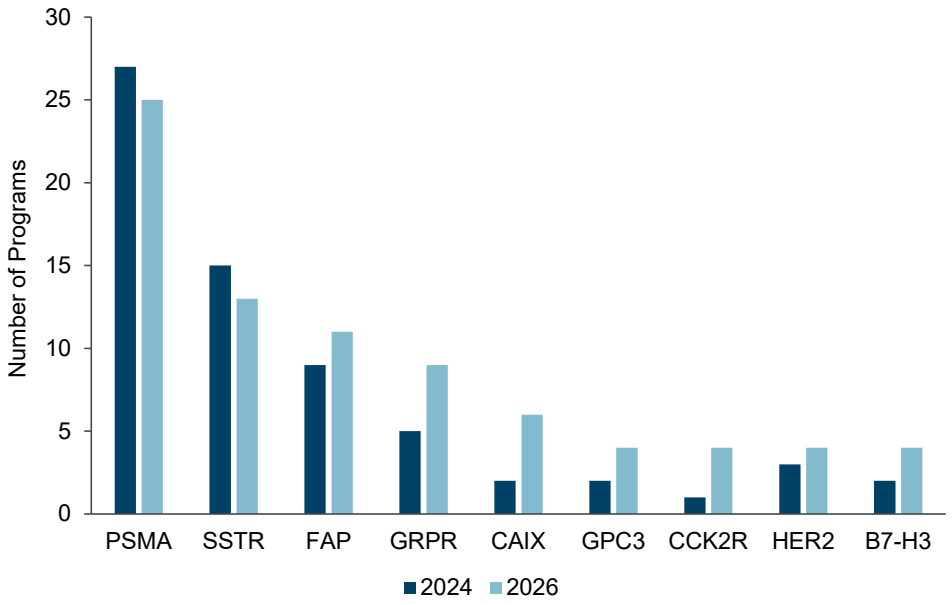
Recognizing both the potential challenges and the benefits (namely, selectivity and specificity) associated with antibodies, there is a trend toward developing targeting moieties that straddle antibodies and smaller-molecule formats. Both small molecules and peptides are recognized for their rapid tumor uptake and quick clearance of excess drug product from the body. Some companies, such as Aktis, are developing targeting moieties that take advantage of key benefits from each type of platform.

The majority of companies currently in operation are more focused on R&D and clinical development than on manufacturing. However, many of the companies that had also been focused on manufacturing, including isotope production, have been previously acquired. Australia-based AdvanCell stands out as being committed to manufacturing, and in June the company announced that U.S. global headquarters had been established. This includes leasing a 128,000-square-foot facility in Andover, part of the Greater Boston area, for U.S.-based manufacturing of lead-212-based ADVC001. AdvanCell will continue building manufacturing capabilities as the company works toward Phase III development and eventual commercialization.

# Targets and Isotopes of Interest

While PSMA and SSTR remain the most popular targets in the therapeutic space, we recognize the growing body of targets under investigation across both alpha- and beta-emitting isotopes. In particular, FAP, GRPR, and CAIX are rising as popular targets, and the number of programs pursuing these targets has notably increased in the past several years while the relative proportion of PSMA and SSTR have decreased (exhibit 14). Within alpha-emitters, the greatest variety of targets resides with actinium-225, and there are Phase III programs for both PSMA and SSTR (exhibit 15). PSMA and SSTR are also the most popular for lead-212, supporting the approach of starting with more validated targets when pursuing new isotopes. However, there is still a broad range of targets being evaluated with lead-212. For astatine-211, we have noted an increase in the number of assets investigating the isotope. We have identified 16 assets in this category; in edition 3 of our radiopharmaceuticals report (published in June 2024), we identified only one astatine-211 asset.

**Exhibit 14**
**Radiopharmaceuticals**
**Number of Assets With Different Targets: 2024 Versus 2026 Comparison**




Source: William Blair Equity Research

**Exhibit 15**
**Radiopharmaceuticals**
**Targets Under Investigation or Being Used in Radiopharmaceuticals With Alpha-Emitting Isotopes (Asset Numbers and Stages Based on Companies Listed in Exhibits 12 and 13)**

| Isotope | Target | Number of Assets | Most Advanced Stage of Development |
|---|---|---|---|
| **Actinium-225** | PSMA | 10 | Phase III |
| *Total assets: 34* | SSTR(2) | 2 | Phase III |
| | FAP | 2 | Phase I/II |
| | CAIX | 2 | Phase I |
| | GPC3 | 2 | Phase I |
| | Not disclosed | 2 | Phase I |
| | GRPR | 1 | Phase I |
| | Nectin-4 | 1 | Phase I |
| | B7-H3 | 1 | Phase I |
| | STEAP2 | 1 | Phase I |
| | hK2 | 1 | Phase I |
| | DLL3 | 1 | Phase I |
| | CD33 | 1 | Phase I |
| | CCK2R | 1 | Preclinical |
| | Cahderin 3 | 1 | Preclinical |
| | Claudin18.2 | 1 | Preclinical |
| | Lipid rafts | 1 | Preclinical |
| | uPAR | 1 | Preclinical |
| | ACP3 | 1 | Preclinical |
| | CD24 | 1 | Preclinical |
| **Lead-212** | Not disclosed | 9 | Preclinical |
| *Total assets: 25* | PSMA | 4 | Phase I/II |
| | SSTR(2) | 2 | Phase II |
| | MC1R | 1 | Phase I/II |
| | FAP | 1 | Phase I/II |
| | DLL3 | 1 | Phase I/II |
| | GRPR | 1 | Phase I |
| | CEA | 1 | Phase I |
| | CCK2R | 1 | Preclinical |
| | Mesothelin | 1 | Preclinical |
| | MT1-MMP | 1 | Preclinical |
| | LDLR1 | 1 | Preclinical |
| | GPC3 | 1 | Preclinical |
| **Astatine-211** | Not disclosed | 5 | Preclinical |
| *Total assets: 16* | PSMA | 2 | Phase I |
| | CAIX | 2 | Phase I |
| | LAT-1 | 2 | Preclinical |
| | GPC3 | 1 | Phase I |
| | CD38 | 1 | Phase I |
| | Sodium iodide symporter | 1 | Phase I |
| | PARP | 1 | Preclinical |
| | FAP | 1 | Not disclosed |

ACP3=Acid phosphatase 3. CAIX=Carbonic anhydrase 9. CCK2R=Cholecystokinin 2 receptor. CEA=Carcinoembryonic antigen. DLL3=Delta-like ligand 3. FAP=Fibroblast activation protein. GPC3=Glypican-3. GRPR=Gastrin releasing peptide receptor. hK2=Human kallikrein-2. LAT-1=L-type amino acid transporter 1. LDLR1=Low-density lipoprotein receptor 1. MC1R=Melanocortin 1 receptor. MT1-MMP=Membrane type-1 matrix metalloproteinase. PARP=Poly-ADP ribose polymerase. PSMA=Prostate-specific membrane antigen. SSTR=Somatostatin receptor. STEAP2=Six-transmembrane epithelial antigen of the prostate 2. uPAR=Urokinase-type plasminogen activator receptor.

Source: William Blair Equity Research

Although there are a number of assets across the three alpha emitters actinium-225, lead-212, and astatine-211, there is a high concentration in lutetium-177 when it comes to beta emitters. Within lutetium-177, FAP actually dominates, though PSMA and GRPR follow closely behind while SSTR lags (exhibit 16). We hypothesize that because lutetium-177 is well established from both clinical and regulatory perspectives, companies are more likely to pursue novel targets within the industry. In these cases, companies avoid the risk of simultaneously exploring uncertain target biology and unvalidated isotope selection. In exhibit 17, we provide a list of targets for which the isotope of interest has not yet been disclosed. Overall, the exact characteristics of what contributes to a "good" target within radiopharmaceuticals remain elusive, but we are encouraged that the target space is expanding. For all our target summary tables and graphs, we note that the exact numbers are based on our research analysis and could differ slightly from the real world but should still illustrate relative numbers and general trends.

**Exhibit 16**
**Radiopharmaceuticals**
**Targets Under Investigation or Being Used in Radiopharmaceuticals With Beta- or Gamma-Emitting Isotopes (Asset Numbers and Stages Based on Companies Listed in Exhibits 12 and 13)**

| Isotope | Target | Number of Assets | Most Advanced Stage of Development |
|---|---|---|---|
| **Lutetium-177** | FAP | 7 | Phase I/II |
| *Total assets: 43* | PSMA | 6 | Approved |
| | GRPR | 6* | Phase I/II |
| | HER2 | 4 | Phase I |
| | SSTR(2) | 3 | Approved |
| | Not disclosed | 3 | Preclinical |
| | CAIX | 2 | Phase II/III |
| | B7H3 | 2 | Phase I/II |
| | CCK2R | 2 | Phase I |
| | CXCR4 | 1 | Phase I/II |
| | CAXII | 1 | Phase I |
| | uPAR | 1 | Phase I |
| | LRRC15 | 1 | Phase I |
| | PD-L1 | 1 | Phase I |
| | GPC-1 | 1 | Phase I |
| | FRα | 1 | Preclinical |
| | Cadherin 3 | 1 | Preclinical |
| **Copper-67** | SSTR(2) | 2 | Phase I/II |
| *Total assets: 5* | PSMA | 2 | Phase I/II |
| | GRPR | 1 | Phase I/II |
| **Iodine-131 (β and γ)** | CD45 | 1 | Phase I |
| | Lipid rafts | 1 | Phase III |
| *Total assets: 3* | LAT-1 | 1 | Phase III |
| **Terbium-161** | Not disclosed | 1 | Preclinical |
| *Total assets: 4* | PSMA | 1 | Phase I |
| | SSTR(2) | 1 | Phase I |
| | KLK3 | 1 | Phase I |
| **Yttrium-90** | CD66 | 1 | Phase II |
| *Total assets: 2* | CXCR4 | 1 | Phase I/II |
| **Samarium-153** | Not disclosed | 1 | Phase I |
| *Total assets: 1* | | | |

*One asset is a GRPR antagonist.

CAIX=Carbonic anhydrase 9. CAXII=Carbonic anhydrase 12. CCK2R=Cholecystokinin 2 receptor. CXCR4=C-X-C chemokine receptor type 4. AP=Fibroblast activation protein. FRα=Folate receptor alpha. GPC-1=Glypican 1. GRPR=Gastrin releasing peptide receptor. HA=Hydroxyapatite. HER2=Human epidermal growth factor receptor 2. KLK3=Kallikrein-related peptidase 3. LAT-1=L-type amino acid transporter 1. LRRC15=Leucine-rich repeat-containing protein 15. PARP=Poly (ADP-ribose) polymerase. PD-L1=Programmed death-ligand 1. PSMA=Prostate-specific membrane antigen. SSTR=Somatostatin receptor. uPAR=Urokinase-type plasminogen activator receptor.

