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# Actinium Highlights New Data at TCT Meetings Demonstrating Effective Lymphodepletion Supporting Iomab-ACT Program Development for Targeted Conditioning Prior to CAR-T and Adoptive Cell Therapy

## - In vivo studies demonstrate CD45 targeting ARC effectively lymphodepletes, allowing cells to expand while sparing bone marrow stem cells, red blood cells and platelets

## - Targeted transient lymphodepletion achieved with non-myeloablative doses administered in a single infusion

NEW YORK, Feb. 21, 2019 /PRNewswire/ -- Actinium Pharmaceuticals, Inc. (NYSE American: ATNM), announced today that it reported data from its Iomab-ACT program in a poster presentation at the 2019 Transplantation & Cellular Therapy Meetings™ of ASBMT and CIBMTR (TCT Meetings). A series of preclinical studies demonstrated that targeting CD45 with an ARC or Antibody Radiation-Conjugate can achieve potent yet transient lymphodepletion in a safe and effective manner. These results support advancement of the Iomab-ACT program into human clinical trials to study it as a single-dose, outpatient lymphodepletion regimen, which is also referred to as conditioning, prior to administration of CAR-T and other adoptive cell therapies. This program has the potential of providing a superior means of conditioning that could displace or replace chemotherapy based conditioning regimens such as Flu/Cy or Fludarabine and Cyclophosphamide that are used as the standard of practice today. The ARC underpinning the Iomab-ACT program is a lower dose version of Actinium's Iomab-B, which is in a pivotal Phase 3 trial for conditioning prior to a bone marrow transplant.

Actinium's preclinical studies showed that a single infusion of an anti-CD45 antibody labelled with Iodine-131 can effectively deplete greater than 90% of lymphocytes, including CD4 and CD8 T cells, CD19 B cells and NK cells, which is necessary for adoptive cell therapies like CAR-T to expand and persist. Tregs or regulatory T cells, including CD4+, CD25+ and FoxP3+ Tregs, which can exert negative pressure on cell therapy expansion and persistence, were suppressed for at least 21 days post lymphodepletion with Iomab-ACT. The multi-modal mechanism of action directed at CD45 expressing cells also depleted macrophages, which are implicated in the development of

CRS or Cytokine Release Syndrome, and splenocytes while red blood cells, platelets, neutrophils and bone marrow stem cells were preserved. Additionally, MicroSPECT/CT imaging showed that Iomab-ACT homed to immune privileged sites including lymph nodes, spleen, liver and bone marrow. Finally, an in vivo animal model showed that adoptively transferred cytotoxic T cells persisted in mice following administration of CD45 targeted lymphodepletion and were able to control tumor cells compared to untreated mice.

Dr. Dale Ludwig, Actinium's Chief Scientific Officer said, "This data provides strong support for advancing the Iomab-ACT program into human clinical trials as a targeted conditioning regimen for lymphodepletion prior to CAR-T or adoptive cell therapy. Targeted lymphodepletion with Iomab-ACT has the potential to create an optimal immune homeostatic environment for cell therapies to expand and persist leading to stronger and more durable responses. It is validating of our initial premise that lymphodepletion was achieved with non-myeloablative doses that spared neutrophils, platelets, red blood cells and bone marrow stem cells, as this could lead to a stronger patient that is able to better withstand treatment with cell therapies, which could also improve patient outcomes and also expand the number of patients eligible for these therapies. To achieve this with a single-infusion, outpatient administration would be an exciting advancement for the field of CAR-T and adoptive cell therapies and for patients that could benefit from them. We look forward to the next phase of development of this program."

Actinium's Iomab-ACT program is an ARC that targets CD45. CD45 is an antigen expressed on many cells that are relevant to CAR-T including lymphocytes, regulatory T cells and macrophages that have been associated with CAR-T challenges such as durability of response, CRS and neurotoxicity. Iomab-ACT is derived from, and is a lower dose of, Actinium's lead program Iomab-B, which has been studied in over 300 patients and is currently being investigated in a pivotal Phase 3 trial for targeted conditioning prior to a BMT or Bone Marrow Transplant. Actinium's Iomab-ACT program is highly differentiated when compared to Flu/Cy or other chemo-based lymphodepletion regimens. Unlike chemotherapy, its targeted nature is expected to improve CAR-T cell expansion more efficiently, potentially resulting in responses that are more durable and reduced CAR-T related toxicities. Also, the Iomab-ACT program enables lymphodepletion through a single-dose, outpatient administration versus Flu/Cy or other chemo-based lymphodepletion regimens that require multiple infusions in an inpatient setting over several days. Because of this potentially superior profile, the Iomab-ACT technology could result in improved access to CAR-T therapy and also better outcomes. A webinar highlighting the Iomab-ACT program can be accessed here.

