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Actinium Highlights First-In-Class HER3 Targeted Radiotherapy Data Demonstrating Potent Anti-Cancer Activity of in Ovarian and Colorectal Cancer Models at the AACR Annual Meeting

- Highly significant ($p<0.0001$) reduction in tumor volume in ovarian cancer model when using HER3-ARC conjugated to either Actinium-225 or Lutetium-177 compared to bevacizumab (Avastin)

- HER3 is expressed at high levels within multiple solid tumors and has been linked to poor survival and drug resistance, providing strong rationale for HER3 targeted radiotherapy in a clinical setting

NEW YORK, April 19, 2023 /PRNewswire/ -- Actinium Pharmaceuticals, Inc. (NYSE AMERICAN: ATNM) (Actinium or the Company), a leader in the development of targeted radiotherapies, announces encouraging preclinical proof of concept data at a poster presentation at the American Association for Cancer Research (AACR) 2023 Annual Meeting being held April 14 - 19, 2023 in Orlando, Florida. The poster showcased the robust anti-tumor effects of HER3-targeted radiotherapy using multiple therapeutic radionuclides in preclinical models of high unmet need malignancies.

Highlights from the AACR poster titled, "Novel HER3 targeting antibody radioconjugates, 225Ac-HER3 ARC and 177Lu-HER3 ARC, exhibit potent antitumor efficacy in HER3-positive solid tumors" include:

- Actinium's HER3-targeted radiotherapy displayed strong anticancer activity when conjugated to either alpha-emitting Actinium-225 or beta-emitting Lutetium-177 in models of two high unmet need cancers, highlighting its therapeutic potential for HER3+ malignancies

- HER3-ARC showed strong target engagement and efficient cellular internalization with compelling cytotoxic activity against established *in vitro* cellular models

- A single dose of HER3-ARC, conjugated to either Actinium-225 ($p<0.0001$) or Lutetium-177 ($p<0.0001$) showed highly significant reductions in tumor burden in a preclinical ovarian cancer model compared to bevacizumab, an anti-VEGF monoclonal antibody indicated in ovarian cancer

- Promising antitumor activity displayed in a preclinical model of colorectal cancer, a highly aggressive malignancy, including a significant reduction in tumor volume ($p<0.0001$) when dosed with 225Ac-HER3-ARC

- The consistent overexpression of HER3 in multiple solid tumor types including ovarian, renal, prostate, urothelial, breast, and lung cancers suggests broad utility of a HER3-targeted agent across oncology indications

"Actinium is committed to developing targeted radiotherapies for patients with unmet needs and our program targeting HER3, a validated, pan-cancer target, is a strong representation of our R&D capabilities", said Sandesh Seth, Actinium's Chairman and CEO. "The new data from our HER3 program once again demonstrate the potent anti-tumor effect and broad utility of targeted radiotherapy in solid tumors. Building on our prior results in lung cancer models, we are excited by the highly significant reduction in tumor burden seen in ovarian cancer and colorectal cancer models, providing much improved treatment options to critical patients with poor clinical outcomes. These data also demonstrate our isotope-agnostic approach to targeted radiotherapy development enabling us to generate optimal therapies, given our strong, industry leading clinical experience with both beta and alpha therapies."

HER3 is a member of the EGFR family, a highly validated cancer target for which there are several approved therapies directed against EGFR and/or HER2. However, there are no approved therapeutics targeting HER3, which is upregulated in response to EGFR and HER2 therapies as part of acquired resistance and is associated with poor survival in multiple solid tumors including breast, colorectal, lung, ovarian and others.

The poster will be available on the presentations page of Actinium's investor relations page of its website: https://ir.actiniumpharma.com/presentations-webinars.

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. Actinium's clinical pipeline is led by targeted radiotherapies 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 bone marrow transplant (BMT), gene therapy or adoptive cell therapy, such as CAR-T, to enable engraftment of these transplanted cells with minimal toxicities. Our lead product candidate, Iomab-B (I-131 apamistamab) has been studied in over four hundred patients, including the pivotal Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. The SIERRA trial was positive with Iomab-B meeting the primary endpoint of durable Complete Remission of 6 months with high statistical significance ($p<0.0001$). Iomab-B enabled 100% of patients to access a BMT and produced higher rates of post-BMT CR. Iomab-B produced positive results for the secondary endpoints of the SIERRA trial including reducing the probability of an event by 78% resulting in an Event-Free Survival (EFS) Hazard Ratio of 0.22 ($p<0.0001$), doubled 1-year overall survival and

median overall survival. 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 with NIH funding. Actimab-A, our second most advanced product candidate has been studied in approximately 150 patients with Acute Myeloid Leukemia or AML, including in combination trials with the chemotherapy regimen CLAG-M and with venetoclax, a targeted therapy. Actimab-A or lintuzumab-Ac225 is an Actinium-225 based antibody radiation conjugate targeting CD33, a validated target in AML. Actinium has entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) to develop Actimab-A as a single agent or combination with chemotherapy, targeted agents or immunotherapy in Phase 1, 2 or 3 trials. The NCI will fund clinical trial expenses under the CRADA while Actinium will supply Actimab-A. The NCI is currently accepting proposals for non-clinical and clinical studies with Actimab-A. Actinium is a pioneer and leader in the field of Actinium-225 alpha therapies with an industry leading technology platform comprising over 200 patents and patent applications including methods of producing the radioisotope AC-225. Our technology and expertise have enabled collaborative research partnerships with Astellas Pharma, Inc. for solid tumor theranostics, with AVEO Oncology Inc., an LG Chem company, to create an Actinium-225 HER3 targeting radiotherapy for solid tumors, and with EpicentRx, Inc. to create targeted radiotherapy combinations with their novel, clinical stage small molecule CD47-SIRPα inhibitor. More information is available on Actinium's website: https://www.actiniumpharma.com/.

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