Source: William Blair Equity Research

**Exhibit 17**
**Radiopharmaceuticals**
**Targets Under Investigation or Being Used in Radiopharmaceuticals With Unspecified Isotopes**

| Isotope | Target | Number of Assets | Most Advanced Stage of Development |
|---|---|---|---|
| **Specific isotope not disclosed** | Not disclosed | 2 | Phase I/II |
| | SSTR(2) | 2 | Phase I |
| *Total assets: 12* | B7H3 | 1 | Phase I |
| | NTSR1 | 1 | Phase I |
| | c-MET | 1 | Phase I |
| | PDGFRα | 1 | Phase I |
| | EphA2 | 1 | Preclinical |
| | TROP-2 | 1 | Preclinical |
| | SSTR2/SSTR5 | 1 | Preclinical |
| | GRPR | 1 | Preclinical |

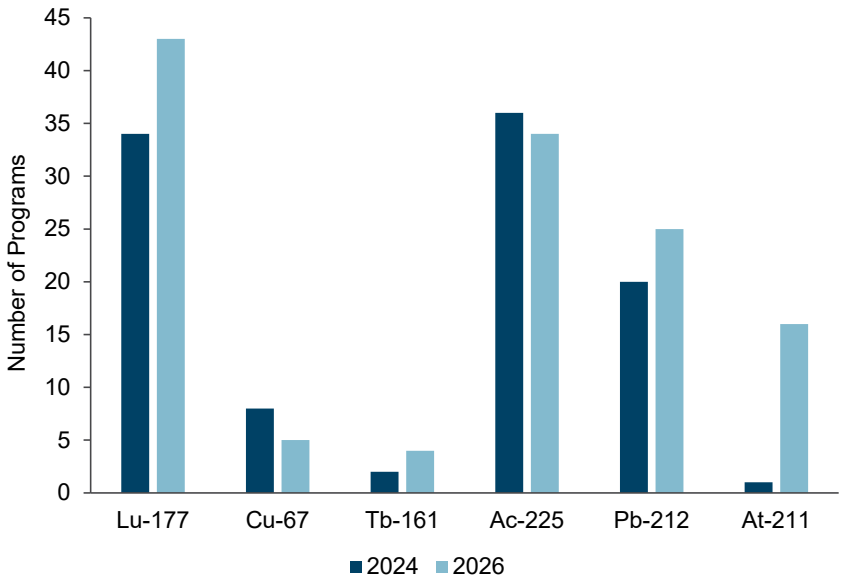
Note: Asset numbers and stages are based on companies listed in exhibits 12 and 13

EphA2=Ephrin type-A receptor 2. GRPR=Gastrin releasing peptide receptor. NTSR1=Neurotensin receptor 1. PDGFRα=Platelet-derived growth factor receptor alpha. SSTR=Somatostatin receptor. TROP-2=Trophoblast cell-surface antigen 2.

Source: William Blair Equity Research

We also conducted an analysis of the number of assets across several of the most investigated isotopes in the industry for both beta and alpha emitters (exhibit 18). Of note, although lead-212 still lags actinium-225, the gap appears to be closing. In addition, as discussed above, we are intrigued by the rapid increase in the number of programs pursuing astatine-211, which is corroborated by the increase in astatine-focused companies.

**Exhibit 18**
**Radiopharmaceuticals**
**Number of Assets With Different Isotopes: 2024 Versus 2026 Comparison**




Source: William Blair Equity Research

# Clinical Trials of Actinium-225, Lead-212, and Terbium-161

As alpha-emitting isotopes gain popularity, there are an increasing number of clinical trials evaluating actinium-225 and lead-212. We have summarized ongoing trials in exhibits 19 and 20 based on the ClinicalTrials.gov registry.

**Exhibit 19**
**Radiopharmaceuticals**
**Ongoing Clinical Trials (Phase I/II Through Phase III) Involving Actinium-225 Assets (Based on ClinicalTrials.gov Registry)**

| Asset/Regimen | Target | Indication | Phase | Company/ Sponsor | Study Title | Trial ID | Status | Estimated Primary Completion |
|---|---|---|---|---|---|---|---|---|
| RYZ101 | SSTR2 | GEP-NETs with prior Lutathera | III | Bristol Myers Squibb | Study of RYZ101 Compared With SOC in Pts w Inoperable SSTR+ Well-differentiated GEP-NET That Has Progressed Following 177Lu-SSA Therapy (ACTION-1) | NCT05477576 | Recruiting | December 2026 |
| $^{225}$Ac-PSMA-617 (AAA817) | PSMA | mCRPC with prior ARPI[1] | III | Novartis | Study Comparing AAA817+ARPI With Standard of Care in Adult Participants With PSMA-Positive mCRPC (AcTFirst) | NCT06855277 | Recruiting | February 2028 |
| $^{225}$Ac-PSMA-617 (AAA817) | PSMA | mCRPC with prior ARPI, taxane, and 177Lu-PSMA therapy | II/III | Novartis | Open-label Study Comparing AAA817 With Standard of Care in the Treatment of Previously Treated PSMA-Positive mCRPC Adults Who Have Disease Progressed on or After [177Lu]Lu-PSMA Targeted Therapy (PSMAcTION) | NCT06780670 | Recruiting | June 2028 |
| $^{225}$Ac-FPI-2265 (PSMA-I&T) | PSMA | mCRPC | II | AstraZeneca | Targeted Alpha Therapy With 225Actinium-Prostate Specific Membrane Antigen (PSMA)-I&T of Castration-resISTant Prostate Cancer (TATCIST) | NCT05219500 | Active, not recruiting | May 2025 (actual) |
| $^{225}$Ac-FPI-2265 (PSMA-I&T) | PSMA | mCRPC with prior 177Lu-PSMA | II | AstraZeneca | FPI-2265 (225Ac-PSMA-I&T) for Patients With PSMA-Positive Metastatic Castration-Resistant Prostate Cancer (mCRPC) (AlphaBreak) | NCT06402331 | Active, not recruiting | December 2026 |
| CONV01-α (J591 antibody) | PSMA | Progressive CRPC (includes part with prior Pluvicto patients) | II | Convergent Therapeutics | Study Evaluating Dosimetry, Randomized Dose Optimization, Dose Escalation and Efficacy of Ac-225 Rosopatamab Tetraxetan in Participants With PSMA PET-Positive Castration-Resistant Prostate Cancer | NCT06549465 | Recruiting | April 2027 |
| $^{225}$Ac-FPI-2265 (PSMA-I&T) | PSMA | mCRPC (both pre and post 177Lu-PSMA | II | AstraZeneca | FPI-2265 (225Ac-PSMA-I&T) and Olaparib for Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC) | NCT06909825 | Active, not recruiting | January 2030 |
| $^{225}$Ac-J591 | PSMA | mCRPC with prior ARPI | I/II | Cornell | Fractionated and Multiple Dose 225Ac-J591 for Progressive mCRPC | NCT04506567 | Active, not recruiting | June 2025 (actual) |
| $^{225}$Ac-LNC1011 | PSMA | mCRPC | I/II | First Affiliated Hospital of Fujian Medical University | Sequential Study of 225Ac-LNC1011 in the Treatment of Metastatic Castration-Resistant Prostate Cancer | NCT07363486 | Recruiting | December 2026 |
| RYZ101 | SSTR2 | Intracranial meningioma | I/II | Joshua Palmar (Ohio State University) | RYZ101 for the Treatment of Progressive or Recurrent Intracranial Meningioma | NCT07150806 | Recruiting | December 2026 |
| $^{225}$Ac-J591 with Keytruda and ARPI | PSMA | mCRPC with prior ARPI | I/II | Cornell | Phase I/II Trial of Pembrolizumab and Androgen-receptor Pathway Inhibitor With or Without 225Ac-J591 for Progressive Metastatic Castration Resistant Prostate Cancer | NCT04946370 | Recruiting | October 2027 |
| $^{225}$Ac-LNC1011 | PSMA | mCRPC | I/II | First Affiliated Hospital of Fujian Medical University | Prospective Clinical Trial of 225Ac-LNC1011 in the Treatment of Metastatic Castration-Resistant Prostate Cancer | NCT07117760 | Active, not recruiting | December 2027 |
| RTX-2358 | FAP | Sof tissue sarcoma | I/II | Ratio Therapeutics | Actinium Therapy for Late-stage Aggressive Sarcomas (ATLAS) | NCT07156565 | Recruiting | January 2028 |
| RYZ101 | SSTR2 | HER2-negative breast cancer | I/II | Bristol Myers Squibb | Trial of 225Ac-DOTATATE (RYZ101) in Subjects With ER+, HER2-Negative Unresectable or Metastatic Breast Cancer Expressing SSTRs. (TRACY-1) | NCT06590857 | Recruiting | October 2028 |
| $^{225}$Ac-rhPSMA-10.1 | PSMA | Prostate cancer | I/II | University College, London | ACTinium in Castrate-RESistant Prostate Cancer After LUTEtium (ACT-RESoLUTE) | NCT07414940 | Recruiting | March 2031 |

[1]No exposure to taxane-based chemotherapy in mCRPC setting.

ARPI=Androgen receptor pathway inhibitor. FAP=Fibroblast activation protein. GEP-NETs=Gastroenteropancreatic neuroendocrine tumors. mCRPC=Metastatic castration-resistant prostate cancer. PSMA=Prostate-specific membrane antigen. SSTR=Somatostatin receptor.
Sources: ClinicalTrials.gov and William Blair Equity Research

**Exhibit 19 (Continued)**
**Radiopharmaceuticals**
**Ongoing Phase I Clinical Trials Involving Actinium-225 Assets (Based on ClinicalTrials.gov Registry)**

