October 27, 2025

Actinium Announces Superior Anti-Tumor Activity of ATNM-400 in Lung Cancer Compared to the Leading First, Second and Third-Line Approved EGFR Mutant Therapies and Mechanistic Synergy with Osimertinib at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics

- ATNM-400 exhibits superior efficacy with 3-5x greater tumor growth inhibition compared to front line therapy osimertinib (EGFR TKI TAGRISSO®), second line therapy Dato-DXd (Trop-2 ADC DATROWAY®) and third line therapy amivantamab (EGFR-cMET bispecific RYBREVANT®)

- Combination of ATNM-400 and osimertinib resulted in complete tumor regression in 100% of tumor bearing animals; synergistic mechanism supported by increased ATNM-400 target antigen expression after EGFR inhibition with osimertinib

- Improved progression free survival has been demonstrated clinically with the combination of osimertinib and external beam radiotherapy providing strong rationale for a combination with targeted alpha-therapy

- Data validates the multi-tumor potential of ATNM-400 in multiple disease and treatment settings that support several blockbuster drugs

NEW YORK, Oct. 27, 2025 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) (Actinium or the Company), a pioneer in the development of differentiated targeted radiotherapies, today announced the presentation of the first ever preclinical data of ATNM-400 in non-small cell lung cancer (NSCLC). ATNM-400 a novel, multi-indication first-in-class antibody radioconjugate armed with the potent alpha-emitter Actinium-225 (Ac-225) is Actinium's lead solid tumor program, which is also being studied in prostate cancer. The data presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics studied ATNM-400 in Epithelial Growth Factor Receptor (EGFR)-mutant NSCLC models.

ATNM-400 demonstrated superior efficacy with 3-5x greater tumor growth inhibition

compared to standard-of-care therapies across EGFR-mutant NSCLC including:

Frontline: Osimertinib (TARGRISSO®, AstraZeneca) an EGFR tyrosine kinase inhibitor (TKI)

Second line: Dato-DXd (DATROWAY®, AstraZeneca/Daiichi Sankyo) a Trop-2 antibody drug conjugate (ADC)

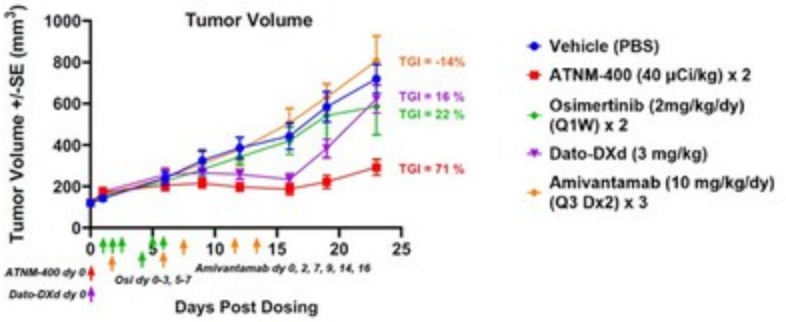
Third line: Amivantamab (RYBREVANT®, J&J), an EGFR-cMET bispecific antibody

ATNM-400 also demonstrated synergistic activity in combination with osimertinib with complete tumor regression in 100% of tumor-bearing animals. The synergistic mechanism of this combination is supported by increased expression of the ATNM-400 target antigen after EGFR inhibition with osimertinib. In addition, previously published data of external beam radiotherapy (EBRT) combined with osimertinib resulted in improved progression free survival (PFS) compared to osimertinib alone, providing a strong clinical rationale for combining targeted alpha-therapy via ATNM-400 with EGFR targeting therapies *Sampath et al. (AstraZeneca & UT Southwestern Harold C. Simmons Comprehensive Cancer Center)*[1].

Dr. Sandip Patel, Professor of Medicine at the University of California San Diego, an author on the poster, stated, "Targeted radiotherapy has transformed the prostate cancer treatment landscape and exemplifies what can be achieved with this technology. ATNM-400 represents a novel and differentiated development candidate for non-small cell lung cancer with EGFR mutations. The positive clinical results with EBRT and osimertinib provide strong support for combining targeted alpha-therapy via ATNM-400 and EGFR therapies to effectively deliver radiation to the target tumors and leverage mechanistic synergies while minimizing off-target effects. I am highly encouraged by these data that demonstrate the potential of ATNM-400 which would be a first-in-class radiotherapy."

