January 5, 2022

# Actinium Pharmaceuticals, Inc. and EpicentRx Announce Strategic Research Collaboration to Combine Targeted Radiotherapies with Next Generation CD47/SIRPα Immunotherapy

### - Collaboration builds on recent data presented by Actinium at SITC demonstrating enhanced activity of targeted radiotherapies in combination with the anti-CD47 targeting antibody magrolimab in blood cancer and solid tumor models

### - Collaboration to explore Actinium's clinical stage CD33 targeting ARC Actimab-A with EpicentRx's clinical stage RRx-001, a CD47-SIRPα regulating small molecule immunotherapy for AML

NEW YORK and SAN DIEGO, Jan. 5, 2022 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium" or the "Company"), a leader in the development of targeted radiotherapies for patients with unmet needs and EpicentRx, Inc. ("EpicentRx"), a San Diego-based clinical cancer immunotherapy company today announced that they have entered into a research collaboration to study Actinium's Actimab-A targeted radiotherapy in combination with RRx-001, EpicentRx's novel small molecule immunotherapy targeting the CD47-SIRPα axis. Under this strategic research collaboration, the two companies will work to determine the benefit of combining Actinium's targeted radiotherapy with EpicentRx's RRx-001, which are both clinical stage drug candidates, in acute myeloid leukemia (AML).

CD47 is a macrophage checkpoint upregulated in certain cancers that acts as a "don't eat me" signal on cancer cells to suppress phagocytosis and evade detection and destruction by the immune system. EpicentRx's RRx-001, currently under investigation in a Phase 3 trial for Small Cell Lung Cancer and in other oncology and non-oncology indications, is a versatile next generation small molecule immunotherapeutic that targets the CD47-SIRPα axis and the NLRP3 inflammasome to alter the tumor microenvironment and optimize immune

response.  Actinium's targeted radiotherapies have shown the ability to upregulate the cell surface "eat me" signal calreticulin, which can result in anti-tumor immune response. This collaboration will explore the mechanistic synergy of RRx-001's CD47–SIRPα downregulation with Actinium's targeted radiotherapy calreticulin upregulation to increase the immune detection and destruction of cancer cells and their potential to improve patient outcomes.

Actinium recently presented data (Link here) at the 36th Annual Society for Immunotherapy of Cancer (SITC) in solid tumor and blood cancer models showing that combining targeted radiotherapy with the anti-CD47 antibody magrolimab resulted in an increase in the pro-phagocytic signal calreticulin and an enhanced innate anti-tumor immune response leading to improved tumor burden and survival outcomes in tumor models.

Actinium's clinical pipeline of targeted radiotherapies, referred to as Antibody Radiation-Conjugates (ARCs), includes Iomab-B and Actimab-A. Collectively, Actinium's ARCs have been studied in nearly 600 patients at leading comprehensive cancer centers including the pivotal Phase 3 SIERRA trial for Iomab-B, which completed patient enrollment in September 2021. Actimab-A has been studied extensively as a single agent and in combination with chemotherapy and targeted agents in approximately 150 patients with AML in Phase 1 and 2 trials. Underpinning Actinium's clinical pipeline is its AWE technology platform, which applies Actinium's extensive intellectual property portfolio of over 160 issued and pending patents, R&D capabilities and know-how to the development of targeted radiotherapies exploiting multiple different radioisotope payloads including the potent alpha-emitter, Actinium-225. Actinium's R&D efforts employ a multidisciplinary approach leveraging its team's expertise and experience in cancer cell biology, radiochemistry, radiation sciences, immunology and oncology drug development. Actinium has utilized its AWE technology platform to create a CD38 targeting ARC using the blockbuster myeloma antibody daratumumab (Darzalex®) and it is also being utilized in collaboration with Astellas Pharma, to create theranostics for solid tumors.

"We are excited to begin this collaboration with EpicentRx as RRx-001 is a highly novel agent that is differentiated from other CD47-SIRPα axis targeting agents, given its multi-modal mechanism of action. As we recently demonstrated at SITC, our R&D efforts have focused on innovative approaches to developing targeted radiotherapy combinations with other therapeutic modalities. When CD47 emerged as a promising immunotherapy target, we quickly worked to explore potential synergies and we are excited that our experiments have demonstrated that targeted radiotherapies not only exert a direct cell killing effect, they also can upregulate calreticulin, a pro-phagocytic signal, resulting in an enhanced anti-tumor immune response. These efforts have also resulted in new intellectual property that we believe will be valuable as we continue our advancement in this field. This collaboration also leverages our extensive clinical experience with Actimab-A, which has produced high rates of remissions and minimal residual disease negativity in patients with AML. With potential synergy and non-overlapping mechanisms of actions, we look forward to generating data from this collaboration and advancing this potentially transformational combination together with EpicentRx", said Sandesh Seth, Chairman and CEO of Actinium.