| Asset/Regimen | Target | Indication | Phase | Company/ Sponsor | Study Title | Trial ID | Status | Estimated Primary Completion |
|---|---|---|---|---|---|---|---|---|
| Ac225-DOTA-M5A | CEA | Advanced or metastatic cancer | I | City of Hope | Actinium 225 Labeled Anti-CEA Antibody (Ac225-DOTA-M5A) for the Treatment of CEA Producing Advanced or Metastatic Cancers | NCT05204147 | Recruiting | July 2026 |
| $^{225}$Ac-ABD147 | DLL3 | SCLC and LCNEC | I | Abdera | Study of 225Ac-ABD147 to Establish Optimal Dose in Patients With SCLC and LCNEC of the Lung That Previously Received Platinum-based Chemotherapy | NCT06736418[1] | Recruiting | August 2026 |
| $^{225}$Ac-FL-020 | PSMA | mCRPC with prior ARPI and taxane | I | Full-Life Technologies | Study With [225Ac]Ac-FL-020 in mCRPC Participants (ProTACT) | NCT06492122 | Recruiting | October 2026 |
| $^{225}$Ac-PSMA-XT | PSMA | mCRPC | I | Xiaorong Sun | A Clinical Study to Evaluate the Safety, Tolerability and Preliminary Efficacy of [225Ac]Ac-PSMA-XT Injection in Patients With Metastatic Castration-resistant Prostate Cancer | NCT07135102 | Recruiting | December 2026 |
| $^{225}$Ac-FAPI-XT | FAP | Advanced solid tumors | I | Xiaorong Sun | A Clinical Study of [225Ac]Ac-FAPI-XT(XT117) Injection in Patients With Advanced Solid Tumors | NCT07135128 | Recruiting | December 2026[2] |
| $^{225}$Ac-PSMA-617 | PSMA | Prostate cancer | I | Endocyte | Study of 225Ac-PSMA-617 in Men With PSMA-Positive Prostate Cancer | NCT04597411 | Active, not recruiting | January 2027 |
| $^{225}$Ac-PSMA-617 | PSMA | mCRPC | I | Novartis | Study of 225Ac-PSMA-617 in Men With PSMA-Positive Prostate Cancer | NCT04597411 | Recruiting | January 2027 |
| RYZ401 | SSTR | Solid tumors | I | Bristol Myers Squibb | Study of RYZ401 in Subjects With Solid Tumors Expressing SSTRs. | NCT07165132 | Recruiting | February 2027 |
| $^{225}$Ac-DOTA-daratumumab | CD38 | Multiple myeloma | I | City of Hope Medical Center | Radioimmunotherapy (111Indium/225Actinium-DOTA-daratumumab) for the Treatment of Relapsed/Refractory Multiple Myeloma | NCT05363111 | Recruiting | March 2027 |
| $^{225}$Ac-DOTA-daratumumab | CD38 | Multiple myeloma | I | City of Hope | Radioimmunotherapy (111Indium/225Actinium-DOTA-daratumumab) for the Treatment of Relapsed/Refractory Multiple Myeloma | NCT05363111 | Recruiting | March 2027 |
| $^{225}$Ac-MTI-201 | MC1R | Uveal melanoma | I | Modulation Therapeutics | Targeted Alpha Particle Radiotherapy for Metastatic Uveal Melanoma | NCT05496686 | Recruiting | March 2027 |
| $^{177}$Lu-PSMA-617 and $^{225}$Ac-PSMA-617 | PSMA | mCRPC | I | Thomas Hope (UCSF) | Comparison of 177Lu-PSMA-617 and 225Ac-PSMA-617 (LUTACT) | NCT07054346 | Recruiting | April 2027 |
| BAY 3563254 | PSMA | mCRPC with prior 177Lu-PSMA | I | Bayer | First-in-Human Study of 225Ac-PSMA-Trillium (BAY 3563254) in Participants With Advanced Metastatic Castration-Resistant Prostate Cancer (mCRPC) (PAnTHA) | NCT06217822 | Recruiting | June 2027 |
| RYZ101 + carboplatin, etoposide, and Tecentriq | SSTR2 | ES-SCLC | I | Bristol Myers Squibb | Study of RYZ101 in Combination With SoC in Subjects With SSTR+ ES-SCLC | NCT05595460 | Recruiting | June 2027 |
| BAY3546828 | PSMA | mCRPC with prior taxane and some with prior 177Lu-PSMA | I | Bayer | A Study to Learn How Safe the Study Treatment Actinium-225-Macropa-Pelgifatamab (BAY3546828) Is, How it Affects the Body, How it Moves Into, Through and Out of the Body, and About Its Anticancer Activity in Men With Advanced Metastatic Castration-Resistant Prostate Cancer (mCRPC) | NCT06052306 | Active, not recruiting | June 2027 |
| $^{225}$Ac-PSMA-62 | PSMA | mCRPC | I | Eli Lilly | [Ac-225]-PSMA-62 Trial in Biochemically Recurrent and Metastatic Castration Resistant Prostate Cancer (ACCEL) | NCT06229366 | Active, not recruiting | September 2027 |
| JNJ-69086420 | human Kallikrein-2 | Prostate cancer | I | Janssen | A Study of JNJ-69086420, an Actinium-225-Labeled Antibody Targeting Human Kallikrein-2 (hK2) for Advanced Prostate Cancer | NCT04644770 | Active, not recruiting | October 2027 |
| $^{225}$Ac-AKY-1189 | Nectin-4 | Solid tumors | I | Aktis | A Study of [225Ac]Ac-AKY-1189 in Patients With Solid Tumors | NCT07020117 | Recruiting | December 2027[3] |
| $^{225}$Ac-J591 with $^{177}$Lu-PSMA-I&T | PSMA | mCRPC with prior ARPI | I | Weill Medical College of Cornell University | Phase I/II 225Ac-J591 Plus 177Lu-PSMA-I&T for Progressive Metastatic Castration Resistant Prostate Cancer | NCT04886986 | Recruiting | December 2027 |
| $^{225}$Ac-AKY-2519 | B7-H3 | mCRPC | I | Aktis | A Study of [225Ac]Ac-AKY-2519 in Patients With Metastatic Castration-Resistant Prostate Cancer (BActinium-1) | NCT07581184 | Recruiting | December 2027 |
| $^{225}$Ac-J591 and $^{177}$Lu-PSMA | PSMA | mCRPC | I | Weill Medical College of Cornell University | Phase I Study of 225Ac-J591 Plus 177Lu-PSMA Small Molecule for Progressive Metastatic Castration Resistant Prostate Cancer | NCT04886986 | Recruiting | December 2027 |
| $^{225}$Ac-A9-3408 | MC1R | Melanoma | I | Alpha-9 | A Phase 1-1b Study to Evaluate the Safety, Efficacy and Dosimetry of Study Drug A9-3408 in Subjects With Metastatic Melanoma | NCT07076550[4] | Recruiting | January 2028 |
| FPI-2068 | EGFR/cMET | Advanced solid tumors | I | AstraZeneca | A Phase 1, Dose-escalation Study of [225Ac]-FPI-2068 in Adult Patients With Advanced Solid Tumours | NCT06147037 | Recruiting | May 2028 |
| $^{225}$Ac-A9-0642 | GRPR | Solid tumors | I | Alpha-9 | A Study of [177Lu]Lu-A9-0631 and [225Ac]Ac-A9-0642 With [68Ga]Ga-A9-6217 or [177Lu]Lu-A9-0631 Imaging in GRPR+ Solid Tumors | NCT07661641 | Recruiting | December 2028 |
| RYZ801 | GPC3 | GPC3-positive HCC | I/Ib | Bristol Myers Squibb | Study of the Theranostic Pair RYZ811 (Diagnostic) and RYZ801 (Therapeutic) to Identify and Treat Subjects With GPC3+ Unresectable HCC (GPC3) | NCT06726161 | Recruiting | March 2029 |
| AZD2284 | STEAP2 | mCRPC | I | AstraZeneca | A Phase I Study of [225Ac]-AZD2284 in Patients With Metastatic Castration-Resistant Prostate Cancer | NCT06879041 | Recruiting | April 2029 |
| PD-32766 | CAIX | Renal cell carcinoma | I | PeptiDream | A Study of Theranostic Pair PD-32766D/T in Participants With Carbonic Anhydrase IX Positive Clear Cell Renal Cell Carcinoma | NCT07688187 | Recruiting | May 2029 |
| $^{225}$Ac-ETN029 | DLL3 | DLL3-expressing solid tumors | I | Novartis | Phase I Study of [225Ac]Ac-ETN029 in Patients With Advanced DLL3-expressing Solid Tumors | NCT07006727 | Recruiting | June 2031 |
| $^{225}$Ac-PSMA-R2 | PSMA | Prostate cancer | I | Novartis | Phase I/II Study of [225Ac]Ac-PSMA-R2 in PSMA-positive Prostate Cancer, With/Without Prior 177Lu-PSMA RLT (SatisfACtion) | NCT05983198 | Active, not recruiting | March 2031 |

[1]Although still listed on clinicaltrials.gov, we are unsure of trial's status given that Abdera is no longer in operation.

[2]Estimated study completion date given that primary completion date has already passed.

[3]Initial data expected in the first quarter of 2027.

[4]Alpha-9 has deprioritized the asset, but the trial is still listed on clinicaltrials.gov.

ARPI=Androgen receptor pathway inhibitor. CAIX=Carbonic anhydrase 9. CEA=Carcinoembryonic antigen. DLL3=Delta-like ligand 3. EGFR=Epidermal growth factor receptor. ES-SCLC=Extensive-stage small-cell lung cancer. GPC-3=Glypican-3. GRPR=Gastrin-releasing peptide receptor. HCC=Hepatocellular carcinoma. LCNEC=Large cell neuroendocrine carcinoma. MC1R=Melanocortin 1 receptor. mCRPC=Metastatic castration-resistant prostate cancer. PSMA=Prostate-specific membrane antigen. RLT=Radioligand therapy. SSTR=Somatostatin receptor.
Sources: ClinicalTrials.gov and William Blair Equity Research

**Exhibit 20**
**Radiopharmaceuticals**
**Ongoing Clinical Trials Involving Lead-212 Assets (Based on ClinicalTrials.gov Registry)**

| Asset/Regimen | Target | Indication | Phase | Company/ Sponsor | Study Title | Trial ID | Status | Estimated Primary Completion |
|---|---|---|---|---|---|---|---|---|
| $^{212}$Pb-DOTAMTATE | SSTR2 | NETs | II | RadioMedix/ Orano Med | Targeted Alpha-emitter Therapy of PRRT Naïve and Previous PRRT Neuroendocrine Tumor Patients (ALPHAMEDIX02) | NCT05153772 | Active, not recruiting | April 2025 |
| [$^{212}$Pb]VMT01-T101 | MC1R | Melanoma | I/II | Perspective Therapeutics | MC1R-Targeted Alpha-Particle Therapy Trial in Adults With Advanced Melanoma | NCT05655312 | Recruiting | December 2027 |
| $^{212}$Pb-ADVC001 | PSMA | mCRPC | I/II | AdvanCell | Dose Escalation and Efficacy Study of 212Pb-ADVC001 in Patients With Metastatic Castration Resistant Prostate Cancer | NCT05720130 | Recruiting | January 2029 |
| [$^{212}$Pb]VMT-α-NET | SSTR2 | Gastrointestinal NETs and Pheochromocytoma/ Paraganglioma | I/II | National Cancer Institute | Somatostatin-Receptors (SSTR)-Agonist [212Pb]VMT-Alpha-NET in Metastatic or Inoperable SSTR+ Gastrointestinal Neuroendocrine Tumor and Pheochromocytoma/Paraganglioma Previously Treated With Systemic Targeted Radioligand Therapy | NCT06427798 | Recruiting | July 2029 |
| [$^{212}$Pb]PSV359 | FAP | Solid tumors | I/IIa | Perspective Therapeutics | Lead-212 PSV359 Therapy for Patients With Solid Tumors | NCT06710756 | Recruiting | January 2028 |
| $^{212}$Pb-MP0712 | DLL3 | SCLC and other solid tumors | I/IIa | Molecular Partners | Study of [212Pb]Pb-DOTAM-MAM279 ([212Pb]Pb-MP0712) in Patients With Small-Cell Lung Cancer and Other DLL3 Expressing Solid Tumors | NCT07278479 | Recruiting | September 2028 |
| [$^{212}$Pb]VMT-α-NET | SSTR2 | NETs | I/IIa | Perspective Therapeutics | Targeted Alpha-Particle Therapy for Advanced SSTR2 Positive Neuroendocrine Tumors (212-Pb-VMT) | NCT05636618 | Recruiting | November 2029 |
| $^{212}$Pb-DOTAM-GRPR1 | GRPR | Solid tumors | I | Orano Med | Safety and Tolerability of $^{212}$Pb-DOTAM-GRPR1 in Adult Subjects With Recurrent or Metastatic GRPR-expressing Tumors | NCT05283330 | Recruiting | January 2027 |
| $^{212}$Pb-CEA-PRIT | CEA | Colorectal cancer | I | Roche | A Study to Investigate CEA-PRIT 2.0 in Participants With Metastatic Colorectal Cancer (mCRC) | NCT07416552 | Recruiting | February 2034 |
| CEA-PRIT 2.0 | CEA | Metastatic colorectal cancer | I | Roche | A Study to Investigate CEA-PRIT 2.0 in Participants With Metastatic Colorectal Cancer (mCRC) | NCT07416552 | Recruiting | February 2034 |
| [$^{212}$Pb]VMT-α-NET | SSTR2 | NETs | Early Phase I | University of Iowa | A Safety Study of 212Pb-VMT-Alpha-NET in Patients With Neuroendocrine Tumors | NCT06148636 | Active, not recruiting | December 2026 |
| $^{212}$Pb-Pentixather | CXCR4 | Lung carcinoid lesions | Early Phase I | University of Iowa | A Safety Study of 212Pb-Pentixather Radioligand Therapy | NCT05557708 | Not yet recruiting | June 2028 |

CEA=Carcinoembryonic antigen. CXCR4=Chemokine receptor type 4. DLL3=Delta-like ligand 3. FAP=Fibroblast activation protein. GRPR=Gastrin-releasing peptide receptor. MC1R=Melanocortin 1 receptor. NETs=Neuroendocrine tumors. mCRPC=Metastatic castration-resistant prostate cancer. PSMA=Prostate specific membrane antigen. SCLC=Small-cell lung cancer. SSTR=Somatostatin receptor.

Sources: ClinicalTrials.gov and William Blair Equity Research

There are several late-stage trials involving actinium-225; one is slated to read out by the end of the year in neuroendocrine tumors (more detail is provided later in this report). Bristol Myers, Novartis, and AstraZeneca are, as expected, sponsoring the majority of the Phase II and later clinical trials, while the earlier-stage studies (Phase I/II or Phase I) are sponsored by a mix of academic centers, smaller biotech, and large pharma. Based on the primary completion dates listed on the clinicaltrials.gov website, most trials complete in 2027 or after; the two late-stage trials from Novartis are slated to read out in 2028.

In our previous analysis of the actinium-225 clinical trial, we highlighted the number of actinium-225 trials employing the J591 antibody, which targets PSMA and to date is one of the most studied targeting moieties for radiopharmaceuticals employing actinium-225. Although J591 is still under investigation in the clinic (including a Phase II trial from Convergent Therapeutics), many of the trials have been previously completed and are not included in the above tables. In our current analysis, we note the increased variety in targets for actinium-225 assets, though PSMA remains the most popular choice, followed by SSTR.

