October 13, 2025

Actinium Pharmaceuticals to Unveil the Multi-Tumor Potential of ATNM-400, a First-in-Class Actinium-225 Radiotherapy, with Data in Non-Small Cell Lung Cancer at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

- ATNM-400 is advancing as a first-in-class, multi-tumor Actinium-225 radiotherapy candidate with activity across prostate and lung cancers, two of the largest cancer indications globally
- New preclinical findings demonstrate ATNM-400 overcomes resistance to the EGFR inhibitor osimertinib in EGFR-mutated NSCLC, addressing a major unmet clinical need

NEW YORK, Oct. 13, 2025 /PRNewswire/ -- Actinium Pharmaceuticals, Inc. (NYSE AMERICAN: ATNM), a leader in the development of differentiated targeted radiotherapies, today announced that the first-ever preclinical data from its ATNM-400 program in non-small cell lung cancer (NSCLC) has been accepted for presentation at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics being held October 22 – 26, 2025, at the Hynes Convention Center in Boston, Massachusetts. ATNM-400 is a highly innovative, first-in-class, Actinium-225 (Ac-225) antibody radioconjugate with preclinical data in both prostate cancer and NSCLC. Together, these two indications represent more than 500,000 new cases annually in the U.S. alone.

ATNM-400 in NSCLC: Addressing Resistance to EGFR TKIs

NSCLC accounts for approximately 85% of lung cancer cases and remains the leading cause of cancer mortality worldwide. While EGFR tyrosine kinase inhibitors (TKIs) such as osimertinib (TAGRISSO®, AstraZeneca) have transformed outcomes for patients with EGFR-mutant NSCLC, virtually all patients develop resistance within 2 to 3 years, leading to

disease progression and a lack of effective therapeutic options.

Preclinical data to be presented at AACR-NCI-EORTC conference demonstrate that ATNM-400 exerts potent anti-tumor activity in EGFR-mutant NSCLC models and is capable of overcoming resistance to osimertinib and is furthermore synergistic in combination osimertinib. This represents a potential breakthrough for patients with relapsed or refractory EGFR-mutant NSCLC, one of the most urgent areas of unmet need in oncology.

In the multicenter, single-arm Phase 2 trial titled "osimertinib plus consolidative radiotherapy for advanced EGFR-mutant non-small cell lung cancer," Sampath et al. (AstraZeneca & UT Southwestern Harold C. Simmons Comprehensive Cancer Center) reported a median progression-free survival (PFS) of 32.3 months. This reflects a notable 12.3-month improvement over the 20.0-month median PFS observed with osimertinib monotherapy, as reported by Watanabe et al. in a real-world clinical setting.

ATNM-400 Presentation Information

Title: ATNM-400, a first-in-class Actinium-225 antibody radioconjugate, demonstrates potent anti-tumor activity and overcomes osimertinib resistance in lung cancer models

Session: Poster Session C

Session Date and Time: Saturday, October 25, 2025, 12:30 – 4:00 PM E.T.

The ATNM-400 abstract will be available for viewing online on October 22, 2025 at 12:00 PM E.T. through a freely available supplement in the *AACR journal Molecular Cancer Therapeutics*.

Expanding Beyond Prostate Cancer: Multi-Indication Potential

ATNM-400 was initially developed in prostate cancer, where it has demonstrated unique differentiation from PSMA-targeting radiotherapies such as 177Lu-PSMA-617 (active ingredient of Pluvicto®, Novartis). Unlike PSMA-directed agents, ATNM-400 targets a distinct receptor implicated in tumor progression and treatment resistance, remaining active in PSMA-low or PSMA-resistant disease - a major limitation of current radiopharmaceuticals. The target antigen of ATNM-400 is overexpressed following ARPI therapy and is associated with a shorter time to castration resistance. This positions ATNM-400 as a differentiated treatment option in the post-ARPI setting, where it has been shown to overcome enzalutamide resistance and enhance the efficacy of ARPI combinations. In preclinical models, synergy with enzalutamide resulted in robust, durable tumor control and significantly improved overall survival.

In both prostate and lung cancer, ATNM-400 leverages the potent, high-linear-energy-transfer emissions of Ac-225 to induce irreparable double-strand DNA breaks, a mechanism expected to overcome conventional resistance pathways and deliver durable tumor control.

