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Actinium Initiates Novel Phase 1/2 Combination Trial of Actimab-A and Venetoclax

Combination trial at UCLA Medical Center supported by demonstrated synergy and mechanistic rationale of targeted radiation from Actimab-A with venetoclax in preclinical studies

Trial adds to Actimab-A and CLAG-M as Actinium's second targeted radiation combination to enter the clinic

NEW YORK, Feb. 5, 2019 /PRNewswire/ -- Actinium Pharmaceuticals, Inc. (NYSE American: ATNM) ("Actinium" or "the Company") announced today that its novel Phase 1/2 combination trial of Actimab-A and venetoclax has been initiated. Gary Schiller, MD, Professor, Hematology-Oncology and Director, Hematologic Malignancy/Stem Cell Transplant Program at the UCLA Medical Center will serve as Principal Investigator for this study. The Phase 1/2 combination trial will enroll patients with relapsed or refractory AML or Acute Myeloid Leukemia that have been previously treated with venetoclax and patients that have never received venetoclax.

Venetoclax is a BCL-2 or B-Cell Lymphoma 2 inhibitor that is jointly developed and marketed by AbbVie and Genentech. BCL-2 is one of several proteins encoded by the BCL2 gene family, which regulates apoptosis or programmed cell death. MCL-1 is another protein encoded by the BCL2 gene family that is also overexpressed in cancers, including relapsed or refractory AML, that prevents apoptosis and promotes resistance to venetoclax, which does not bind to MCL-1. It has been demonstrated that MCL-1 levels can be depleted with radiation, but only external radiation was used in these studies. Actinium believes that the targeted radiation from Actimab-A can more effectively deplete MCL-1 levels thereby removing the AML cells' resistance mechanism and rendering them more susceptible to venetoclax. In preclinical studies, Actinium demonstrated this synergistic effect when combining Actimab-A with venetoclax that led to increased cancer cell death, the results of which were highlighted in a webinar hosted by Actinium that can be accessed here.

Dr. Dale Ludwig, Actinium's Chief Scientific Officer said, "The ability to deplete MCL-1, a known resistance mechanism to venetoclax, by selectively targeting AML cells that express CD33 with Actimab-A and hitting them with potent alpha radiation from Actinium-225 is very compelling. I am excited to see this study enter the clinic as I believe Actimab-A's targeted radiation will prove to be synergistic with venetoclax as we have shown in our preclinical work. With our powerful Antibody Warhead Enabling technology platform we are excited to deploy targeted radiation as a weapon against cancer cells by exploiting their susceptibility to radiation and leveraging potential synergies with other therapeutic modalities."

Dr. Mark Berger, Chief Medical Officer of Actinium said' "Despite advancements and recent approvals of AML therapies including venetoclax, there is a real need to improve their incremental benefits and produce more durable responses as well as curative outcomes for patients with relapsed and refractory disease. We are excited about this trial as our recent phase 2 study with Actimab-A demonstrated an ability to produce complete responses in difficult to treat AML patients. We attribute this efficacy to ARCs being agnostic to cytogenetic factors, the ubiquitous expression of CD33 in AML and potency of the Actinium-225 warhead. We are hopeful that the combination of Actimab-A and venetoclax will in the clinic will validate our preclinical studies showing synergy and result in improved patient outcomes."

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 Radio-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 acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS).

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. Iodine-131 apamistamab (Iomab-B), 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 500 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 and our Twitter feed @ActiniumPharma, 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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