The library of lead-212 trials is notably smaller but, in our view, likely to grow in the coming years as this isotope is being increasingly explored by radiopharmaceutical companies. We also believe that the interest in lead-212 could be bolstered, at least in the short term, by concerns about the actininium-225 supply chain. The potential convenience of producing lead-212 with generators could help combat manufacturing headwinds plaguing the industry. Furthermore, there is increasing enthusiasm about lead-212's simple decay chain, direct imaging through SPECT, and short half-life, which could facilitate fractionated, intensified, and/or adaptive dosing regimens.

The number of trials for terbium-161 is also relatively small but growing (exhibit 21). All but one trial is investigator-sponsored, and the vast majority target PSMA; the PSMA-I&T ligand is particularly popular. However, there are also PSMA assets that incorporate albumin binding or are designed with long-circulating ligands. Beyond prostate cancer, neuroendocrine tumors appear to currently be the only other indication under clinical investigation for terbium-161-based radiopharmaceuticals. We suspect that this is inspired by the success of Pluvicto in prostate cancer and that the indication space could expand in the future pending initial results of terbium-161 in prostate cancer.

**Exhibit 21**
**Radiopharmaceuticals**
**Ongoing Clinical Trials Involving Terbium-161 Assets (Based on ClinicalTrials.gov Registry)**

| Asset/Regimen | Target | Indication | Phase | Company/ Sponsor | Study Title | Trial ID | Status | Estimated Primary Completion |
|---|---|---|---|---|---|---|---|---|
| $^{161}$Tb-DOTATATE | SSTR | NETs | II | Tata Memorial Hospital | Study to Assess the Safety and Effectiveness of Novel Radiopharmaceutical Terbium-161 DOTATATE in Metastatic Neuroendocrine Tumors (TENET) | NCT07404176 | Recruiting | February 2028 |
| $^{161}$Tb-PSMA-I&T | PSMA | Pluvicto-Naïve mCRPC | II | Ankara University | Terbium 161 PSMA in Lutetium-177 PSMA Naive Patients (TeLuNa) | NCT07441837 | Not yet recruiting | August 2028 |
| $^{161}$Tb-PSMA-I&T | PSMA | mCRPC | II | National Taiwan University Hospital | Exploring Auger-Enhanced PSMA-Targeted Radioligand Therapy: A First-in-Taiwan Clinical Study of 161Tb-PSMA-I&T | NCT07621692 | Recruiting | December 2030 |
| $^{161}$Tb-PSMA-I&T | PSMA | mCRPC | I/II | Peter MacCallum Cancer Centre | EValuation of radIOLigand Treatment in mEn With Metastatic Castration-resistant Prostate Cancer With [161Tb]Tb-PSMA-I&T (VIOLET) | NCT05521412 | Recruiting | December 2026[1] |
| $^{161}$Tb-NYM032 | PSMA | mCRPC | I/II | Zhengguo Chen | Study on the Safety, Tolerability, and Preliminary Efficacy of 161Tb-NYM032 in Patients With Metastatic Castration-Resistant Prostate Cancer | NCT06827080 | Not yet recruiting | December 2026 |
| $^{161}$Tb-PSMA-I&T | PSMA | Locally advanced prostate cancer | I/II | Rabin Medical Center | Tb-PSMA-I&T Radionuclide Before Radical Prostatectomy in Patients With Locally Advanced Prostate Cancer - TbeforePROST Trial. | NCT07208240 | Recruiting | August 2028 |
| $^{161}$Tb-RAD402 | KLK3 | CRPC | I/IIa | Radiopharm Theranostics | A Study of Terbium 161 (161Tb)-RAD402 in Participants With CRPC (RAD402) | NCT07259213 | Recruiting | November 2028 |
| $^{161}$Tb-SibuDAB (long-circulating ligand) | PSMA | Metastatic prostate cancer | I | University Hospital, Basel, Switzerland | Targeted Radionuclide Therapy in Metastatic Prostate Cancer Using a New PSMA Ligand Radiolabelled With Terbium-161 (161Tb-SibuDAB) - Dose Identification/Escalation Phase Ia/b Study (PROGNOSTICS) | NCT06343038 | Recruiting | June 2028 |
| $^{161}$Tb-LNC1011 (albumin binding) | PSMA | mCRPC | Early Phase I | Peking Union Medical College Hospital | Safety, Tolerability and Preliminary Efficacy of 161Tb-LNC1011 (PSMA Radioligand) in Patients With Metastatic Castration-Resistant Prostate Cancer (mCRPC) (161Tb-LNC1011) | NCT07381582 | Not yet recruiting | October 2027 |

[1]Estimated study completion date since primary completion date was August 2025.

KLK3=Kallikrein-related peptidase 3. NETs=Neuroendocrine tumors. mCRPC=Metastatic castration-resistant prostate cancer. PSMA=Prostate specific membrane antigen. SSTR=Somatostatin receptor.

Sources: ClinicalTrials.gov and William Blair Equity Research

# Recent Datasets in the Radiopharmaceuticals Industry

In our view, the most practice-changing recent dataset was the Phase III PSMAddition trial of Pluvicto in the mHSPC setting, which was presented at ESMO 2025. While we are encouraged that the trial was positive, we recognize that enthusiasm about the results was relatively muted initially, owing to the lack of a significant overall survival (OS) benefit (though the survival data was immature at the time of presentation; a subsequent analysis continued to show a positive trend in OS without statistical significance). Furthermore, the discussant for the presentation highlighted that the trial may never demonstrate a significant survival benefit, owing to the crossover design of the study. When including several additional considerations, the discussant did not believe that the data warranted widespread use of Pluvicto in the tested disease setting and held the view that patients should be carefully selected based on PSMA biomarkers (e.g., PSMA $SUV_{mean}$ and PSMA total tumor volume). Despite mixed views of the results, Pluvicto was approved in the mHSPC setting in July 2026.

Below, we highlight several datasets presented during 2025 and early 2026 that showcase recent advancements in the field. Overall, we are encouraged by the progress in expanding the isotope toolbox, with particular attention drawn to lead-212 and some advancements for both actinium-225 and terbium-161.

**Lutetium-177 Updates**

***Novartis's Phase III PSMAddition Trial in mHSPC***

The Phase III PSMAddition trial evaluated Pluvicto (dosed at 7.4 GBq every 6 weeks for 6 cycles) administered in conjunction with standard of care (comprising androgen deprivation therapy and a novel hormone therapy) versus standard of care alone in patients with metastatic hormone-sensitive prostate cancer (HSPC). Patients randomized to standard of care are also allowed to cross over to the Pluvicto-containing arm. Based on top-line results announced in June, the trial met the primary endpoint of radiographic PFS (rPFS) at an interim analysis, and a positive trend in the OS secondary endpoint was also highlighted. Pluvicto was subsequently approved in this setting on July 31, 2026.

A total of 1,144 patients were enrolled in the trial, with 572 randomized to the Pluvicto arm and an additional 572 enrolled to the control arm. Across all patients, the median age was 68 years, the majority (70%) of patients had an ECOG performance status of 0, 70% had a Gleason score of 8-10, and half had de novo disease. Bone metastases were present in 91% of patients, while 41% had visceral metastases and 59% had soft-tissue disease.

Median rPFS was not reached in either arm, and the hazard ratio was 0.72 ($p$=0.002). All subgroups analyzed favored the Pluvicto arm in terms of rPFS benefit, though in some subgroups, the upper bound of the 95% confidence interval crossed 1. For OS, there was a trend toward favoring the Pluvicto treatment with a hazard ratio of 0.84, but the upper end of the 95% confidence interval was 1.13 (the $p$-value for OS was 0.125). Once again, median OS was not reached for either arm. The ORR in patients with measurable soft-tissue disease at baseline slightly favored Pluvicto at 85% (57% complete response rate), versus 81% (42% complete response rate) for the control arm.

TRAEs occurring at grade 3 or higher were reported in 23% of patients in the Pluvicto arm and 12% of patients in the control arm. Adverse events leading to discontinuation of any drug treatment occurred in 8.2% and 4.1% of patients in the Pluvicto and control arms, respectively. No treatment-related deaths were reported. Dry mouth occurred in 46% of patients treated with the Pluvicto regimen (versus 3.7% for the control arm), but all cases were grade 1 or 2. Grade 3 or higher adverse events occurring in at least 5% of patients were hypertension (6.0% for the Pluvicto arm versus 6.2% for the control arm), anemia (5.0% versus 2.7%), and decreased lymphocyte count (5.0% versus 1.2%).

The trial results are outlined in exhibit 22. A subsequent updated analysis was conducted, and results were disclosed upon approval in mHSPC. Like the initial data, risk of progression or death was reduced by 28% with a hazard ratio of 0.72, and OS continued to favor Pluvicto with a hazard ratio of 0.80. Although the upper end of the 95% confidence interval was lower compared to the initial data disclosure, it still crossed 1, albeit barely, at 1.01.

**Exhibit 22**
**Novartis AG**
**Phase III PSMAddition Trial of Pluvicto in Metastatic Hormone-Sensitive Prostate Cancer**

**Trial Results (NCT04720157)**

| | | | |
|---|---|---|---|
| **Mechanism of Action** | | PSMA-targeting radioligand incorporating lutetium-177 | |
| **Enrollment Criteria** | | ECOG PS 0 to 2<br>Treatment naïve or minimally treated[1]<br>PSMA-positive by PSMA PET | |
| **Study Arm** | | Pluvicto<br>(7.4 GBq +/- 10% every 6 weeks for 6 cycles) + ADT + ARPI | ADT + ARPI[2] |
| **Enrollment** | | 572 patients | 572 patients |
| **Patient Baseline Characteristics** | | *Median age* = 68 years<br>*ECOG PS:* 0 / 1 / 2 = 69% / 30% / 0.2%<br>*Gleason score of 8-10:* 68%<br>*Median PSA* = 12.1 µg/L<br>*Site of disease:* soft tissue / bone / visceral = 60% / 91% / 39% | *Median age* = 68 years<br>*ECOG PS:* 0 / 1 / 2 = 71% / 27% / 1.2%<br>*Gleason score of 8-10:* 71%<br>*Median PSA* = 11.6 µg/L<br>*Site of disease:* soft tissue / bone / visceral = 59% / 91% / 42% |
| **Radiographic Progression-Free Survival** | | **Not reached**<br>**(HR=0.72, *p* =0.002)** | **Not reached** |
| **Overall Survival (intent-to-treat analysis)** | | Not reached<br>(HR=0.84; *p* =0.125) | Not reached |
| **Objective Response Rate[3]** | | 85%<br>(out of 224 patients)<br><br>*Complete response rate: 57%* | 81%<br>(out of 213 patients)<br><br>*Complete response rate: 42%* |
| **Grade 3+ Treatment-Related Adverse Events (TRAEs)** | | 23% | 12% |
| **Common (≥20%) Treatment-Emergent Adverse Events (TEAEs; all grades)** | *Dry mouth* | 46% | 3.7% |
| | *Fatigue* | 35% | 28% |
| | *Nausea* | 34% | 9.4% |
| | *Hot flash* | 29% | 36% |
| | *Anemia* | 27% | 13% |
| | *Arthralgia* | 20% | 23% |
| | *Back pain* | 18% | 20% |
| | *Constipation* | 18% | 16% |
| | *Asthenia* | 16% | 13% |
| | *Hypertension* | 14% | 17% |
| **Serious Adverse Events (all grades)** | | 32%<br>(treatment-related=6.9%) | 29%<br>(treatment-related=2.5%) |
| **Grade 5 TEAEs** | | 2.7%<br>(treatment-related=0%) | 2.5%<br>(treatment-related=0%) |
| **TEAEs Leading to Discontinuation** | | 16% | 9.0% |

ADT=Androgen deprivation therapy. ARPI=Androgen receptor pathway inhibitor. ECOG PS=Eastern Cooperative Oncology Group performance status. HR=Hazard ratio. PSMA=Prostate-specific membrane antigen.