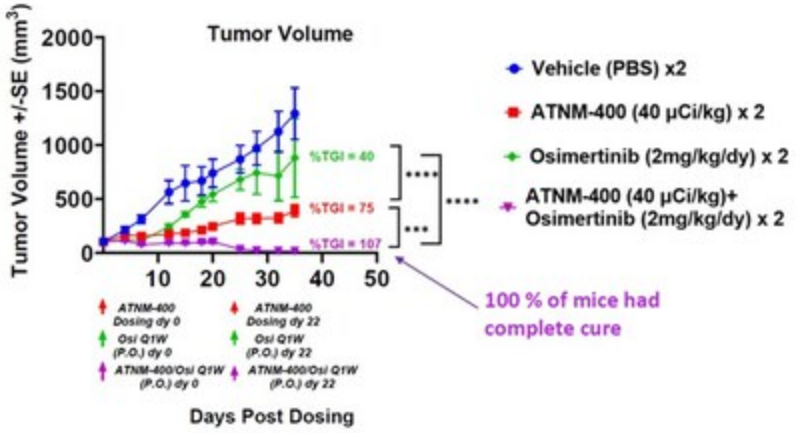
Notable ATNM-400 NSCLC Data

Superior Monotherapy Efficacy Compared to Standard-of-Care Therapies



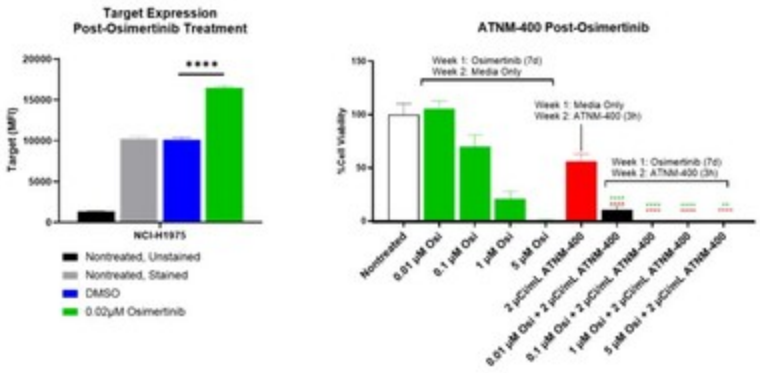
- ATNM-400 produced superior tumor growth inhibition (TGI) in animals bearing human lung cancer NCI-H1975, which carry L858R and T790M EGFR mutations
- TGI with ATNM-400 was 3-5 times higher than what was achieved with the current standard of care EGFR-mutant NSCLC therapies including TAGRISSO®, DATROWAY® and RYBREVANT®

Synergy in Combination with Osimertinib Resulting in Complete Tumor Growth Inhibition



- The combination of ATNM-400 and osimertinib produced cures in all tumor-bearing animals with complete tumor regression, outperforming either agent alone and suggesting synergistic activity

Significance of the ATNM-400 Target in NSCLC Post Osimertinib



- The ATNM-400 target antigen is overexpressed in NSCLC and is linked to treatment resistance including to osimertinib

- Osimertinib treatment significantly increased the expression of the ATNM-400 target antigen in NCI-H1975 lung cancer cells

- This increased target expression post-osimertinib notably increased ATNM-400's in vitro cytotoxic effect when combined post-osimertinib

Sandesh Seth, Actinium's Chairman and CEO, stated, "Improving outcomes for patients with non-small cell lung cancer remains a major challenge evidenced by the significant number of therapies and modalities in development. ATNM-400 represents a truly innovative approach that leverages the potent Ac-225 alpha-emitter payload against a target that is overexpressed in lung cancer and linked to treatment resistance. These results strongly support ATNM-400's differentiated profile and its potential for development in first, second and third-line treatment settings, alone or in combination with some of the most successful drugs that compete with each other in the EGFR-mutant segment. ATNM-400's potential

against difficult to treat and common mutations in lung cancer and the recent data updates in prostate cancer at the Prostate Cancer Foundation meeting further validate the multi-tumor potential of ATNM-400 in several disease and treatment settings that support several blockbuster drugs. We look forward to providing further updates on this exciting pipeline candidate as we progress into clinical development."

Potential for ATNM-400 in NSCLC

Lung cancer is the most common cancer worldwide with more than 200,000 new cases estimated in 2025 in the U.S. and over 2 million new cases globally. NSCLC accounts for approximately 85 percent of all lung cancer cases with EGFR mutations detected in approximately 10-15 percent of Western cases and 40-60 percent of some Asian populations. Approved therapies for EGFR-mutant NSCLC collectively generated approximately $7 billion in sales in 2024, including EGFR tyrosine kinase inhibitor osimertinib (TARGRISSO®, AstraZeneca) in the frontline setting that led the class with sales of $6.6 billion in 2024, Trop-2 antibody drug conjugate Dato-DXd (DATROWAY®, AstraZeneca/Daiichi Sankyo) that was approved in January 2025 in the second line setting, and the EGFR-cMET bispecific antibody amivantamab (RYBREVANT®, J&J) in later lines that had sales of $0.3 billion in 2024. Despite their success, nearly all patients eventually develop resistance within two to three years, underscoring the urgent need for novel, differentiated therapies to overcome resistance and improve survival outcomes. ATNM-400 is designed to address this significant unmet need by combining the high-affinity targeting of a monoclonal antibody directed against an antigen overexpressed in NSCLC, associated with poor prognosis and osimertinib resistance, with the potent alpha-emitting isotope Ac-225, which induces irreversible double-strand DNA breaks. The preclinical data showed ATNM-400's differentiated potential as monotherapy, combination therapy with EGFR-inhibitors like osimertinib and in post-EGFR-resistance settings.

Sources:

1. Sampath et al. Osimertinib plus consolidative radiotherapy for advanced *EGFR* mutant non-small cell lung cancer: a multicenter, single-arm, phase 2 trial. The Lancet eClinicalMedicine, Volume 87, 103435. https://www.thelancet.com/journals/eclinm/article/PIIS2589-5370(25)00367-0/fulltext. https://clinicaltrials.gov/study/NCT03667820

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 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 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 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 and over 2 million cases globally. NSCLC accounts for approximately 85% of all lung cancer cases. EGFR targeting therapies had sales of approximately $7 billion in 2024 with the EGFR TKI Osimertinib (TAGRISSO®, AstraZeneca) generating 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. 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. 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 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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