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Actinium Pharmaceuticals, Inc. Announces Research Collaboration with Columbia University to Study Actimab-A in AML Following Transplant of Engineered Hematopoietic Stem Cells Gene Edited to be CD33 Negative

- Collaboration builds on the groundbreaking research of Columbia University oncologist Dr. Siddhartha Mukherjee that uses gene-editing to remove the CD33 surface protein from hematopoietic stem cells

- Actimab-A to be used post-transplant of these engineered stem cells to prevent relapse by selectively targeting residual CD33 positive leukemia cells while sparing the engineered stem cells

- High rates of measurable residual disease negativity demonstrated by Actimab-A + CLAG-M validates merits of Actimab-A's use to prevent disease relapse post gene edited stem cell transplant

- Actimab-A + CLAG-M data to be presented in oral presentation at American Society of Hematology Annual Meeting on Saturday, December 10th highlighting 53% 1-year and 32% 2-year overall survival, 67% Overall Response Rate and 72% MRD negativity in patients with relapsed or refractory acute myeloid leukemia

NEW YORK, Dec. 8, 2022 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium" or the "Company"), a leader in the development of targeted radiotherapies, today announced that it has entered into a research collaboration with Columbia University to study Actimab-A, its clinical-stage CD33 targeting radiotherapeutic, with engineered hematopoietic stem cells (eHSCs) modified by CRISPR/Cas9 gene editing technology to knock out CD33 expression. Dr. Siddhartha Mukherjee, MD, DPhil, Assistant Professor of Medicine at Columbia University Medical Center in the Department of Medicine and Division of Hematology/Oncology and his research group developed the technology. Technology from Dr. Mukherjee's lab has been licensed and is currently being developed by Vor Biopharma, Inc., including trem-cel (formerly VOR33). Vor is currently using Mylotarg, a CD33 targeting antibody drug conjugate (ADC), in its clinical trial to target residual CD33 positive leukemia cells post-transplant.

Dr. Siddharth Mukherjee, MD, DPhil, stated, "I am very excited to be collaborating with Actinium to study Actimab-A targeted radiotherapy with our eHSCs to prevent relapse and improve post-transplant outcomes. Actimab-A is highly differentiated from other CD33 targeting agents including the ADC Mylotarg, which demonstrates resistance with repeated use. Actimab-A due to its radiation modality is agnostic to cytogenetics and molecular mutations and the Actinium-225 warhead can produce double strand DNA breaks for which there is no known resistance or repair mechanism. With AML cells being highly sensitive to radiation, we believe Actimab-A has great potential given the potency of the Actinium-225 isotope warhead, its validated CD33 targeting ability and its strong clinical data to date. My team and I look forward to progressing this collaboration with Actinium to generate first ever data with a targeted radiotherapy following engineered HSC transplant to advance to this novel combination to the clinic."

Dr. Avinash Desai, Actinium's Chief Medical Officer, added, "We are honored to be working with Dr. Mukherjee and his team at Columbia University in this exciting collaboration. This is another attractive setting for Actimab-A that builds on our leading-edge, combination focused development efforts that includes chemotherapy, targeted agents and immune checkpoint inhibitors. We are eager to show that Actimab-A will produce better post-eHSC transplant outcomes than other modalities including ADCs like Mylotarg given the specificity and potency of the Actinium-225 warhead. Recently, Actimab-A, in combination with the chemotherapy CLAG-M, produced deep remissions by wiping out residual leukemia cells resulting in high rates of MRD negativity rate in very difficult to treat relapsed or refractory AML patients, including patients with TP53 mutations and those receiving multiple lines of prior therapy including Venetoclax. These results give us confidence that Actimab-A will effectively eliminate any residual leukemia cells in this post-transplant setting where the leukemia burden is expected to be much lower. In addition to improved leukemia cell killing, Actimab-A's highly targeted nature has been shown to be well tolerated with minimal extramedullary toxicities. We look forward the oral presentation at ASH and to advancing this collaboration and furthering Actimab-A's utility in treating patients with AML."

Under this collaboration, Actimab-A will be administered following transplantation of the eHSCs with the goal of eliminating any CD33 positive residual AML cells. eHSCs are intended to engraft and reconstitute patients' blood and immune systems with cells that do not express cancer-specific targets such as CD33. This would then allow a patient to receive CD33 targeting therapy post-transplant to eradicate any residual CD33 positive leukemia cells and prevent relapse while sparing newly formed blood cells that do not express CD33. Actimab-A has been studied in over 150 AML patients in six clinical trials. It has the most clinical experience of any Actinium-225 based drug candidate in development. Actinium-225 is an alpha-particle emitting radioisotope that has the most potent cell killing ability of any medical grade isotope but has a short pathlength that limits potential off-target effects. Recently, Actimab-A demonstrated high rates MRD negativity following CLAG-M therapy in relapsed or refractory AML patients with adverse risk features including over 50% with a TP53 mutation and over 50% who received prior treatment with Venetoclax. This resulted in

a 53% 1-year overall survival and 32% 2-year overall survival in a patient group that has an expected overall survival of less than 3 months.

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 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. In October 2022, we announced that the SIERRA trial met its primary endpoint of 6-month durable Complete Remission (dCR) with a high degree of statistical significance ($p<0.0001$). Additional data from the SIERRA trial is expected to be presented at a BMT focused medical conference in 2023. 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 AML, including in combination trials with the chemotherapy regimen CLAG-M and with Venetoclax, a targeted therapy. Actimab-A (lintuzumab-Ac-225) is an Actinium-225 based antibody radiation conjugate targeting CD33, a validated target that is expressed in virtually all patients with AML. Actinium is a pioneer and leader in the field of Ac-225 alpha therapies with an industry leading technology platform comprising over 190 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 Ac-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/.

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.

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