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Actinium Presents Data Demonstrating Actimab-A's Potential Use Against Solid Tumors by Selectively Depleting Immunosuppressive MDSCs, a Key Component of the Tumor Microenvironment, at the AACR Annual Meeting

- Actimab-A displayed robust MDSC depletion at statistically superior levels to other CD33-targeted therapeutics, including unconjugated Lintuzumab and Mylotarg™

- Myeloid derived suppressor cells (MDSCs) are ubiquitous across multiple cancer indications and exert strongly immunosuppressive effects through inhibition of immune responses by T cells, B cells and NK cells

- Data support the potential for Actimab-A to be a backbone therapy to broadly improve antitumor activity of immunotherapies and other therapeutic modalities in multiple solid tumor indications

NEW YORK, April 19, 2023 /PRNewswire/ -- Actinium Pharmaceuticals, Inc. (NYSE AMERICAN: ATNM) (Actinium or the Company), a leader in the development of targeted radiotherapies, announced today the first ever data demonstrating the utility of Actimab-A to depleted myeloid derived suppressor cells (MDSCs), which are ubiquitously present within the solid tumor microenvironment as well as blood cancers. The new data were showcased in a poster presentation at the American Association for Cancer Research (AACR) 2023 Annual Meeting, which is being held April 14 - 19, 2023 in Orlando, Florida.

Sandesh Seth, Actinium's Chairman and CEO, said, "Significant research and development activities are being applied to understanding the complex biological activities within the tumor microenvironment in order to generate better treatment responses and patient outcomes. MDSCs are recruited to sites of chronic inflammation, such as the tumor microenvironment, where they exert immunosuppressive effects including inhibition of

immune responses mediated by T cells, B cells, and NK cells. At Actinium, we believe Actimab-A can play an important role in the tumor microenvironment by depleting MDSCs, which express CD33, in a targeted manner. In doing so, Actimab-A can mitigate a major immunosuppressive contributor and potentially improve response rates as well as the duration of responses for a wide array of immunotherapies. With the substantial number of immunotherapies in development or currently in clinical use, we see multiple opportunities to synergize with immunotherapies such as checkpoint inhibitors and T and NK cell therapies. These data are an important step forward and we are excited to continue development of Actimab-A for MDSC depletion and beyond."

Highlights from the AACR poster titled, "Targeting myeloid-derived suppressor cells with actinium-225 lintuzumab, a CD33 antibody radioconjugate to enhance antitumor immunity", include:

- Actimab-A demonstrated efficient depletion of *ex vivo* human MDSCs derived from colorectal and lung cancer patient samples *in vitro* in addition to an *in vivo* humanized mouse model of Non-Small Cell Lung Cancer

- Colorectal cancer blood MDSCs treated with Actimab-A were more effectively cleared ($p<0.01$) compared to depletion by Mylotarg, a CD33-targeted antibody-drug conjugate, highlighting the powerful cytotoxicity and potential therapeutic benefit of radiotherapy compared to naked antibodies or ADCs

- Flow cytometry data confirmed an upregulation of CD33+ MDSCs in both lung and colorectal cancer patient samples compared to healthy donor controls. Following Actimab-A treatment in mice, a specific and robust depletion of *ex vivo* CD33+ MDSCs was observed

- These results suggest that targeted blockade of MDSC activity via treatment with Actimab-A can alleviate their pro-tumorigenic and immunosuppressive activities to bolster the efficacy of immunotherapy such as checkpoint inhibitors.

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. 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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