December 1, 2025

Actinium Pharmaceuticals Announces ATNM-400 Data Demonstrating Potent Efficacy in Triple-Negative Breast Cancer and Ability to Overcome Endocrine and HER2-Targeted Therapy Resistance Being Presented at the San Antonio Breast Cancer Symposium

- Presentation to include new data in triple-negative disease, a breast cancer subtype with poor outcomes and limited viable treatment options
- ATNM-400 overcomes HER2 therapy resistance and represents a novel targeted radiotherapy with the potential to avoid off-target toxicities including ILD that constrains other therapeutic modalities such as antibody drug conjugates
- ATNM-400 has demonstrated the potential to overcome resistance to first-line tamoxifen endocrine therapy
- Data to be presented on December 11, 2025 at 5:00 PM CT

NEW YORK, Dec. 1, 2025 /PRNewswire/ -- Actinium Pharmaceuticals, Inc. (NYSE American: ATNM), a leader in the development of differentiated targeted radiotherapies, today announced compelling preclinical data for ATNM-400, a first-in-class Actinium-225 (AC-225) antibody radioconjugate, in hormone receptor positive (HR+), HER2 positive (HER2+) and triple-negative breast cancer (TNBC) that will be presented at the San Antonio Breast Cancer Symposium (SABCS) being held December 10-14, 2025 in San Antonio, Texas. The data demonstrates significant anti-tumor activity in breast cancer models resistant to standard-of-care therapies including endocrine therapy tamoxifen and HER2-targeted therapy trastuzumab (Herceptin, Roche) as well as potent tumor growth inhibition in TNBC models. The data highlight ATNM-400's potential to address critical unmet needs in patients who have exhausted treatment options following endocrine therapy or HER2-targeted therapy failure. These data add to ATNM-400's robust preclinical data package that also encompasses metastatic castrate-resistant prostate cancer (mCRPC) and non-small cell lung cancer (NSCLC).

Breast cancer remains the most commonly diagnosed cancer among women, with hormone receptor positive (HR+) disease representing more than 70% of cases. Despite the widespread use of tamoxifen and other endocrine therapies, approximately 20-30% of patients experience disease recurrence. Similarly, resistance to HER2-targeted therapies such as trastuzumab develops in a significant proportion of HER2+ breast cancer patients. While HER2-targeted antibody drug conjugates (ADCs) like trastuzumab deruxtecan (Enhertu®, Daiichi-Sankyo/AstraZeneca) have demonstrated efficacy, their clinical utility is constrained by dose-limiting toxicities, including interstitial lung disease (ILD). TNBC is associated with poor outcomes with approximately 40 percent of patients having rapid disease relapse.

ATNM-400's Differentiated Profile and Mechanism of Action in Breast Cancer

ATNM-400 represents a fundamentally different therapeutic approach, leveraging the potent alpha-particle emission of Actinium-225 to deliver targeted radiation to breast cancer cells. ATNM-400's target antigen is overexpressed in breast cancer and linked to disease progression, metastasis, and poor clinical outcomes. Importantly, expression of this target is significantly elevated in patients who develop resistance to both endocrine therapy and HER2-targeted treatments, providing a strong mechanistic rationale for ATNM-400 in resistant disease settings.

Unlike conventional ADCs, ATNM-400 via its Ac-225 isotope payload has the potential to provide potent tumor killing while potentially reducing off-target lung toxicity—a critical differentiating factor that could expand treatment options for patients unable to tolerate current therapies.

ATNM-400's Pan Tumor Potential Extends to Prostate and Lung Cancer

In addition to breast cancer, ATNM-400 has demonstrated potent efficacy and the ability to overcome treatment resistance in metastatic castrate resistant prostate cancer (mCRPC) and non-small cell lung cancer (NSCLC). By targeting a distinct, non-PSMA antigen associated with treatment resistance and poor outcomes, ATNM-400 represents a mechanistically differentiated alpha-radiotherapy approach that has potential in various treatment settings in prostate cancer as a monotherapy, combination therapy or sequential therapy after androgen receptor pathway inhibitor (ARPI) therapy or PSMA-targeted radioligand therapy such as Pluvicto® (Novartis). ATNM-400's target antigen is also overexpressed in NSCLC, associated with poor prognosis and treatment resistance Preclinical data showed ATNM-400's differentiated potential as monotherapy, combination therapy with EGFR-inhibitors like osimertinib (TAGRISSO®, AstraZeneca) and in post-EGFR-resistance settings.

ATNM-400 SABCS Presentation Details

Abstract Title: Anti-tumor activity of ATNM-400, a first-in-class Actinium-225 antibody radioconjugate, in tamoxifen and trastuzumab resistant breast cancer models

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Date & Time: December 11, 2025, 5:00 PM – 6:30 PM CT
Abstract Number: 2069
Presentation Number: PS4-04-26
Date/Time: Thursday, December 11, 2025, 5:00 PM–6:30 PM CT
Session: Poster Session 4

Key Preclinical Findings

Actinium's preclinical studies to date evaluated ATNM-400 across multiple breast cancer subtypes, including HR+, HER2+, and triple-negative disease, with particular focus on models resistant to tamoxifen and trastuzumab. Key findings include:

