April 3, 2019

# Actinium Highlights Actimab-A and Venetoclax Synergies Observed in New Studies Presented at AACR

### - Studies observed increase in double-stranded DNA breaks and reduction in MCL-1 levels in cell lines resistant to venetoclax following Actimab exposure

### - Combination of Actimab-A and venetoclax resulted in increased cell death compared to individual treatment in cell lines resistant to venetoclax and tumor regression, leading to complete responses and 100% survival in an in vivo tumor model of acute myeloid leukemia

### - Actinium has initiated a Phase 1/2 clinical trial to study Actimab-A in combination with venetoclax and is planning to initiate a Phase 1/2 trial of Actimab-A with venetoclax and a hypomethylating agent

NEW YORK, April 3, 2019 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) highlighted data from its poster presentation at the AACR or American Association of Cancer Research annual Meeting 2019 demonstrating that the targeted radiation delivered by Actimab-A to CD33 expressing cells can deplete MCL-1 levels in tumor cells, thereby removing a mechanism of resistance and rendering them more susceptible to venetoclax. Further, the induction of direct AML cell death via double-stranded DNA breaks by Actimab-A provides a second mechanism for enhancing synergistic potency with venetoclax. Actimab-A is an ARC or Antibody Radiation Conjugate comprised of the anti-CD33 monoclonal antibody lintuzumab and the potent alpha-particle emitting radioisotope Ac-225 or Actinium-225. Venetoclax is a BCL-2 or B-Cell Lymphoma 2 inhibitor that is jointly developed and marketed by AbbVie and Genentech and is approved for patients with AML or Acute Myeloid Leukemia, Chronic Lymphocytic Leukemia, and Small Lymphocytic Leukemia. The poster can be viewed on Actinium's website here.

Highlight's of Actinium's poster presentation are as follows:

- Actimab-A treatment of venetoclax resistant AML cells led to a decrease in MCL-1

levels. MCL-1 is a protein in the BCL-2 family of anti-apoptotic proteins, which is overexpressed in relapsed or refractory AML cells and has been shown to mediate resistance to venetoclax.
- The same Actimab-A treatment reduced BCL-XL. BCL-XL is another protein in the BCL-2 family and also been proposed to mediate resistance to venetoclax.
- Additional studies demonstrated that Actimab-A produced double-stranded DNA breaks in two cell lines resistance to venetoclax.
- At all dose levels and time points, Actimab-A significantly increased double-stranded DNA breaks compared to cells treated with lintuzumab alone.
- In a venetoclax resistant AML *in vivo* tumor model, statistically significant reduction in tumor size was observed in animals receiving the combination of Actimab-A and venetoclax compared to venetoclax alone.
- At evaluation on day 38, complete responses were reported in 3 of 5 animals receiving the combination of Actimab-A and venetoclax while no animals receiving venetoclax alone achieved a complete response at any time point.
- 100% survival at day 40 was observed in cohorts receiving Actimab-A and venetoclax while no animals treated with venetoclax alone survived beyond day 30.

Dr. Dale Ludwig, Actinium's Chief Scientific Officer, said, "The results of these studies further our enthusiasm for the combination of Actimab-A and venetoclax. Expanding on our previous in vitro work, it is validating to observe multiple synergies derived from Actimab-A's unique targeted radiation mechanism of action including MCL-1 reduction. Given the role this protein plays in AML cell resistance to venetoclax, it is exciting to see its depletion with Actimab-A, resulting in increased cell death and tumor control in these studies. We are also excited to demonstrate that Actimab-A causes double-stranded DNA breaks for which there is no known resistance or repair mechanism. It is important to note that these findings were observed in cell lines and xenograft animal models based on venetoclax resistant cell lines. These data further support the advancement of the combination of Actimab-A and Venetoclax into clinical trials as we are doing with two distinct clinical trials."

Actinium has filed a patent on the combination of a targeted alpha-emitting therapeutic such as Actimab-A together with a BCL-2 inhibitor, which includes venetoclax, as a method to treat cancer. Actinium has initiated a Phase 1/2 trial that is studying Actimab-A in combination with venetoclax for patients with relapsed or refractory AML and is planning a Phase 1/2 trial that will study Actimab-A and venetoclax with a hypomethylating agent also for patients with relapsed or refractory AML, which is expected to be initiated in the first half of 2019.

Sandesh Seth, Actinium's Chairman and CEO, said, "As we advance towards the clinic with our second Actimab-A venetoclax combination trial, it is encouraging to see multiple synergies in robust pre-clinical models. With many patients not responding to or having limited duration of their responses with venetoclax treatment, these important findings together with our extensive clinical data with Actimab-A will be beneficial to the advancement of our two combination trials. This work also showcases Actinium's integration of our research and development and clinical development efforts that can result in rapid translation to the clinic.  With a robust intellectual property portfolio around our AWE technology platform, we see a multitude of opportunities to leverage targeted radiation via our ARC's in combination with other therapeutic modalities to generate potential therapies for patients with high unmet medical needs that are underserved by current therapeutic

approaches."

**About Actinium Pharmaceuticals, Inc.**

Actinium Pharmaceuticals Inc. is focused on improving patient access and outcomes to cellular therapies such as BMT or Bone Marrow Transplant 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 ARC's 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 ARC's are designed to 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 and 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, 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 may 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. Notable trials include the planned pivotal program for Actimab-MDS for targeted conditioning prior to a BMT for patients with high-risk MDS, that is expected to initiate in 2019, and two Actimab-A venetoclax combination trials including the initiated Phase 1 doublet trial and the planned triplet trial with a hypomethylating agent.

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 110 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 contains "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 performance of Actinium which Actinium 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 Food and Drug Administration 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, including without limitation its annual report on Form 10-K for the period ended December 31, 2018, subsequent quarterly reports on Form 10-Q and current reports on Form 8-K, each as amended and supplemented from time to time.

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