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Actinium Pharmaceuticals Announces Iomab-ACT Program Gene Therapy Collaboration with UC Davis in Ongoing Clinical Trial for Patients with HIV-Related Lymphoma

- Trial will replace currently used chemotherapy conditioning with apamistamab-I-131, Actinium's targeted conditioning ARC, to selectively eliminate lymphoma cancer cells and stem cells to enable engraftment of stem cell gene therapy

- Anti-HIV stem cell gene therapy intended to simultaneously treat patients' HIV-related lymphoma and develop immune cells resistant to HIV

NEW YORK, Jan. 13, 2020 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium"), announced today that it has entered into an agreement with the University of California, Davis (UC Davis) to utilize Actinium's Antibody Radiation-Conjugate or ARC apamistamab-I-131 for targeted conditioning and replace the chemotherapy conditioning being used in an ongoing Phase 1/2 stem cell gene therapy clinical trial. In the trial, patients with relapsed or refractory HIV-related lymphoma are being treated with autologous stem cell gene therapy. This is the first gene therapy clinical trial that will utilize ARC based conditioning. The clinical trial will be conducted at UC Davis and may be expanded to additional sites in the future.

Dr. Mehrdad Abedi, Professor, Hematology and Oncology at UC Davis and study lead, said, "This collaboration represents an exciting combination of revolutionary technologies that could further our ability to treat patients with HIV and other life-threatening diseases with gene therapy. Despite the advances made in the field of gene therapy, the reliance on non-targeted chemotherapy and external radiation as conditioning regimens is less than optimal and poses a problem that we hope to reduce or eliminate as part of this collaboration by

replacing our conditioning regimen in this study with Actinium's ARC based targeted conditioning. Advances in HIV therapies have dramatically improved patient survival, but current therapies require life-long daily use to keep the HIV virus at bay, can have severe side effects, may be overcome by HIV resistance and do not address the needs of all patients like those in this study with HIV-related lymphomas. We envision a future where a single treatment of our stem cell gene therapy can cure patients of their lymphoma and HIV leaving the patient with a new immune system that can fight, be resistant to and prevent the mutation of HIV. Apamistamab-I-131's demonstrated antitumor effect against lymphoma and ability to condition patients in a targeted manner with a demonstrated tolerable safety profile in the bone marrow transplant setting makes it an ideal conditioning agent for this patient population. Based on these factors and extensive supporting clinical data in the Iomab-B program, we selected this ARC as the conditioning agent for the next phase of our trial as we believe antibody radiation-conjugates are more advanced and hold distinct advantages over novel but unproven conditioning technologies such as Antibody Drug Conjugates and naked antibodies that are beginning to be developed albeit at the preclinical stage."

In the current clinical trial, the anti-HIV stem cell gene therapy is produced by taking a patient's own or autologous, blood forming stem cells and genetically modifying them via gene therapy with a combination of three anti-HIV genes. The intended result is for the gene modified bone marrow stem cells to produce a new immune system and newly arising immune cells that are resistant to HIV via a single treatment. Conditioning is necessary prior to adoptive cell therapies such as gene therapy to eliminate certain cell types such as immune cells and stem cells in the bone marrow so the transplanted cells can engraft. Until now, conditioning in this trial, as is typical, used a multi-drug chemotherapy regimen administered over several days. This approach is non-targeted, associated with toxicities that impairs patients and restricts the use and efficacy of cellular therapy. Apamistamab-I-131, which requires just one therapeutic administration, will displace the non-targeted chemotherapy to condition patients in a targeted manner with the goal of reducing conditioning related toxicities and improving patient outcomes. Actinium and UC David will cross-reference their respective Investigational New Drug applications and will work collaboratively to obtain necessary regulatory and institutional approvals. In this clinical collaboration, Actinium will provide drug product, support for its administration and certain trial costs. UC Davis will be responsible for the production of the anti-HIV stem cell gene therapy and overall conduct of the study and its cost.