[1]ADT allowed in the neo-adjuvant/adjuvant setting. ADT/ARPI also allowed if used for up to 45 days for metastatic disease.

[2]Can cross over to Pluvicto arm following centrally reviewed radiographic progression. After crossover, ADT/ARPI is not required.

[3]In patients with measurable soft-tissue disease at baseline, accounting for bone disease.

Sources: ESMO 2025

***Telix's Phase III ProstACT Trial Part 1 in mCRPC***

At ASCO 2026, preliminary results were presented from part 1 of the global Phase III ProstACT trial of TLX591 in mCRPC. The trial randomized 36 patients with mCRPC who progressed following treatment with one prior androgen receptor pathway inhibitor across three dosing cohorts: TLX591 in combination with the standard-of-care treatments Xtandi (cohort 1, n=11) or Zytiga (cohort 2, n=11), or TLX591 dosing followed by docetaxel (cohort 3, n=14). Part 1 of the trial was designed as a safety and dosimetry lead-in to part 2, establishing safety profiles, dosimetry, and pharmacokinetics across the three cohorts.

The enrolled patient population was slightly older compared to other trials (median age 77 years), and the majority of enrolled patients were in the second-line treatment setting. The most common prior androgen receptor pathway inhibitor was Xtandi (47%; 17/36 patients), followed by Zytiga (28%; 10/36 patients), Nubeqa (17%; 6/36 patients), and Erleada (8%; 3/36 patients). Average PSA levels at baseline were 60.3 ng/dL, and we note a higher degree of viscera metastases (36%; 13/36 patients).

The most common treatment-related adverse events were hematological in nature, which included thrombocytopenia in 78% of patients (grade 3=5 patients; grade 4=11 patients), neutropenia in 64% (grade 3=8 patients; grade 4=9 patients), anemia in 44% (grade 3=1 patient; grade 4=0 patients), white blood cell count decrease in 42% (grade 3=6 patients; grade 4=5 patients), and lymphopenia in 56% (grade 3=8 patients; grade 4=7 patients). Of these patients, most self-resolved, with 5.6% receiving red blood cell transfusion, 13.9% receiving platelet transfusion, and 8.3% receiving G-CSF. Hematological profiles were transient, with platelet counts recovering to grade 1 or lower levels over the course of 15 days following treatment. Common nonhematological events included mostly mild to moderate fatigue (53%, grade 3=2 patients), nausea (28%, grade 3=1 patient), and dry mouth (25%). Notably, management previously indicated that investigators did not attribute all cases of dry mouth to TLX591 itself.

Pharmacokinetic profiles appeared to be consistent across cohorts, showing high blood concentrations that slowly decline over the course of 15 days. In parallel, lesion radioactivity gradually increases and plateaus, showing sustained uptake out to 15 days. Organ radiation exposure remained within safe levels, with the highest uptake seen in the liver, left colon, rectum, right colon, spleen, and kidney. Lesion dosimetry across all tumor sites (n=132) was about 4.83 Gy on average. Bone lesions (n=122) had absorbed dose of 5.0 Gy on average, and lymphatic nodes (n=8) and soft tissues (n=2) were 2.01 Gy and 5.73 Gy, respectively.

Part 2 of the ProstACT GLOBAL trial is currently enrolling outside the U.S., and in early July 2026 Telix announced that based on the part 1 safety data and part 2 trial design, it had aligned with the FDA during a Type B meeting. Therefore, Telix plans to submit an IND amendment to officially allow ProstACT to progress to part 2 in the U.S. The company also plans to look at progression-free survival as an exploratory endpoint, with potential for results later this year or early next (once 81 disease progression events have occurred).

The part 1 safety results are outlined in exhibit 23 and are compared to the Phase III PSMAfore trial of Pluvicto.

**Exhibit 23**
**Telix Pharmaceuticals Limited**
**Comparison of Phase III Part 1 Safety Results of TLX591 Versus Pluvicto in Metastatic Castration-Resistant Prostate Cancer**

| | ProstACT GLOBAL Trial (NCT06520345) - Part 1 | PSMAfore Trial (NCT04689828) | |
|---|---|---|---|
| **Mechanism of Action** | PSMA-targeting radiolabeled (with lutetium-177) antibody | PSMA-targeting radiolabeled (with lutetium-177) small molecule | |
| **Inclusion Criteria** | PSMA-positive tumor by PET scan (gallium-based)<br>Progression after Xtandi or Zytiga plus prednisone (at least 12 weeks of therapy)<br>Chemotherapy-naïve (except in mCSPC setting if ≥ 6 months prior to screening)<br>ECOG PS: 0, 1, or 2 | PSMA-positive tumor by PET scan (gallium-based)<br>Progression after Xtandi or Zytiga plus prednisone<br>Taxane-naïve (adjuvant/neoadjuvant setting if >12 months ago)<br>ECOG PS: 0 or 1 | |
| **Study Arm** | TLX591<br>(76 mCi every 2 weeks for 2 cycles)<br>+<br>Best standard of care<br>(ARPI or taxane) | Pluvicto<br>(200 mCi every 6 weeks for 6 cycles) | ARPI change |
| **Patient Baseline Characteristics** | Median age=77 years<br>Second line=72%<br>Median baseline PSA=18.2 ng/dL<br>ECOG PS 0/1=53%/47%<br>Metastases=lymph node/bone/visceral=39 /47%/36%<br>Prior ARPI=Xtandi/Zytiga/other=47%/28%/25%<br>Prior taxane=25% | Median age=71 years<br>Second-line=82%<br>Median baseline PSA=18.4 ng/dL<br>ECOG PS 0/1=62%/37%<br>Site of disease=lymph node/bone/liver=32%/88%/6%<br>Prior ARPI=Xtandi/Zytiga/other=40%/51%/9% | Median age=72 years<br>Second-line=80%<br>Median baseline PSA=14.9 ng/dL<br>ECOG PS 0/1=50%/49%<br>Site of disease=lymph node/bone/liver=31%/87%/3%<br>Prior ARPI=Xtandi/Zytiga/other=35%/56%/9% |
| **Enrollment** | 36 patients | 227 patients | 232 patients |
| **All-Grades (Grade 3/4) Non-Hematologic Treatment-Emergent Adverse Events** | Fatigue: 53% (6%)<br>Nausea: 28% (3%)<br>Dry mouth: 25% (0%)<br>Diarrhea: 22% (0%)<br>Back pain: 22% (3%)<br>Headache: 14% (0%) | Fatigue: 23% (<1%)<br>Nausea: 32% (0%)<br>Dry mouth: 58% (0.9%)<br>Diarrhea: 17% (0%)<br>Back pain: 14% (1.3%)<br>Headache: 8.4% (0%) | Fatigue: 25% (1.7%)<br>Nausea: 12% (<1%)<br>Dry mouth: 3% (0%)<br>Diarrhea: 9% (<1%)<br>Back pain: 20% (2.6%)<br>Headache: 4.7% (0%) |
| **All-Grades (Grade 3+) Hematologic Treatment-Emergent Adverse Events** | Thrombocytopenia: 78% (45%)<br>Neutropenia: 64% (47%)<br>Anemia: 44% (3%)<br>WBC decrease: 42% (31%)<br>Lymphopenia: 56% (41%) | Thrombocytopenia: 7.5% (2.2%)<br>Neutropenia: 5.7% (1.3%)<br>Anemia: 27% (6.2%)<br>WBC decrease: N/A*<br>Lymphopenia: N/A* | Thrombocytopenia: 3.0% (0.9%)<br>Neutropenia: 0.9% (<1%)<br>Anemia: 19% (6.9%)<br>WBC decrease: N/A*<br>Lymphopenia: N/A* |

ARPI=Androgen receptor pathway inhibitor. ECOG PS=Eastern Cooperative Oncology Group performance status. mCi=Millicurie. mCRPC=Metastatic castration-sensitive prostate cancer. PET=Positron emission tomography. PSA=Prostate specific antigen. PSMA=Prostate-specific membrane antigen. WBC=White blood cell.

*Not specifically disclosed (included in broad myelosuppression category).

Sources: Telix reports, Morris, M. et al. *Lancet* (2024), and clinicaltrials.gov

**Lead-212 Updates**

***AdvanCell's Phase I/II TheraPb Trial in mCRPC***

In our view, one of the highlights for radiopharmaceuticals during 2025, from a data perspective, was AdvanCell's I/II TheraPb trial data of lead-212-powered ADVC001 in mCRPC, which was presented at ESMO. Despite the early nature of the results, the data marked the first clinical dataset (aside from a previously reported case study) for a lead-212-based therapy that targets PSMA, and we believe it set a new bar for PSMA radioligand therapy in mCRPC. We are impressed by the initial results and believe that they lay the foundation for lead-212 to become an important isotope for radiopharmaceuticals targeting prostate cancer (and potentially additional cancer indications, pending future data).

The Phase Ib dose-escalation portion enrolled 22 patients across 7 dose cohorts (60 MBq, 120 MBq, 160 MBq, and 200 MBq were tested across various administration schedules from once every 6 weeks for 4 cycles to every week for 4-6 cycles). The median age was 73 years, and 77% had an ECOG performance status of 1. The majority (91%) were treated with 1 prior line of androgen receptor pathway inhibitors, and 36% were treated with 1 prior line of chemotherapy (an additional 36% were treated with 2 or 3 lines of prior chemotherapy, while 27% had no prior chemotherapy exposure). Overall, half of the patients had 3 or more prior lines of systemic therapy. Most (86%) had bone metastases, and the median $SUV_{mean}$ was 8.9.

The $PSA_{50}$ was 80% in 15 patients who were treated with a dose of 160 MBq or more of ADVC001, and the $PSA_{80}$ in these patients was 60%. Across all 22 patients, the $PSA_{50}$ was 64%. In six patients with RECIST-measurable lesions at baseline, the ORR was 100%, with two patients (33%) achieving complete responses.

While TheraPb includes patients both with and without prior chemotherapy, we highlight that the $PSA_{50}$ response in patients treated with 160 MBq or higher was notably higher than both the Phase III VISION trial (post-chemotherapy) at 46% and the Phase III PSMAfore trial (pre-chemotherapy) at 51% (though we acknowledge all the caveats and limitations associated with cross-trial comparison, including that the TheraPb data is based on small patient numbers and in an earlier phase of development compared to the Pluvicto studies). While recognizing the small sample size, we also emphasize the impressive ORR, which outperforms both VISION (51%, based on patients with measurable disease at baseline based on RECIST v1.1 criteria) and PSMAfore (50%, again based on measurable disease patients).

The maximum tolerated dose was not reached during dose escalation. In addition, no treatment-related serious adverse events were reported, and there were no discontinuations or dose modifications due to TRAEs. Across the 22 patients enrolled in the study, grade 3 TRAEs occurred in 9% of patients (1 case of anemia and 1 case of hypophosphatemia), and no grade 4 or grade 5 TRAEs were reported. Treatment-related dry mouth at grade 1 and grade 2 occurred in 59% and 23% of patients, respectively.

Based on pharmacokinetic measurements, the blood concentration of ADVC001 rapidly diminished with an elimination half-life of about six hours. We believe this encouraging pharmacokinetic profile could increase the feasibility of incorporating powerful alpha-emitting payloads into the cancer treatment paradigm. Dosimetry measurements also revealed a low radiation absorbed dose to healthy organs. Of particular note, the absorbed dose to the kidneys was estimated to be 1.7 Gy for the 160 MBq dose of ADVC001 and 2.4 Gy for the maximum 200 MBq dose (for reference, the limit for radiation to the kidneys that was set by external beam radiation therapy is 23 Gy to 28 Gy).

The Phase II dose expansion portion of the study will investigate the two highest doses of ADVC001 (160 MBq and 200 MBq) and will incorporate adaptive dosing. In addition to pre-chemotherapy mCPRC, post-$^{177}$Lu-PSMA mCRPC and mHSPC will also be investigated. We are encouraged to see the broad range of settings being tested as it provides multiple avenues for showcasing the potential power of lead-212.