As the flagship of EpicentRx's CyNRGY™ platform, RRx-001 is a first-in-class investigational treatment sourced from an exclusively licensed portfolio of aerospace-derived small molecules. It is a hypoxia activated prodrug with antioxidant and anti-inflammatory

properties in oxygenated healthy tissues through its inhibition of the NLRP3 inflammasome. Under hypoxic conditions, however, which is a hallmark of tumors, RRx-001 fragments, generating immunostimulatory and radiation-sensitizing activities. This hypoxia-triggered 2-stage mechanism places RRx-001 in a class of its own.

"AML's pervasive resistance to treatment requires strategic collaborations and combinations of treatment to increase the likelihood of a good outcome. We are excited to begin this collaboration with Actinium, a company with whom we have good chemistry. As a radiosensitizer which antagonizes CD47, RRx-001 should pair well with Actinium's ARC. This combination is a recipe for success," said Tony R. Reid, M.D., Ph.D., Chief Executive Officer of EpicentRx."

**About Actinium Pharmaceuticals, Inc.**

Actinium Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing targeted radiotherapies to deliver cancer-killing radiation with cellular level precision to treat patients with high unmet needs not addressed by traditional cancer therapies. Actinium's current clinical pipeline is led by ARCs or Antibody Radiation-Conjugates that are being applied to targeted conditioning, which is intended to selectively deplete a patient's disease or cancer cells and certain immune cells prior to a BMT or Bone Marrow Transplant, Gene Therapy or Adoptive Cell Therapy (ACT) such as CAR-T to enable engraftment of these transplanted cells with minimal toxicities. Actinium's targeted conditioning ARCs seek to improve patient outcomes and access to these potentially curative treatments by eliminating or reducing the non-targeted chemotherapy that is used for conditioning in standard practice currently. Our lead product candidate, I-131 apamistamab (Iomab-B) has been studied in several hundred patients including in the recently completed, 150-patient, pivotal Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. Iomab-ACT, low dose I-131 apamistamab is being studied as a targeted conditioning agent in a Phase 1 study with a CD19 CAR T-cell Therapy with Memorial Sloan Kettering Cancer Center. In addition, we are leaders in the field of Actinium-225 alpha therapies. Actimab-A, our clinical stage CD33 targeting ARC alpha therapy has been studied in nearly 150 patients including our ongoing combination trials with the salvage chemotherapy CLAG-M and the Bcl-2 targeted therapy venetoclax. Underpinning our clinical programs is our proprietary AWE (Antibody Warhead Enabling) technology platform. This is where our intellectual property portfolio of over 160 patents, know-how, collective research and expertise in the field are being leveraged to construct and study novel ARCs and ARC combinations such as with CD47 immunotherapies to bolster our pipeline for strategic purposes. Our AWE technology platform is currently being utilized in a collaborative research partnership with Astellas Pharma, Inc. Website: https://www.actiniumpharma.com/

**About EpicentRx Inc.**

EpicentRx is a leading-edge biopharmaceutical company with a complementary pipeline of small molecule and cancer targeting virus platforms that represent the next frontier in treating patients with diseases of significant unmet need. With two platforms, CyNRGY and AdAPT, EpicentRx has developed novel therapies and drug delivery devices with emphasis on not just treating the disease but improving quality of life. For more information, visit www.epicentrx.com.

**Forward-Looking Statements for Actinium Pharmaceuticals, Inc.**

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:**
Hans Vitzthum
LifeSci Advisors, LLC
Hans@LifeSciAdvisors.com
(617) 430-7578

**EpicentRx Media Contact:**
Caitlin Chase, Taft Communications
caitlin@taftcommunications.com
(210) 386-1735

View original content to download multimedia: https://www.prnewswire.com/news-releases/actinium-pharmaceuticals-inc-and-epicentrx-announce-strategic-research-collaboration-to-combine-targeted-radiotherapies-with-next-generation-cd47sirp-immunotherapy-301454275.html

SOURCE Actinium Pharmaceuticals, Inc.