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Actinium Pharmaceuticals Announces Initiation of Actimab-A Triplet Combination Frontline Trial Under NCI CRADA with Venetoclax and Taiho Oncology's Hypomethylating Agent ASTX-727 in Patients with Newly Diagnosed AML

- Represents first ever triplet combination using targeted radiotherapy as a backbone therapy in AML with initial clinical data expected in 2H:2025
- Expansion into frontline setting greatly expands potential addressable patient opportunity for Actimab-A
- Triplet combination supported by previously completed Phase 1 trials of Actimab-A + Venetoclax and Actimab-A + CLAG-M demonstrating Actimab-A's mutation agnostic and synergistic potential

NEW YORK, March 11, 2025 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) (Actinium or the Company), a pioneer in the development of targeted radiotherapies, today announced that the first clinical trial under its previously announced Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) for Actimab-A has been initiated. The trial (NCT06802523) 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. Venetoclax in combination with HMAs (Ven-HMA) is approved for patients with newly diagnosed AML. Actimab-A, a humanized anti-CD33 antibody conjugated to Actinium-225 (Ac-225) targets CD33, a marker expressed ubiquitously on myeloid blasts in patients with AML and other hematologic malignancies. The potent alpha-particle payload Ac-225 causes lethal double strand DNA breaks for which there are no known resistance or repair mechanisms. This study will evaluate the rate and duration of Complete Remission (CR), as well as safety, including the optimal dose of Actimab-A in combination with Venetoclax and ASTX-727 for potential future studies.

Dr. Avinash Desai, Actinium's Chief Medical Officer, commented, "We are incredibly excited that the first Actimab-A trial initiated under our CRADA with the NCI is this triplet combination with Venetoclax and Taiho's ASTX-727. While Ven-HMA has positively impacted outcomes in AML, a significant number of patients have poor responses or relapse quickly resulting in dismal outcomes. We believe Actimab-A's potentially synergistic, and mutation agnostic mechanism of action can improve clinical outcomes for these patients by producing deeper remissions, including measurable residual disease negativity, that are more durable. Due to its mutation agnostic mechanism, Actimab-A can overcome high-risk features, such as TP53 mutations, and has demonstrated the ability to improve outcomes in these patients where Ven-HMA has had limited success. This triplet regimen can be conveniently administered in the outpatient setting as Venetoclax and ASTX-727 are both oral agents and Actimab-A does not require isolation given that it is an alpha-particle emitter. We are eager to collaborate with NCI on this important study to evaluate earlier intervention with a CD33 targeted radiotherapy in patients with AML."

Actimab-A in combination with Venetoclax was previously studied in a multi-center Phase 1 trial. The combination was shown to be well tolerated with manageable adverse events. Preclinical studies showed that Actimab-A can synergize with Venetoclax by depleting MCL-1, which mediates Venetoclax resistance.

Sandesh Seth, Actinium's Chairman & CEO, said, "We believe 2025 will be a transformational year for Actimab-A and that the initiation of this triplet trial is a significant catalyst. It is our objective to establish Actimab-A as a backbone therapy across the treatment continuum of AML and other myeloid malignancies leveraging the broad expression of CD33 and the mutation agnostic Ac-225 payload. Driven by the compelling clinical results in over 150 patients in multiple treatment settings and the high visibility of our NCI CRADA, we are seeing strong enthusiasm from investigators for Actimab-A. As the only CD33 targeted radiotherapy in development for myeloid malignancies, we are focused on capitalizing on the tremendous opportunity to improve outcomes for a significant patient population that continues to have high unmet medical needs that are not addressed by current therapies. Over the course of 2025, we expect to generate preclinical data and initiate additional clinical trials that will further differentiate Actimab-A and demonstrate material progress in establishing Actimab-A as a first-in-class backbone radiotherapy for the over 100,000 patients with AML and other myeloid malignancies in the U.S. and other major international markets."

About Actinium Pharmaceuticals, Inc.

Actinium is a pioneer in developing targeted radiotherapies intended to meaningfully improve patient outcomes. Actinium is advancing its lead product candidate Actimab-A, a CD33 targeting therapeutic ARC as potential backbone therapy in 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) including measurable residual disease (MRD) negativity with improved survival outcomes. In addition, Actinium is engaged with the National Cancer Institute (NCI) under the Cooperative Research and Development Agreement (CRADA) for development of Actimab-A in AML and other myeloid malignancies. 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 in 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 230 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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