***Orano Med's/RadioMedix's ALPHAMEDIX 02 Trial in GEP-NETs***

At ESMO 2025, there were also two datasets presented for Orano Med's/RadioMedix's Phase II ALPHAMEDIX 02 trial of 212Pb-DOTAMTATE in gastroenteropancreatic neuroendocrine tumors (GEP-NETs). The trial includes two cohorts: cohort 1 evaluates the agent in patients naïve to radioligand therapy, while cohort 2 is investigating the post-radioligand setting. In both cohorts, 212Pb-DOTAMTATE was dosed at 67.6 µCi/kg every 8 weeks for up to 4 cycles.

Based on prior data from cohort 1 (presented at the 2024 American Society of Clinical Oncology annual meeting), the ORR was 56% in 36 patients. The 24-month PFS and OS were 74% and 91%, respectively, in patients from both cohort 1 of ALPHAMEDIX 02 and the Phase I ALPHAMEDIX 01 trial. Hematologic toxicity was generally grade 3 or 4 lymphocytopenia that was reversible. This year at ESMO, long-term follow-up of cohort 1 from ALPHAMEDIX 02 was presented.

In 35 patients, the median age was 60 years, 23% had grade 1 disease while 66% had grade 2 (5.7% had grade 3), all had prior somatostatin analog (SSA) therapy, and 83% had prior surgery. With the longer-term follow-up, the ORR increased slightly to 60% (all partial responses). For comparison, the response rate in the Phase III NETTER-1 trial of Lutathera was 18%. Most patients (72%) experienced responses of 2 years or more, and 86% of patients received all 4 doses of treatment. The 36-month PFS and OS rates of 72% and 88%, respectively, were similar to the previously reported 24-month rates. In NETTER-1 the final median OS for Lutathera was 48 months.

Grade 3 and higher TEAEs occurred in 54% of patients, although only one patient (2.9%) discontinued due to TEAEs. The one death due to sepsis was described as likely unrelated to treatment. Grade 3 or higher TEAEs that were reported in at least 5% of patients were lymphopenia (26%), decreased weight (8.6%), chronic kidney disease (8.6%), decreased glomerular filtration rate (8.6%), fatigue (5.7%), and decreased appetite (5.7%). Dysphagia (described as a chronic adverse event) of all grades occurred in 49% (2.9% grade 3) of patients.

Cohort 2 enrolled 26 patients with a mean age of 62 years. Half of the patients had grade 2 disease, while 27% had grade 1 and 12% had grade 3. In addition to prior radioligand therapy, 96% had prior SSA therapy, 89% had prior surgery, 58% had prior chemotherapy, and 58% had prior TKIs. The ORR was 35% (again, all were partial responses), and all patients experienced a duration of response of 18 months or more. Similar to cohort 1, most patients (85%) received all 4 doses of the treatment. The 18-month PFS was 83%, while 18-month OS was 85%.

Grade 3 or higher TEAEs occurred in 42% of patients, and there were no discontinuations or deaths due to TEAEs. Grade 3 or higher TEAEs that were reported in at least 5% of patients were lymphopenia (15%), dysphagia (12%), vomiting (7.7%), and chronic kidney disease (7.7%). Dysphagia (58% all grade) was described as an unexpected side effect that is still under investigation, and it was highlighted that a longer follow-up may be needed to obtain a comprehensive picture of renal toxicity (therefore, the reported renal toxicities from the longer-term follow-up of cohort 1 may be more comprehensive).

Sanofi removed $^{212}$Pb-DOTAMTATE from its pipeline in early 2026, although Orano Med is continuing to develop the asset. Although speculation on our part, we believe that Sanofi's decision could be rooted in the high rates of chronic kidney disease (grade 4 or higher requires dialysis or transplant) and other renal events.

***Perspective Therapeutics' Update of VMT-α-NET in NETs***

Interim data from Perspective's Phase I/IIa trial of [$^{212}$Pb]VMT-α-NET in NETs was also presented at ESMO 2025, with updated data disclosed at ASCO GI 2026. The study includes three main cohorts in the dose-finding phase: four doses of [$^{212}$Pb]VMT-α-NET at 2.5 mCi (cohort 1), 5 mCi (cohort 2), or 6 mCi (cohort 3). First disclosed at the American Association for Cancer Research annual meeting in March 2026, another cohort in the trial will test a front-loaded regimen with an initial dose of 6 mCi, followed by two doses of 5 mCi and a final dose of 4 mCi.

The data from ASCO GI included 56 patients across the first three cohorts (2 patients in cohort 2, 46 patients in cohort 2 [split into two halves based on extent of follow up], and 8 patients in cohort 3). The median age range across all patients was 63 years; 23% had an ECOG performance status of 1 (the rest had a status of 0); 59% of the GEP-NET patients (which were 95% of all patients) had non-pancreatic GEP-NETs; and the median number of prior systemic therapies was 1. A total of 11% of patients had grade 3 tumors, while 70% and 20% had grade 2 and grade 1 tumors, respectively.

Focusing on the 23 patients in the first half of cohort 2 (patients with a median follow-up of 11 months), 9 patients (39%) had a partial response (35% confirmed response rate). Of the 16 patients in the first half of cohort 2 who had SSTR2 expression in all tumors, 7 (44%) had a partial response. For the two patients in cohort 1, stable disease has been ongoing for two years.

There were no treatment-related discontinuations, and serious adverse events (none deemed related to treatment) were reported in five patients. Grade 3 or higher adverse events occurred in 38% of patients (no grade 5 events were reported), and the most common grade 3/4 adverse event was decreased lymphocyte count. No serious renal complications were reported.

Additional updated results were presented later in the year at the annual ASCO meeting. Based on an April 17 data cutoff, 68 patients were treated, 46% of which had pancreatic GEP-NETs and 50% of which had non-pancreatic GEP-NETs. The median number of prior systemic therapies was one, and the proportion of patients that were grade 1, grade 2, and grade 3 was 22%, 65%, and 13%, respectively. No dose-limiting toxicities or treatment-related discontinuations were reported. There were also no reports of serious renal complications, clinically meaningful myelosuppression, or dysphagia. In the first half of cohort 2 (5 mCi dose), the confirmed objective response rate was 39% (9 of 23 patients), with an unconfirmed response rate of 43%.

***Perspective's Phase I/IIa Trial of $^{212}$Pb-VMT01 in Melanoma***

At the ASCO 2026 meeting, preliminary results were presented for both part 1 (monotherapy) and part 2 (in combination with Opdivo) of the Phase I/IIa trial. The asset targets MC1R and has been granted fast-track designation by the FDA. Participants received up to three cycles of 212Pb-VMT01 at a dose of 1.5 mCi, 3 mCi, or 5 mCi (only 1.5 mCi or 3 mCi for part 2). As of the data cutoff of March 25 of this year, 27 patients were enrolled with a median of four lines of prior systemic therapy. No treatment-related serious adverse events were reported, and there were no discontinuations due to adverse events. The most common treatment-emergent adverse events were fatigue (52%), nausea (37%), dyspnoea (19%), abdominal pain (15%), anemia (15%), and increased AST (15%). Based on preliminary efficacy data in patients treated with monotherapy, 2 of the 7 patients (29%) treated at the 3 mCi dose achieved a confirmed partial response. No confirmed responses were observed at the other two doses.

Taken together, we believe Perspective's lead-212-based therapies have demonstrated encouraging safety, especially in regard to renal toxicity that could limit other lead-212-based therapies in NETs. From an efficacy perspective, it is our view that more mature data, especially in melanoma, is needed to inform a view on the potential of these assets. We are particularly intrigued by the front-loaded dosing cohort for $^{212}$Pb-VMT-α-NET in NETs as we believe it supports the trend of alternative dosing schemes that could ultimately lead to improved patient outcomes.

**Actinium-225 Updates**

***Novartis's Phase I AcTION Trial in mCRPC***

At ASCO 2026, Dr. Louise Emmett presented results for Novartis's Phase I AcTION trial of $^{225}$Ac-PSMA-617 in mCRPC both with and without prior Pluvicto or other $^{177}$Lu-PSMA therapy (abstract 5010). Novartis's $^{225}$Ac-PSMA-617 was administered every 8 weeks for up to 6 cycles at a dose of 4 MBq, 6 MBq, 8 MBq, or 10 MBq (dose escalation) or 8 MBq or 10 MBq (dose expansion). Three patient groups were tested: group A patients had prior taxane and ARPI but were naïve to $^{177}$Lu-PSMA; group B patients had no prior exposure to taxane, ARPI, or $^{177}$Lu-PSMA; and group C patients had exposure to prior $^{177}$Lu-PSMA, while prior exposure to taxane and ARPI was not required.

Across all dose levels, $PSA_{50}$ responses in group A (34 patients), B (27 patients), and C (40 patients) were 59%, 85%, and 53%, respectively, while overall $PSA_{90}$ was 44%, 82%, and 18%, respectively. Objective response rate in group A was 43% (of 14 patients), in group B was 33% (of 9 patients), and in group C was 42% (of 12 patients). Treatment-related adverse events of grade 3 or higher occurred in 24% of group A patients, 11% of group B patients, and 15% of group C patients. The rate of treatment-emergent adverse events that led to discontinuation in groups A, B, and C was 2.9%, 0%, and 10%, respectively. Dry mouth (all grade 1 or 2) was the most common adverse event, occurring in 90% to 97% of patients across the three groups. The recommended Phase II dose for all groups was 10 MBq every 8 weeks for up to 6 cycles.

The discussant highlighted the high rates of dry mouth, which can have a significant negative impact on patients' quality of life. However, it was also noted that no cases of grade 3 dry mouth (characterized by lack of ability to swallow and need for a feeding tube) were reported. Meanwhile, the discussant was enthusiastic that $PSA_{50}$ was reported in up to 100% of group B patients at the 10 MBq dose, along with a $PSA_{90}$ of 91% at the same dose and in the same patient group. We are also encouraged to see responses, albeit lower, in the Pluvicto-experienced group C patients, suggesting the ability for alpha therapy to rescue patients who relapse on or who do not respond to beta therapy.

Comparing group A to other trials in prostate cancer with similar patient populations, we highlight that $PSA_{50}$ responses are similar to AdvanCell's Phase Ib TheraPb trial of $^{212}$Pb-ADVC001 and Bayer's Phase I PAnTHA trial of $^{225}$Ac-PSMA-Trillium. On the safety side, rates of xerostomia were also comparable between the three trials (though numerically higher in AcTION, and the majority of patients did not recover), and hematologic toxicities appear lowest for $^{212}$Pb-ADVC001.

There are two ongoing Phase III trials evaluating $^{225}$Ac-PSMA-617 in mCRPC. The PSMAcTION is in the post-Pluvicto setting, while AcTFIRST is combining with ARPI in the frontline setting. Both are expected to read out in 2028.

**Convergent's Phase II CONVERGE-01 Trial in mCRPC**

At ASCO 2026, results from part 3 of the Phase II CONVERGE-01 trial from Convergent Therapeutics were presented. The study is evaluating two doses (45 kBq/kg and 55 kBq/kg) administered two weeks apart of CONV01-α, a PSMA-directed antibody rosopatamab conjugated to actinium-225 (or indium-111 for imaging), in mCRPC. Part 3 of the study is designed to determine the recommended Phase II dose. All patients were exposed to prior $^{177}$Lu-PSMA and ARPI therapy, and 80% had prior taxane exposure.

In 25 evaluable patients, $PSA_{50}$ was 40%. At a median follow-up of 8.1 months, preliminary median rPFS was 8.4 months in 11 patients treated at the future fixed target dose of 9 MBq. No dose-limiting toxicities were observed, and no treatment-related adverse events led to discontinuation. The most common treatment-emergent adverse event was dry mouth, all grade 1 or 2 and occurring in 63% of patients, though it was noted that about 49% of patients had experienced dry mouth

previously due to prior treatment with $^{177}$Lu-PSMA or had dry mouth at screening. There was also evidence of hematologic toxicity; the most common grade 3 adverse events were decreased lymphocyte count (49%), anemia (26%), decreased platelet count (23%), and decreased neutrophil count (11%). Nephrotoxicity was not observed.

