



Actinium Pharmaceuticals CD33 Program to Focus on Actimab-MDS Pivotal Trial Enabling Study for Targeted Conditioning and Novel Combination Trials with Actimab-A and Venetoclax

- Positive FDA discussions for Actimab-MDS program enable accelerated pivotal trial pathway and broaden target patient population
- Actimab-A development strategy in combinations with Venetoclax for AML informed by company research indicating potential synergy and support from leading physicians

NEW YORK, Oct. 30, 2018 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc. (NYSE American: ATNM)** announced today that the next stage of development for its CD33 ARC (Antibody Radiation Conjugate) Ac-225-Lintuzumab program, after successful completion of the Actimab-A phase 2 trial in Acute Myeloid Leukemia (AML), will incorporate two key initiatives; a pivotal trial pathway for its Actimab-MDS program for Myelodysplastic Syndromes (MDS), and also in two combination trials with Venetoclax for AML. Actinium's development strategy for its CD33 program is being informed by: clinical data from 4 trials totaling over 100 patients including the recent Actimab-A Phase 2 trial in AML; positive interactions with the FDA regarding its Actimab-MDS trial; company research findings regarding potential synergy with Venetoclax; support from leading physicians; and attractiveness of the targeted indications given the unmet medical need and potential of its differentiated ARC modality in combination with chemotherapy.



Actinium highlighted the outcome of its successful discussions with the FDA for the Actimab-MDS program, which resulted in guidance for an accelerated pathway to a pivotal trial after a short dose finding Phase 1 portion. Actinium's initial proposal to the FDA was to conduct a larger Phase 2 trial prior to a pivotal trial in patients with a TP53 mutation, however, the company was encouraged by the FDA to expand the trial to include all high-risk patients with

poor or very poor and complex cytogenetics. The program will use the ARC Ac-225-lintuzumab for targeted conditioning in combination with a reduced intensity dose of fludarabine and melphalan prior to a BMT or Bone Marrow Transplant in patients with high-risk Myelodysplastic Syndrome (MDS).

Dr. Mark Berger, Actinium's Chief Medical Officer said, "In our studies to date, we've seen that Ac-225 – Lintuzumab can achieve remissions with minimal extramedullary toxicities even in patients progressing to AML from MDS. Typically, high-risk MDS patients undergoing a BMT do poorly with standard conditioning resulting in poor outcomes. The goal of the Actimab-MDS program is to use our ARC AC-225 – Lintuzumab to target cells of the myeloid lineage including progenitor cells in combination with reduced intensity conditioning with the goal of achieving improved conditioning and BMT outcomes, as successful BMT is the only potentially curative treatment option for these patients. We are building on the data we already have from our CD33 program and we are excited to have a quicker pathway to a pivotal trial that targets a larger patient population than originally envisaged."

Actinium's two combination trials with Venetoclax, a BCL-2 inhibitor that was jointly developed by AbbVie and Genentech, will leverage Actimab-A's unique and differentiated mechanism of action to explore synergies between the two agents for patients with relapsed or refractory AML. Venetoclax is an approved drug for patients with chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) and a supplemental New Drug Application (NDA) has been submitted to the FDA for patients newly diagnosed with AML.

The first proposed study will evaluate Actimab-A in combination with Venetoclax and will be led by Dr. Gary Schiller, Director, Hematology/Stem Cell Transplantation at UCLA Medical center. The second study will evaluate Actimab-A in combination with Venetoclax and hypomethylating agents and will be conducted in collaboration with Dr. Hagop Kantarjian and Dr. Tapan Kadia of the MD Anderson Cancer Center. The company is pursuing these combination trials with Actimab-A and Venetoclax on the basis of internal preclinical studies which have demonstrated a synergistic effect between these two agents that is supported by a mechanistic rational. Specifically, patients with AML have high levels of MCL-1, a protein that mediates resistance to Venetoclax, which is known to be depleted by DNA damage caused by external radiation treatment. Preclinical studies have demonstrated that MCL-1 is effectively depleted by DNA damage caused by external radiation and Actinium believes that Actimab-A's targeted radiation mechanism will therefore lead to a greater effect of Actimab-A plus Venetoclax, as demonstrated in the Company's preclinical work.

