

July 31, 2025



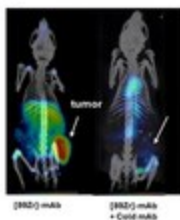
# **Actinium Presents Data Supporting Paradigm Changing Potential of ATNM-400 in Prostate Cancer Demonstrating Its Superior Efficacy and Improved Survival in Treatment Resistant Tumor Models versus Pluvicto and ARPI Therapy, and Also Enhanced Efficacy in Combination with ARPI Therapy at the 4th Annual Targeted Radiopharmaceuticals Summit**

- ATNM-400 demonstrates robust efficacy in prostate cancer tumor models with acquired resistance to Pluvicto® and enzalutamide, follow-up continues
- ATNM-400 significantly improved survival compared to the approved prostate cancer treatment Pluvicto®, the first blockbuster radiotherapy
- In combination with enzalutamide, an approved ARPI therapy, ATNM-400 produced enhanced efficacy with 40% of prostate cancer tumor-bearing animals achieving complete cures

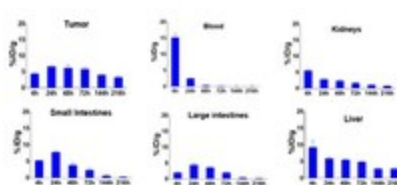
NEW YORK, July 31, 2025 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) (Actinium or the Company), a pioneer in the development of targeted radiotherapies, today reported additional preclinical data supporting its ATNM-400 radiotherapy prostate cancer candidate at the 4<sup>th</sup> Annual Targeted Radiopharmaceuticals Summit (TRP) being held July 29 – 31, 2025 in San Diego, CA. ATNM-400 is a novel, first-in-class targeted radiotherapy designed to deliver potent Actinium-225 (Ac-225), an alpha-emitter radioisotope, to prostate cancer cells by targeting a non-Prostate Specific Membrane Antigen (PSMA), disease-driving protein overexpressed in advanced and treatment-resistant disease. Unlike PSMA-targeted agents that primarily serve as imaging and targeting tools, the ATNM-400 target is directly implicated in tumor progression, survival signaling, and resistance to androgen receptor (AR) pathway inhibitor (ARPI) therapy. The presentation titled, "*Building a Transformative Ac-225 Portfolio for Next-Generation Precision Oncology*" on Wednesday, July 30, 2025, highlighted new PET imaging data showing tumor-specific uptake of ATNM-400, robust tumor control and improved survival outcomes in preclinical studies.

## ATNM-400 Demonstrated Sustained Tumor-Specific Uptake

PET imaging in Prostate Cancer Tumor-bearing Animals



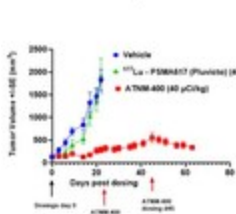
In vivo Biodistribution in Prostate Cancer model



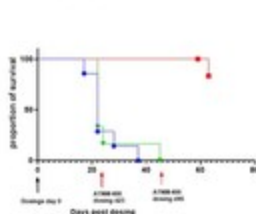
- PET imaging confirmed tumor-specific uptake of the ATNM-400 antibody
- The ATNM-400 antibody showed sustained tumor uptake up to 216 hours with rapid clearance from normal tissues