Sandesh Seth, Actinium's Chairman and CEO, said, "We are excited to share the first data demonstrating that ATNM-400 can overcome resistance to osimertinib in NSCLC, one of the most challenging settings in oncology today. ATNM-400 has demonstrated compelling multi-indication potential in both mCRPC and NSCLC, showing greater efficacy as a monotherapy than standard-of-care agents including ^{177}Lu-PSMA-617, enzalutamide, and osimertinib. In

combination with enzalutamide, ATNM-400 delivered superior anti-tumor activity compared to enzalutamide alone, including complete tumor regressions in 40% of prostate cancer-bearing animals and significantly extended their survival. Notably, ATNM-400 also overcame resistance to standard of care therapies in relapse settings, highlighting its promise in treatment-refractory disease." Mr. Seth added, "This data in NSCLC expands the potential of ATNM-400 far beyond prostate cancer into another major cancer indication with significant unmet patient need. By leveraging the Actinium-225 alpha-emitter payload and targeting a receptor implicated in multiple tumor types, ATNM-400 has the potential to become a transformative therapy across two of the largest and most difficult-to-treat solid tumors."

About ATNM-400

ATNM-400 is a highly innovative, first-in-class, and multi-indication Actinium-225 (Ac-225) targeted radiotherapy candidate in development for prostate cancer and non-small cell lung cancer (NSCLC). ATNM-400 is highly differentiated in prostate cancer as it targets a distinct non-PSMA protein strongly implicated in prostate cancer progression and treatment resistance. Unlike 177Lu-PSMA-617, the active agent in Pluvicto® and the majority of radiotherapies under development, which rely on PSMA targeting, ATNM-400 is designed to maintain efficacy in PSMA-low or PSMA-resistant disease, a major unmet clinical need. Ac-225 delivers high-linear-energy-transfer alpha particles that induce irreparable double-strand DNA breaks, offering superior potency over beta emitters like Lutetium-177 (177Lu), and has a shorter tissue path length that may reduce off-target toxicity. The receptor specifically targeted by ATNM-400 continues to be expressed at a high level even after androgen receptor inhibitor (ARPI) and ATNM-400 has shown to overcome resistance to the ARPI therapy enzalutamide and work synergistically in combination with enhanced tumor control including complete tumor regression. In NSCLC, ATNM-400 has shown to overcome resistance to osimertinib, an EGFR tyrosine kinase inhibitor (TKI) that is a standard of care therapy.

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®, which had sales of over $1.3 billion in 2024, yet many patients either lack PSMA expression or develop resistance to Pluvicto®. In the U.S., 40,000–60,000 mCRPC patients annually progress after ARPI therapy, which as a class had sales of over $10.0 billion in 2024 including enzalutamide (Xtandi®) that led the ARPI class with sales of over $5.9 billion in 2024, highlighting a significant unmet need. Lung cancer is the leading cause of cancer deaths and there are there are over 200,000 new cases expected in the U.S. in 2025. NSCLC accounts for approximately 85% of all lung cancer cases. The EGFR TKI Osimertinib (TAGRISSO, AstraZeneca) generated sales of $6.6 billion in 2024. Across prostate cancer and NSCLC, there are approximately 500,000 new cases in the U.S. alone.

About Actinium Pharmaceuticals, Inc.

Actinium is a pioneer in the development of targeted radiotherapies intended to meaningfully improve patient outcomes. ATNM-400, Actinium's lead product candidate, is a novel, first-in-class, and multi-indication Actinium-225 (Ac-225) in development for prostate cancer and

non-small cell lung cancer (NSCLC). The antigen 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® treatment. ATNM-400 is supported by preclinical data demonstrating tumor-specific uptake, higher efficacy than androgen receptor inhibitor enzalutamide (Xtandi®) and 177Lu-PSMA-617 radiotherapy, the active agent in Pluvicto®, durable tumor control and potent efficacy in prostate cancer models resistant to both enzalutamide and 177Lu-PSMA-617. In addition, ATNM-400 has demonstrated synergy with enzalutamide. The data generated to date with ATNM-400 supports its potential to be used either as a monotherapy, or in combination or sequenced with other therapies. 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® and OPDIVO® by depleting myeloid derived suppressor cells (MDSCs), which represents a potential multi-billion-dollar addressable market. 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.

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