One of the potential advantages of targeting PSMA with an antibody is limited exposure of salivary glands to radiation as PSMA-targeted antibodies are said to be more specific to PSMA expressed on the tumor versus on healthy tissues. Given that a considerable proportion of patients in CONVERGE-01 may have had baseline xerostomia, we concede that it is difficult to fully characterize rates of dry mouth reported in the study given the potentially cumulative effect. Similarly, although rates of grade 3 or higher hematologic adverse events appear to be high, prior radiation exposure could have influenced patients' ability to recover from hematologic toxicity given the cumulative nature of these events. Regarding renal toxicity, we are encouraged that meaningful nephrotoxicity was not observed, supporting the hypothesis that liver-based clearance of antibodies, compared to renally cleared peptides, may help spare the radiation-sensitive kidneys. Regarding efficacy, we are encouraged by the 40% $PSA_{50}$ response given the heavily pretreated nature of the population (all had prior Pluvicto and at least one prior ARPI, and 80% had a prior taxane).

A Phase III trial in Pluvicto-experienced patients is under preparation.

**Terbium-161 Updates**

***First-in-Human Data From Phase I/II VIOLET Trial in mCRPC***

Presented at the ASCO 2025 annual meeting, the first-in-human Phase I/II VIOLET study of $^{161}$Tb-PSMA-I&T evaluated the radioligand at starting doses of 4.4 GBq, 5.5 GBq, or 7.4 GBq every 6 weeks for up to 6 cycles; the dose was reduced by 0.4 GBq each cycle. Patients with mCRPC were eligible if they had progressed following prior therapy with at least one line of taxane (if suitable) and an androgen receptor pathway inhibitor (ARPI). Tumors were required to be PSMA positive with an $SUV_{max}$ of 20 or higher (no FDG-positive/PSMA-negative disease was allowed). The primary endpoints were maximum tolerated radioactivity and safety.

A total of 30 patients were treated, with 24 patients treated at the highest 7.4 GBq dose, and 70% of patients completed all 6 cycles. Median age was 69 years, and regarding prior therapy, 67% received prior taxane-based chemotherapy (67% docetaxel and 13% cabazitaxel) and all patients received prior ARPI. The PSA level at screening was 27 ng/mL.

A $PSA_{50}$ was achieved in 70% of patients, and the $PSA_{90}$ response rate was 40%. Radiographic PFS at a follow-up of 11.0 months was 11.1 months, while median PSA-PFS was 9.0 months. Mean radiation absorbed dose to normal organs was evaluated in the parotid glands, kidneys, liver, and spleen, and found to be 0.15 Gy/GBq, 0.36 Gy/GBq, 0.08 Gy/GBq, and 0.06 Gy/GBq, respectively.

The majority of adverse events from treatment with $^{161}$Tb-PSMA-I&T were grade 1 or 2 and none were grade 4. Grade 3 or 4 TRAEs occurred in 2 patients (7%), which included 1 case of lymphocytopenia and 1 case of pain. No dose-limiting toxicities were observed, and all cases of dry mouth (occurring in 70% of patients) were grade 1.

While acknowledging all the caveats and limitations associated with cross-trial comparison, we highlight that the $PSA_{50}$ is numerically higher than the 46% rate from the Phase III VISION trial of Pluvicto and the 58% reported from the Phase III PSMAfore trial. The rPFS was greater than the 8.8 months from VISION and similar to but numerically lower than the 12.0 months from PSMAfore. While more studies are needed, we view these additional results as encouraging and providing support for expanding the beta-emitting radioisotope toolbox.

# Upcoming Radiopharmaceutical Readouts

In this section, we highlight select therapeutic readouts that we expect later this year or next year and that we believe could have important implications for the radiopharmaceuticals field as a whole.

**Bristol's Phase III ACTION-1 Trial in GEP-NETs**

Perhaps the most anticipated radiopharmaceuticals data update in 2026 is the top-line data from the Phase III portion of ACTION-1, which is evaluating RYZ-101 in GEP-NETs. The results will represent the first Phase III dataset for actinium-225 and therefore could be instrumental in shaping investors' view of the isotope's long-term and commercial potential. The data is slated for release by the end of the year.

Enrollment in ACTION-1 requires prior treatment with Lutathera or another lutetium-177-labeled somatostatin analogue. RYZ101 is being evaluated at 10.2 MBq (the recommended Phase III dose from the Phase Ib portion of the trial) every eight weeks for up to four cycles. The active comparator arm is standard-of-care, which can include Afinitor, Sutent, or a high-dose long-acting somatostatin analogue. Progression-free survival is the primary endpoint, with OS as a secondary endpoint. The trial design is summarized in exhibit 24.

**Exhibit 24**
**Bristol Myers Squibb Company**
**Phase III ACTION-1 Trial of RYZ101 in Well-Differentiated GEP-NETs**

| Trial Design (NCT05477576) | | |
|---|---|---|
| **Mechanism of Action** | SSTR-targeting radioligand incorporating actinium-225 | |
| **Enrollment Criteria** | ECOG PS 0 to 2, grade 1 or 2, Ki67 ≤20<br>SSTR-positive by PET<br>2-4 cycles prior Lutathera/$^{177}$Lu-labeled SSA | |
| **Study Arm** | RYZ101<br>(10.2 MBq every 8 weeks for 4 cycles) | Standard of care<br>(Afinitor, Sutent, or high-dose long-acting SSA) |
| **Estimated Enrollment** | 338 patients (randomized 1:1) | |
| **Primary Endpoint** | **Progression-free survival** | |
| **Key Secondary Endpoints** | Overall survival<br>Objective response rate<br>Duration of response | |
| **Timeline** | Top-line data: 2H 2026 | |

GEP-NETs=Gastroenteropancreatic neuroendocrine tumors. SSA=Somatostatin analogue.
Sources: clinicaltrials.gov, NANETS 2023 Symposium abstracts

**Telix's Phase III ProstACT Trial Part 2 in mCRPC**

As reported above, the part 1 safety data from ProstACT has already been disclosed, but we await the part 2 efficacy data to inform our view on the potential of TLX591. We are intrigued by the simplified dosing schedule—two doses administered two weeks apart—but we also recognize investor skepticism about the antibody modality. Therefore, we believe the efficacy data will be critical in defining the role of TLX591 among incumbents like Pluvicto and potentially Curium's $^{177}$Lu-PSMA-I&T. Although the exact timing of the initial data release has not been disclosed, we

believe it could occur as early as the end of 2026 (once 81 disease progression events have occurred). Part 2 of the trial has not yet initiated within the U.S., although Telix has aligned with the FDA and expects to submit an IND in the near term.

**AstraZeneca's Phase II AlphaBreak Trial in mCRPC**

The AlphaBreak trial evaluates zadavotide guraxetan, which AstraZeneca gained access to through its acquisition of Fusion Pharmaceuticals. Zadavotide guraxetan targets PSMA with the PSMA-I&T ligand and incorporates actinium-225. An estimated 110 patients with prior exposure to Pluvicto or other lutetium-PSMA therapy were enrolled and randomized to one of several dosing regimens. The primary endpoints are $PSA_{50}$ response and safety. Zadavotide guraxetan has also advanced to Phase III development in the VECTRA-01 trial in heavily pretreated mCRPC (prior lutetium-PSMA therapy, prior chemotherapy, and prior ARPI).

**Aktis's Phase Ib Nectinium-2 Trial in Bladder Cancer**

Another potential showcase for actinium-225 could occur in the first quarter of 2027 with Aktis's Phase Ib Nectinium-2 trial of AKY-1189, which targets nectin-4. Although early stage, the data will represent one of the first actinium-225 datasets with a target other than PSMA or SSTR (excluding Johnson & Johnson's human kallikrein-2 targeted asset, which employs an antibody). Given that the asset is being positioned in second-line bladder cancer, we view the objective response rate from post-Padcev chemotherapy (roughly 20%) as the benchmark for initial efficacy results. The trial design is outlined in exhibit 25.

**Exhibit 25**
**Aktis Oncology, Inc.**
**Phase Ib NECTINIUM-2 Trial of AKY-1189 in Locally Advanced or Metastatic Solid Tumors**

| Trial Design (NCT07020117) | | |
|---|---|---|
| **Mechanism of Action** | Radiopharmaceutical that incorporates actinium-225 and targets nectin-4 | |
| **Enrollment Criteria** | ECOG PS 0 or 1<br>No prior radiopharmaceutical treatment<br>No prior nectin-4-targeted therapy (except for Padcev)<br>Nectin-4-positive based on copper-64 imaging | |
| **Enrollment** | 150 patients | |
| **Study Portion** | Part 1: Dose escalation and backfill | Part 2: Dose expansion |
| **Population** | Locally advanced or metastatic solid tumors | Cohort 1: Metastatic UC<br>Cohort 2: TNBC<br>Cohort 3: Basket of solid tumors |
| **Treatment Regimen** | Up to 6 cycles of AKY-1189 across 5 dose levels | AKY-1189 at the RP2D |
| **Primary Endpoints** | Safety and tolerability<br>Determine RP2D | Objective response rate |
| **Secondary Endpoints** | Objective response rate<br>Progression-free survival<br>Duration of response | Safety and tolerability<br>Progression-free survival<br>Duration of response |
| **Timing** | Initial data: 1Q 2027 | NA |

ECOG PS=Eastern Cooperative Oncology Group Performance Status. NSCLC=Non-small-cell lung cancer. RP2D=Recommended Phase II dose. TNBC=Triple-negative breast cancer. UC=Urothelial carcinoma.
Sources: Company reports, clinicaltrials.gov

### Aktis's Phase Ib BActinium-1 Trial in Prostate Cancer

Although the exact timing of the readout is uncertain, Aktis has guided to initial data from the Phase Ib BActinium-1 trial of AKY-2519 in mCRPC in 2027. AKY-2519 targets B7-H3 and also incorporates actinium-225. Therefore, the initial data will again expand actinium-225's data pool to more novel targets in the radiopharmaceuticals industry. The trial design for the Phase Ib study of AKY-2519 is provided in exhibit 26.

**Exhibit 26**
**Aktis Oncology, Inc.**
**Phase Ib BActinium-1 Trial of AKY-2519 in mCRPC**

| Trial Design (NCT07581184) | | |
|---|---|---|
| **Mechanism of Action** | Radiopharmaceutical that incorporates actinium-225 and targets B7-H3 | |
| **Enrollment Criteria** | ECOG PS of 0 or 1<br>B7-H3-positive[1]<br>Cohort B: ≥2 doses prior Pluvicto | |
| **Cohorts** | A: Pluvicto-naive | B: Pluvicto-experienced |
| **Dose Escalation** | 6 MBq<br>9 MBq<br>12 MBq | |
| **Backfill** | Selected doses from escalation | |
| **Estimated Enrollment** | 138 patients | |
| **Initiation** | Early May 2026 | |
| **Primary Endpoint** | **Safety and tolerability**<br>**Occurrence of DLTs** | |
| **Key Secondary Endpoints** | Objective response rate<br>Duration of response<br>Progression-free survival<br>$PSA_{50}$ / $PSA_{90}$ responses | |
| **Next Catalyst** | Initial data: 2027 | |

DLTs=Dose-limiting toxicities. ECOG PS=Eastern Cooperative Oncology Group Performance Status. mCRPC=Metastatic castration-resistant prostate cancer.