## ATNM-400 Produced Robust Tumor Control, Improved Survival and Superior Efficacy After Pluvicto® Resistance

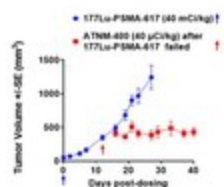
In vivo efficacy: head-to-head



In vivo overall survival: head-to-head



In vivo efficacy: Post-177Lu-PSMA-617 failure

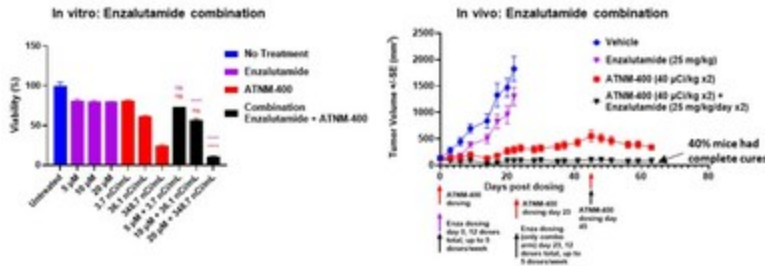


- ATNM-400 is more efficacious than Pluvicto® (Lu-177-PSMA-617) with potent tumor control
- ATNM-400 significantly improved survival compared to Pluvicto® with continued follow-up ongoing
- ATNM-400 is highly effective in prostate cancer tumors with acquired Pluvicto® resistance, halting tumor growth and producing potent tumor cell killing after Pluvicto® stops working, highlighting its potential in advanced disease settings that are resistant to standard treatments

## Enhanced Efficacy of ATNM-400 with Enzalutamide Supports Potential for Novel Combinations

- ATNM-400 demonstrated significant in vitro tumor cell killing when used in combination with AR-targeting agents, such as enzalutamide (Xtandi®)
- The ATNM-400 enzalutamide combination produced superior anti-tumor efficacy and durable tumor control compared to enzalutamide alone with 40% of prostate cancer tumor-bearing animals having complete cures
- Actinium previously highlighted that ATNM-400 inhibited tumor growth of enzalutamide resistant tumors whereas re-treatment with Pluvicto® or additional enzalutamide did

not



Actinium highlighted that follow-up continues to further evaluate the durability of ATNM-400's anti-tumor efficacy in prostate cancer with additional data expected in the second half of 2025. Actinium's TRP presentation can be accessed via the Investor Relations page of Actinium's website [HERE](#).

Sandesh Seth, Actinium's Chairman and CEO, said, "We are highly encouraged by the growing body of data supporting the therapeutic potential of ATNM-400 and the significance of its target being directly implicated in tumor progression, survival signaling, and resistance to ARPI therapy. The new data presented at TRP highlight the utility of the differentiated mechanism of action of ATNM-400 via the Ac-225 alpha-emitter payload evidenced by durable tumor control, improved survival rates compared to Pluvicto<sup>®</sup>, and efficacy in enzalutamide and Pluvicto<sup>®</sup> resistant models. We believe ATNM-400 has the potential to redefine the treatment paradigm in the high-value, advanced disease, and metastatic castrate-resistant prostate cancer settings, which impact tens of thousands of patients annually. We look forward to presenting additional data in the second half of this year and further highlighting ATNM-400's differentiated potential in treatment settings with high unmet needs."

## About ATNM-400

ATNM-400 is a highly innovative, first-in-class, non-PSMA targeting Actinium-225 (Ac-225) radiotherapy candidate for prostate cancer. In comparison to Pluvicto<sup>®</sup> (Lu-177-PSMA-617) and the majority of radiotherapies in development for prostate cancer, which target prostate specific membrane antigen (PSMA) and are either non-differentiated or barely differentiated, ATNM-400 targets a distinct non-PSMA disease-driving protein overexpressed in advanced and treatment-resistant disease. The receptor specifically targeted by ATNM-400 is highly expressed in metastatic castration-resistant prostate cancer (mCRPC), contributes directly to disease progression, poorer survival outcomes, and continues to be expressed at a high level even after androgen receptor inhibitor (ARPI) and Pluvicto<sup>®</sup> treatment. ATNM-400 leverages the alpha-particle emitter Ac-225, which can cause lethal irreversible double-stranded DNA breaks and is more potent compared to the beta-particle emitter Lutetium-177 (Lu-177) used by Pluvicto<sup>®</sup>, as well as a shorter path length that could result in fewer off-target effects.

Prostate cancer is the most commonly diagnosed cancer in men, with ~1.5 million new cases globally and over 313,000 expected in the U.S. in 2025. While early-stage disease is typically managed with surgery, radiation, and ARPI therapy, up to 20% of cases progress to mCRPC - a lethal stage with limited treatment options. Targeted radiotherapy is a growing

field in prostate cancer, dominated by PSMA-targeting agents like Pluvicto<sup>®</sup>, which had sales of over \$1.3 billion in 2024, yet many patients either lack PSMA expression or develop resistance to Pluvicto<sup>®</sup>. In the U.S., 40,000–60,000 mCRPC patients annually progress after ARPIs such as Xtandi<sup>®</sup>, which had sales of over \$5.9 billion in 2024, highlighting a significant unmet need.