- **Robust Tumor Growth Inhibition:** In HR+ MCF-7 xenograft models triple-negative and MDA-MB-468 models, ATNM-400 achieved robust tumor growth inhibition (TGI) across dose levels with TGI exceeding 100% at higher doses.
- **Activity in Resistant Models:** ATNM-400 retained significant efficacy in both tamoxifen-resistant and trastuzumab-resistant cell lines and xenograft models, demonstrating its ability to overcome established resistance mechanisms that limit current therapies.
- **Enhanced Target Expression in Resistant Disease:** Target protein expression was significantly elevated in tamoxifen- and trastuzumab-resistant cell lines compared to parental lines, supporting the mechanistic link between target expression and therapeutic resistance.
- **Combination Potential:** In vitro studies demonstrated that ATNM-400's potent, dose-dependent cytotoxicity as monotherapy was further enhanced when combined with standard-of-care agents, suggesting potential for rational combination regimens.
- **Favorable Tolerability Profile:** ATNM-400 was well tolerated across efficacious dose ranges in all xenograft models tested.

Addressing Critical Unmet Needs in Breast Cancer

"These preclinical data that will be presented at SABCS underscore ATNM-400's potential to transform outcomes for breast cancer patients who have limited therapeutic options after developing resistance to endocrine or HER2-targeted therapies and those with triple-negative disease," said Sandesh Seth, Chairman & CEO of Actinium Pharmaceuticals. "The combination of ATNM-400's differentiated mechanism of action, which has the potential to avoid off-target toxicities such as ILD that limit the use of ADCs and its activity across multiple breast cancer subtypes including resistant disease positions this program as a highly differentiated first-in-class targeted radiotherapy. We are excited to culminate 2025 with our presentation at SABCS that firmly establishes ATNM-400 as a pan-tumor program

with potential across multiple disease subtypes with high unmet needs across mCRPC, NSCLC and Breast Cancer."

Actinium noted that ATNM-400's target demonstrates elevated expression specifically in resistant disease settings, potentially enabling patient selection strategies that could optimize clinical benefit as either a monotherapy or in combinations. This precision approach aligns with Actinium's broader strategy of developing targeted radiotherapies that address validated biology in areas of high unmet medical need.

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, non-small cell lung cancer (NSCLC) and breast cancer. ATNM-400 is highly differentiated in prostate cancer as it targets a distinct non-PSMA protein strongly implicated in prostate cancer disease biology including 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 low-PSMA or high-PSMA resistant disease, a major unmet clinical need as up to 30% of patients do not respond to PSMA radioligand therapies and up to 60% of patients have at least one PSMA-negative tumor lesion. 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 superior efficacy compared to approved first, second- and third-line EGFR therapies including small molecules, antibody drug conjugates and bispecific antibodies that is synergistic with osimertinib, an EGFR tyrosine kinase inhibitor (TKI) that is a standard of care therapy approved for treatment of patients in the frontline setting and is also able to overcome osimertinib resistance.

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 up to 30% of patients either lack or have no PSMA expression and virtually all patients develop resistance to Pluvicto® within 1-year. In the U.S., 40,000–60,000 mCRPC patients annually progress after ARPI therapy with approximately 35% of patients progressing within 1-year. As a class, ARPI therapies had sales of over $10.0 billion in 2024 including enzalutamide (Xtandi®) that led the 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 and over 2 million cases globally. NSCLC accounts for approximately 85% of all lung cancer cases. EGFR targeting therapies including front-line osimertinib (TAGRISSO®, AstraZeneca) an EGFR tyrosine kinase inhibitor (TKI), second-line Dato-DXd

(Datroway®, AstraZeneca/Daiichi Sankyo) a Trop-2 ADC, and third-line amivantamab (Rybrevant®, Johnson & Johnson) an EGFR-cMET bispecific had sales of approximately $7 billion in 2024 with the EGFR TKI Osimertinib (TAGRISSO®, AstraZeneca) generating sales of $6.6 billion in 2024. Breast cancer is the most diagnosed cancer among woman in the United States with approximately 316,950 women expected to be diagnosed with the disease in 2025 according to the National Cancer institute. It is estimated that approximately 200,000 women are living with metastatic breast cancer in 2025, which is expected to grow to 250,000 in 2030. Of those diagnosed, hormone receptor-positive, HER2-negative (HR+/HER2-) breast cancer accounts for 70-75% of breast cancer, representing the largest subtype. In this setting, tamoxifen and trastuzumab (Herceptin®, Roche and biosimilars) generated sales of approximately $4.0 billion in 2024. ATNM-400 also demonstrated potency in triple negative breast cancer (TNBC), which accounts for up to 15% of all breast cancer cases is associated with poor patient outcomes. Across prostate cancer, NSCLC and breast cancer, ATNM-400 has demonstrated treatment paradigm changing potential in these indications, which have over 800,000 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, non-small cell lung cancer (NSCLC) and breast cancer. 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. In NSCLC, ATNM-400 showed superior efficacy to EGFR targeting therapies including osimertinib (TARGRISSO®, AstraZeneca), Dato-DXd (DATROWAY®, AstraZeneca/Daiichi Sankyo) and amivantamab (RYBREVANT®, J&J) with synergistic activity in combination with osimertinib. In breast cancer, Actinium has been studied in hormone and HER-2 resistant settings with data to be presented at the San Antonio Breast Cancer Symposium in December 2025. The data generated to date with ATNM-400 supports its potential across treatment settings 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 250 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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