### Molecular Partners' Phase I/IIa Data for DLL3-Targeted Asset

This dataset will likely have read-through to lead-212 more broadly given that MP0712 (developed in collaboration with partner Orano Med) incorporates the isotope. The DLL3-targeting moiety is a designed ankyrin repeat protein (DARPin), and Molecular Partners believes that DARPins are an ideal targeting vector that can be tuned for compatibility with specific targets and cancer biology. The Phase I/IIa study is investigating MP0712 in small-cell lung cancer (SCLC) and other neuroendocrine cancers, and each patient is receiving up to four doses of the radiopharmaceutical. Initial data is expected by the end of the year, while a comprehensive dataset that includes both safety and efficacy is slated for release in 2027. We are particularly intrigued by the DLL3 target given the success of T-cell engagers like Imdelltra, though we also recognize that these agents have raised the bar for efficacy in the SCLC disease setting. Regardless, we view the upcoming dataset as intriguing given that DLL3 is a commercially validated target that remains more novel in radiopharmaceuticals.

**Perspective Therapeutics' Phase I/IIa Updates**
Expected data updates across Perspective's lead-212-focused pipeline in late 2026 will also have read-through to lead-212. This will include updated Phase I/IIa data in NETs for lead program VMT-α-NET, which targets SSTR; initial Phase I/IIa data in melanoma for VMT01, which targets MC1R; and initial Phase I/IIa data in solid tumors for PSV359, which targets FAP. We look forward to continued data from the lead-212 field, from both safety and efficacy perspectives.

# Outlook

Based on our conversations with biotech executives, physicians, and investors, there has been a substantial rise in interest in radiopharmaceuticals over the past several years. Propelled by the highly successful Phase III VISION and PSMAfore trials and the remarkable commercial launch and continued momentum of Pluvicto, we believe it is a watershed moment for the space that will encourage additional investment in R&D and expanded clinical trial activities. This has been bolstered by the investment in, and progress in procurement of, medically relevant radioisotopes and the further advancement of just-in-time manufacturing. This has helped alleviate supply constraints for currently available products and opens avenues for new radionuclides to potentially enter the market in the future. In parallel, clinical trials for assets incorporating a wide variety of novel targets, radionuclides, and targeting moieties continue to propel the industry.

Enthusiasm in the field is exemplified by continued strong funding, and based on year-to-date funding across private and public sectors, 2026 is the strongest year of radiopharmaceuticals financings since at least 2020. Based on our updated analysis, our base-case assumption for the total addressable market for radiopharmaceuticals could reach $35 billion in the United States alone (bull case of $68 billion and a bear case of $4.6 billion). Overall, it is our view that investors should see the market as a budding sector that could benefit from material long-term secular growth. While not without risks, especially pertaining to complicated logistics required for supply chain optimization and limited data outside PSMA- and SSTR-targeted assets, we believe the risk/reward symmetry is skewed to the upside. As the fifth edition in an annual periodical series, this report serves as a continued resource for the investment community interested in conducting due diligence on this exciting and fledgling field in biotech.

The prices of the common stock of other public companies mentioned in this report follow:

| | |
|---|---|
| Actinium Pharmaceuticals, Inc. | $1.01 |
| Aktis Oncology, Inc. (Outperform) | $25.78 |
| AstraZeneca PLC | $162.70 |
| Bayer AG | $14.02 |
| Bicycle Therapeutics PLC | $4.20 |
| Bristol Myers Squibb Company (Market Perform) | $66.58 |
| Cellectar Biosciences, Inc. | $2.53 |
| Clarity Pharmaceuticals Ltd. | A$2.51 |
| Eli Lilly and Company | $1,174.61 |
| Immunome, Inc. | $27.57 |
| Johnson & Johnson | $268.04 |
| Lantheus Holdings, Inc. (Market Perform) | $100.77 |
| Novartis AG | $153.81 |
| Perspective Therapeutics, Inc. | $3.11 |
| Radiopharm Theranostics Limited | A$0.01 |
| Roche Holdings Ltd. | $55.19 |
| Telix Pharmaceuticals Limited (Outperform) | $11.29 |

**IMPORTANT DISCLOSURES**

William Blair or an affiliate is a market maker in the security of Lantheus Holdings, Inc., Telix Pharmaceuticals Limited and Aktis Oncology, Inc.

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DOW JONES: 53185.90
S&P 500: 7686.14
NASDAQ: 26370.90



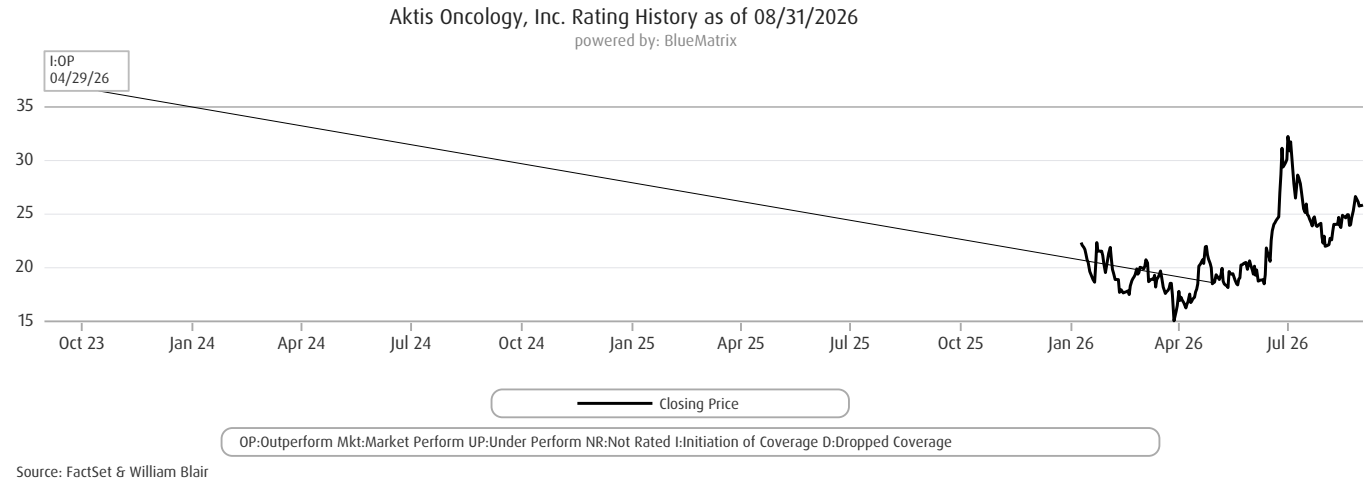

Source: FactSet & William Blair

**Current Rating for LNTH: Market Perform**




Source: FactSet & William Blair

**Current Rating for TLX: Outperform**




Source: FactSet & William Blair

**Current Rating for AKTS: Outperform**

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| Coverage Universe | Percent | Inv. Banking Relationships * | Percent |
|---|---|---|---|
| Outperform (Buy) | 72 | Outperform (Buy) | 14 |
| Market Perform (Hold) | 28 | Market Perform (Hold) | 4 |
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William Blair

# Equity Research Directory

**John Kreger, Partner Director of Research +1 312 364 8612**

**Kyle Harris, CFA, Partner Operations Manager +1 312 364 8230**

## CONSUMER

**Sharon Zackfia, CFA, Partner +1 312 364 5386**
Group Head–Consumer
*Lifestyle and Leisure Brands, Restaurants, Automotive/E-commerce*

**Jon Andersen, CFA, Partner +1 312 364 8697**
*Consumer Products*

**Phillip Blee, CPA +1 312 801 7874**
*Home and Outdoor, Automotive Parts and Services, Discount and Convenience*

**Dylan Carden +1 312 801 7857**
*E-commerce, Specialty Retail*

## ECONOMICS

**Richard de Chazal, CFA +44 20 7868 4489**

## ENERGY AND POWER TECHNOLOGIES

**Jed Dorsheimer +1 617 235 7555**
Group Head–Energy and Power Technologies
*Generation, Efficiency, Storage*

**Neal Dingmann +1 312 801 7835**
*Oil and Gas, Rare Earth*

**Tim Mulrooney, Partner +1 312 364 8123**
*Energy and Environmental Services*

**Mark Shooter +1 617 235 7593**
*Generation, Storage*

## FINANCIAL SERVICES AND TECHNOLOGY

**Adam Klauber, CFA, Partner +1 312 364 8232**
Group Head–Financial Services and Technology
*Financial Analytic Service Providers, Insurance Brokers, Property & Casualty Insurance*

**Andrew W. Jeffrey, CFA +1 415 796 6896**
*Fintech*

**Cristopher Kennedy, CFA +1 312 364 8596**
*Fintech, Specialty Finance*

**Jeff Schmitt +1 312 364 8106**
*Wealthtech, Wealth Management, Capital Markets Technology*

## GLOBAL SERVICES

**Tim Mulrooney, Partner +1 312 364 8123**
Group Head–Global Services
*Commercial and Residential Services*

**Andrew Nicholas, CPA +1 312 364 8689**
*Consulting, HR Technology, Information Services*

**Trevor Romeo, CFA +1 312 801 7854**
*Staffing, Waste and Recycling*

## HEALTHCARE

### Biotechnology

**Matt Phipps, Ph.D., Partner +1 312 364 8602**
Group Head–Biotechnology

**Sami Corwin, Ph.D. +1 312 801 7783**

**Lachlan Hanbury-Brown +1 312 364 8125**

**Andy T. Hsieh, Ph.D., Partner +1 312 364 5051**

**Myles R. Minter, Ph.D., Partner +1 617 235 7534**

### Healthcare Technology and Services

**Ryan S. Daniels, CFA, Partner +1 312 364 8418**
Group Head–Healthcare Technology and Services
*Healthcare Technology, Healthcare Services*

**Jared Haase, CFA +1 312 364 5135**
*Healthcare Delivery, Pharmaceutical Outsourcing and Services*

**Steven Lichtman +1 646 561 9373**
*Medical Technology*

**Brandon Vazquez, CFA +1 212 237 2776**
*Dental, Animal Health, Medical Technology*

### Life Sciences

**Matt Larew, Partner +1 312 801 7795**
*Life Science Tools, Bioprocessing, Healthcare Delivery*

## INDUSTRIALS

**Brian Drab, CFA, Partner +1 312 364 8280**
Co-Group Head–Industrials
*Advanced Manufacturing, Industrial Technology*

**Ryan Merkel, CFA , Partner +1 312 364 8603**
Co-Group Head–Industrials
*Building Products, Specialty Distribution*

**Louie DiPalma, CFA, Partner +1 312 364 5437**
*Aerospace and Defense, Smart Infrastructure*

**Ross Sparenblek, CFA +1 312 364 8361**
*Diversified Industrials, Robotics, and Automation*

## TECHNOLOGY, MEDIA, AND COMMUNICATIONS

**Jason Ader, CFA, Partner +1 617 235 7519**
Co-Group Head–Technology, Media, and Communications
*Infrastructure Software*

**Arjun Bhatia, Partner +1 312 364 5696**
Co-Group Head–Technology, Media, and Communications
*Software*

**Dylan Becker, CFA +1 312 364 8938**
*Software*

**Louie DiPalma, CFA, Partner +1 312 364 5437**
*Government Technology*

**Jonathan Ho, Partner +1 312 364 8276**
*Cybersecurity, Security Technology*

**Patrick McIlwee, CFA +1 312 364 8655**
*Software*

**Sebastien Naji +1 212 245 6508**
*Infrastructure Software, Semiconductor and Infrastructure Systems*

**Maggie Nolan, CPA, Partner +1 312 364 5090**
*IT Services*

**Ralph Schackart III, CFA, Partner +1 312 364 8753**
*Internet and Digital Media*

**Stephen Sheldon, CFA, CPA, Partner +1 312 364 5167**
*Vertical Technology – Real Estate, Education, Restaurant/Hospitality*

## EDITORIAL AND SUPERVISORY ANALYSTS

**Steve Goldsmith, Head Editor and SA +1 312 364 8540**
**Katie Anderson, Editor and SA +44 20 7868 4451**
**Audrey Majors, Editor and SA +1 312 364 8992**
**Beth Pekol Porto, Editor and SA +1 312 364 8924**
**Lisa Zurcher, Editor and SA +44 20 7868 4549**