Sandesh Seth, Actinium's Chairman and CEO said, "The TCT meetings are the ideal venue to showcase this exciting new data and we are excited to have had the opportunity to present it to thought leading physicians and industry leaders that are advancing the field of cellular therapy. These data are the catalyst enabling advancement into the clinic with the first single-dose, outpatient targeted conditioning program for lymphodepletion and also support our collaborative efforts. With recently filed IP and now this new data, we are excited to see Iomab-ACT advancing in tandem with other programs in our targeted conditioning portfolio including our pivotal programs Iomab-B and Actimab-MDS. Clearly, at the TCT Conference, this poster and our other activity is gaining recognition that we are

building a highly differentiated, industry leading portfolio in targeted conditioning that has value in serving major unmet or underserved medical needs."

**About Actinium Pharmaceuticals, Inc.**

Actinium Pharmaceuticals Inc. is focused on improving patient access and outcomes to cellular therapies such as bone marrow transplant (BMT) and CAR-T with its proprietary, chemotherapy free, targeted conditioning technology. Actinium is the only company with a multi-disease, multi-target, drug development pipeline focused on targeted conditioning. Its targeted conditioning technology is enabled by ARCs or Antibody Radiation-Conjugates that combine the targeting ability of monoclonal antibodies with the cell killing ability of radioisotopes. Actinium's pipeline of clinical-stage targeted conditioning ARCs target the antigens CD45 and CD33 for patients with a broad range of hematologic malignancies including AML or Acute Myeloid Leukemia, MDS or Myelodysplastic Syndrome and MM or Multiple Myeloma.

Iomab-B, Actinium's lead targeted conditioning product candidate, is currently enrolling patients in the pivotal Phase 3 SIERRA trial in patients age 55 or older, with active, relapsed or refractory AML. Iomab-B (Iodine-131 apamistamab), combines the anti-CD45 monoclonal antibody labeled with iodine-131 for myeloablation prior to a bone marrow transplant. CD45 is expressed on leukemia, lymphoma and normal immune cells. Iomab-B has been studied in over 300 patients in 10 clinical trials in numerous hematologic diseases. Actinium's Iomab-ACT program is an expansion of its CD45 program that is intended to be a universal, chemo-free solution for targeted lymphodepletion prior to CAR-T. Through targeted lymphodepletion, the Iomab-ACT program is expected to improve CAR-T cell expansion, reduce CAR-T related toxicities and expand patient access to CAR-T treatment and potentially other adoptive cell therapies. Due to its lower payload dose, lymphodepletion with the Iomab-ACT program can be accomplished through a single outpatient infusion. Actinium intends to advance its Iomab-ACT program with CAR-T focused collaborators from academia and industry.

Actinium's pipeline also includes a potentially best-in-class CD33 program with its ARC comprised of the anti-CD33 antibody lintuzumab labeled with the alpha-particle emitter actinium-225. Its CD33 program is currently being studied in multiple Phase 1 clinical trials for targeting conditioning, in combinations and as a therapeutic in multiple diseases and indications including AML, MDS and MM.

Actinium is also developing its proprietary AWE or Antibody Warhead Enabling technology platform which utilizes radioisotopes including iodine-131 and the highly differentiated actinium-225 coupled with antibodies to target a variety of antigens that are expressed in hematological and solid tumor cancers. The AWE technology enables Actinium's internal pipeline and with the radioisotope Actinium-225 is being utilized in a collaborative research partnership with Astellas Pharma, Inc. Actinium's clinical programs and AWE technology platform are covered by a portfolio of over 75 patents covering composition of matter, formulations, methods of use and also methods of manufacturing the radioisotope Actinium-225 in a cyclotron.

More information is available at[www.actiniumpharma.com](http://www.actiniumpharma.com) and our Twitter feed @ActiniumPharma, [www.twitter.com/actiniumpharma](http://www.twitter.com/actiniumpharma).

**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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