### **About Actinium Pharmaceuticals, Inc.**

Actinium is a pioneer in the development of targeted radiotherapies intended to meaningfully improve patient outcomes. Actinium's most advanced product candidate in development is Actimab-A, a CD33 targeting therapeutic, that is a potential backbone therapy for acute myeloid leukemia (AML) and other myeloid malignancies leveraging the mutation agnostic alpha-emitter radioisotope payload Actinium-225 (Ac-225). Actimab-A has demonstrated potential activity in relapsed and refractory acute myeloid leukemia (r/r AML) patients in combination with the chemotherapy CLAG-M including high rates of Complete Remissions (CR) and measurable residual disease (MRD) negativity leading to improved survival outcomes and is being advanced to a pivotal Phase 2/3 trial. In addition, Actinium is engaged with the National Cancer Institute (NCI) under a Cooperative Research and Development Agreement (CRADA) for development of Actimab-A in AML and other myeloid malignancies. The first clinical trial under the CRADA will evaluate the triplet combination comprised of Actimab-A, Venetoclax (Abbvie/Roche) an oral Bcl-2 inhibitor and ASTX-727 (Taiho Oncology, an Otsuka holdings company) a novel oral hypomethylating agent (HMA) in frontline acute myeloid leukemia (AML) patients. Additionally, Actinium is developing Actimab-A as a potential pan tumor therapy in combination with PD-1 checkpoint inhibitors including KEYTRUDA<sup>®</sup> and OPDIVO<sup>®</sup> by depleting myeloid derived suppressor cells (MDSCs), which represents a potential multi-billion-dollar addressable market. ATNM-400 is Actinium's novel, first-in-class, non-PSMA targeting Ac-225 radiotherapy for prostate cancer. The receptor specifically targeted by ATNM-400 is highly expressed in metastatic castration-resistant prostate cancer (mCRPC), contributes directly to disease progression, poorer survival outcomes, and continues to be expressed at a high level even after androgen receptor inhibitor (ARPI) and Pluvicto<sup>®</sup> treatment. ATNM-400 is supported by preclinical data demonstrating tumor-specific uptake, higher efficacy than androgen receptor inhibitor enzalutamide (Xtandi<sup>®</sup>) and the radiotherapy Pluvicto<sup>®</sup> (Lu-177-PSMA-617), durable tumor control, potent efficacy in prostate cancer models resistant to both enzalutamide and Pluvicto<sup>®</sup> and potential to be used in combination with other therapies. Iomab-ACT, Actinium's next generation conditioning candidate, is being developed with the goal of improving patient access and outcomes for potentially curative cell and gene therapies. Iomab-B is an induction and conditioning agent prior to bone marrow transplant in patients with r/r AML, which Actinium is seeking a potential strategic partner for the U.S. In addition, the company's R&D efforts are primarily focused on advancing several preclinical programs for solid tumor indications. Actinium holds approximately 240 patents and patent applications including several patents related to the manufacture of the isotope Ac-225 in a cyclotron.

For more information, please visit: <https://www.actiniumpharma.com/>

### **Forward-Looking Statements**

This press release may contain projections or other "forward-looking statements" within the

meaning of the "safe-harbor" provisions of the private securities litigation reform act of 1995 regarding future events or the future financial performance of the Company which the Company undertakes no obligation to update. These statements are based on management's current expectations and are subject to risks and uncertainties that may cause actual results to differ materially from the anticipated or estimated future results, including the risks and uncertainties associated with preliminary study results varying from final results, estimates of potential markets for drugs under development, clinical trials, actions by the FDA and other governmental agencies, regulatory clearances, responses to regulatory matters, the market demand for and acceptance of Actinium's products and services, performance of clinical research organizations and other risks detailed from time to time in Actinium's filings with the Securities and Exchange Commission (the "SEC"), including without limitation its most recent annual report on form 10-K, subsequent quarterly reports on Forms 10-Q and Forms 8-K, each as amended and supplemented from time to time.

**Investors:**

[investorrelations@actiniumpharma.com](mailto:investorrelations@actiniumpharma.com)



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