Dr. Dale Ludwig, Actinium's Chief Scientific Officer, said, "We are excited to be working with Dr. Abedi on this clinical study and we appreciate his recognition of the value of our Iomab-ACT targeted conditioning program may provide in support of gene stem cell therapy. This targeted approach using our CD45 ARC, enables both anti-tumor activity and effective conditioning with the potential for reduced toxicity compared to non-targeted chemotherapy and external radiation in the bone marrow transplant setting. Supported by extensive clinical investigation in 12 trials and over 300 patients, a single therapeutic dose of apamistamab-I-131 is sufficient for conditioning and, due to its dual activity, even a patient with active disease could expect to receive therapy within two weeks, which is anticipated to lead to better outcomes compared to chemotherapy, external beam radiation, or exploratory approaches such as naked antibodies or Antibody Drug Conjugates. In addition, CD45, the target of apamistamab-I-131, is ideal for targeted conditioning, as it is not expressed outside of the haemopoietic system and, because it is a poorly internalizing receptor. An ARC

approach which does not require internalization of its radionuclide warhead for target cell killing, is anticipated to be more viable and more effective than Antibody Drug Conjugate approaches which need to internalize their payloads. Given the potential of this ARC targeted conditioning technology for bone marrow transplant, we are grateful to Dr. Abedi for the opportunity to advance the Iomab-ACT program into the promising field of gene stem cell therapy."

Sandesh Seth, Actinium's Chairman and Chief Executive Officer, said, "Actinium is thrilled to be working with UC Davis and honored to now be part of this important trial. It has become evident that better conditioning regimens are needed for cell and gene therapies to reach their full potential. Our team is proud to be the first company to establish a clinical stage targeted conditioning portfolio for both cell and gene therapy. We are pleased to extend our ARC technology for targeted conditioning into these rapidly advancing fields and we are committed to establishing a strong leadership position in enabling these adoptive cell therapies fully realize their great potential for improving patients' lives."

Apamistamab-I-131's demonstrated conditioning and antitumor effect in lymphoma[1]

Actinium's apamistamab-I-131 ARC has been studied as a targeted conditioning agent in over 300 patients in the bone marrow transplant setting in the Iomab-B Program and is currently being studied in a pivotal Phase 3 clinical (SIERRA) trial in patients with relapsed or refractory acute myeloid leukemia. Clinical proof of concept has been established with Iomab-B for targeted conditioning in high-risk, relapsed or refractory lymphoma patients prior to an autologous stem cell transplant where a favorable safety profile with no dose limiting toxicities and minimal non-hematologic toxicities observed and promising efficacy with median overall survival not reached (range: 29 months to infinity) and 31% of patients in prolonged remission at a median of 36 months follow up (range: 25 – 41 months)[1].

1) Cassaday et al. Phase I Study of a CD45-Targeted Antibody–Radionuclide Conjugate for High-Risk Lymphoma. AACR *Clin Cancer Res* Published OnlineFirst September 3, 2019

About Actinium Pharmaceuticals, Inc.

Actinium Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing ARCs or Antibody Radiation-Conjugates, which combine the targeting ability of antibodies with the cell killing ability of radiation. Actinium's lead application for our ARCs is 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. With our ARC approach, we 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, apamistamab-I-131 (Iomab-B) is being studied in the ongoing pivotal Phase 3 **S**tudy of **I**omab-B in **E**lderly **R**elapsed or **R**efractory **A**cute Myeloid Leukemia (SIERRA) trial for BMT conditioning. The SIERRA trial is over fifty percent enrolled and promising single-agent, feasibility and safety data has been highlighted at ASH, TCT, ASCO and SOHO annual meetings. Apatmistamamb-I-131 will also be studied as a targeted conditioning agent in a Phase 1/2 anti-HIV stem cell gene therapy with UC Davis and is expected to be studied with a CAR-T therapy in 2020. In addition, we are developing a multi-disease, multi-target

pipeline of clinical-stage ARCs targeting the antigens CD45 and CD33 for targeted conditioning and as a therapeutic either in combination with other therapeutic modalities or as a single agent for patients with a broad range of hematologic malignancies including acute myeloid leukemia, myelodysplastic syndrome and multiple myeloma. Ongoing combination trials include our CD33 alpha ARC, Actimab-A, in combination 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 100 patents, know-how, collective research and expertise in the field are being leveraged to construct and study novel ARCs and ARC combinations to bolster our pipeline for strategic purposes. Our AWE technology platform is currently being utilized in a collaborative research partnership with Astellas Pharma, Inc.

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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