Dr. Berger added, "Many therapeutic advances in oncology, and also in AML, have been the result of combination therapies. We are excited to be advancing our Actimab-A program in combination with Venetoclax, which has the potential to lead the next evolution of AML therapy, in collaboration with top thought leaders from leading medical institutions. As indicated by our collaborators during the [CD33 Update webinar](#), while results with Venetoclax in patients with AML are encouraging, there remains a high unmet need for durable responses and curative outcomes. We believe Actimab-A can be used in combination with Venetoclax to improve patient outcomes, which is based on a strong scientific rationale supporting the combination as well as preclinical and clinical data. Our proposed trials with these combinations demonstrate the strong investigator interest we have seen for working with Ac-225 – Lintuzumab as an Antibody Radiation Conjugate is a new therapeutic modality for patients with radiation sensitive cancers such as AML, MDS and Multiple Myeloma that has the potential to improve their outcomes."

Sandesh Seth, Actinium's Chairman and Chief Executive Officer said, "Having a clear and relatively quick pathway to a pivotal trial for Actimab-MDS materially strengthens our targeted conditioning pipeline. It also enhances our outlook for building a business focused on developing and launching multiple products for targeted conditioning prior to BMT or CAR-T that can improve both patient access and outcomes due to their superior safety and efficacy balance compared to non-targeted chemotherapy that is current standard of care. With the solid progress of the Iomab-B Phase 3 trial for BMT, the recent launch of the Iomab-ACT program for CAR-T and the solid impetus for a near-term Actimab-MDS pivotal trial, our pipeline prospects for targeted conditioning have never been better."

Mr. Seth added, "The Actimab-A trial which was recently closed has been a big success as it has provided the foundation for the near-pivotal Actimab-MDS program in an area where there is high unmet need, no competing development programs by other companies and a larger patient population than originally envisaged. Additionally, our combination trials with Venetoclax and Actimab-A are very exciting as we have the opportunity to validate our preclinical research showing superiority of the combination in two highly relevant clinical settings where the unmet medical need continues to be high. Based on these recent developments, our CD33 Program has evolved much beyond the narrow AML focused CD33 programs in the industry due to the versatility of our ARC technology. The ARC approach has allowed us to expand into other radiation sensitive diseases such as multiple myeloma and MDS, and into targeted conditioning using high doses of the ARC as well as therapeutic combinations at lower ARC doses which allow incorporation of targeted radiation as another modality to treat highly radiation sensitive cancers."

"In addition," said Mr. Seth, "from a strategic perspective, the Actimab-MDS targeted conditioning trial strengthens our go-it-alone outlook. However, the other CD33 program developments including combination trials increase its attractiveness to potential collaborators and are expected to provide our company with attractive optionality going forward, as the period between now and 2019 are expected to yield several valuable clinical milestones and data readouts. We look forward to providing updates as value in this program continues to build."

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 or sparing, 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 ARC's 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), myelodysplastic syndrome (MDS) and multiple myeloma (MM), acute lymphoblastic leukemia (ALL), Hodgkin's lymphoma and Non-Hodgkin's lymphoma. Actinium's Iomab-ACT program is designed to be a universal lymphodepletion technology intended to eliminate the need for chemotherapy-based conditioning prior to CAR-T or other adoptive cellular therapies.

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, chemotherapy-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 clinical trials for targeting conditioning and as a therapeutic as a single agent or in combination in multiple diseases and indications including AML, MDS and MM. Actinium applies its CD33 program at high doses to target CD33+ cells of the myeloid lineage in combination with reduced intensity conditioning (RIC), which together are intended to result in myeloablative outcomes with a more benign and well tolerated profile than high intensity chemotherapy myeloablation. Actinium is focused on applying its CD33 program at low doses in combination with other therapeutic modalities including chemotherapy, targeted agents and immunotherapies.

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 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.

Contact:

Actinium Pharmaceuticals, Inc.

Steve O'Loughlin
Principal Financial Officer
soloughlin@actiniumpharma.com

Investor Relations

Rx Communications Group
Paula Schwartz
917-322-2216
pschwartz@rxir.com

View original content to download multimedia <http://www.prnewswire.com/news-releases/actinium-pharmaceuticals-cd33-program-to-focus-on-actimab-mds-pivotal-trial-enabling-study-for-targeted-conditioning-and-novel-combination-trials-with-actimab-a-and-venetoclax-300740769.html>

SOURCE Actinium Pharmaceuticals, Inc.