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# **Actinium Pharmaceuticals Announces Phase 3 SIERRA Trial Dosimetry Results Support Low Dose lomab-B for Targeted Lymphodepletion Prior to Adoptive Cell Therapy**

- Clinical data predicts dose level, administration window beginning 6.1 days post infusion and potential outpatient use for the lomab-ACT program that Actinium intends to advance into human clinical studies
- lomab-ACT program is intended to provide a universal chemotherapy-free solution for lymphodepletion and conditioning prior to adoptive cell therapy such as CAR-T at low dose and gene therapy at higher doses

NEW YORK, Dec. 9, 2019 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium") presented new findings from its pivotal Phase 3 SIERRA trial for lomab-B (Iodine-131 apamistamab) at the 2019 American Society of Hematology (ASH) annual meeting on Sunday, December 8, 2019 in a poster presentation. Actinium is advancing the development of low dose Iodine-131 apamistamab, a CD45 targeting antibody radiation-conjugate (ARC), as an alternative to today's standard practice of chemotherapy-based lymphodepletion regimens like fludarabine/cyclophosphamide (Flu/Cy), which have been implicated in CAR-T toxicities including cytokine release syndrome (CRS) and neurotoxicity.



The analysis of dosimetric results with lomab-B in the pivotal Phase 3 SIERRA trial was conducted to model a non-myeloablative dose level to be used for lymphodepletion prior to CAR-T, as well as the time frame in which an adoptive cell therapy such as CAR-T could be administered. Based on the results from 56 evaluable patients that received a dosimetric dose of Iodine-131 apamistamab, including patients initially randomized to receive lomab-B and those that received lomab-B upon crossover from the control arm, it was determined that a single 75 mCi dosage of Iodine-131 apamistamab would deliver approximately 200 cGy to the bone marrow, the threshold that is considered non-myeloablative. At this dose level, it expected that an adoptive cell therapy could be administered approximately six days

following lomab-ACT lymphodepletion. Actinium intends to advance its lomab-ACT program into human proof-of-concept clinical trials in conjunction with an adoptive cell therapy. The poster can be accessed on Actinium's investor relations page of its website [HERE](#).

Key findings presented in the poster include:

- At fractional dose levels of Iodine-131 apamistamab (median 10mCi) used for dosimetry analysis in the SIERRA trial, approximately 1/10 of the targeted lymphodepletion dose, a significant but transient reduction in lymphocytes and white blood cells was observed compared to pre-dosimetry infusion levels
- 85% reduction in lymphocytes was observed at the post-dosimetry infusion time point, a 67% decrease at day 1 post-dosimetric infusion, and a 43% decrease one week later just prior to the lomab-B therapeutic infusion, demonstrating potent yet reversible lymphodepletion at this dose level
- 35% reduction in peripheral leukemic blasts was observed at the post-dosimetry infusion time point, suggesting a rapid anti-leukemic effect with single-agent Iodine-131 apamistamab consistent with findings from SIERRA presented at ASCO 2019
- The levels of platelets, red blood cells, and neutrophils did not significantly change between pre-infusion and post-dosimetry infusion
- Based on the analysis of the 56 treated patients, a non-myeloablative dosage of 75 mCi has been proposed as a starting dose for human clinical testing in combination with a CAR-T
- Analysis of the dosimetry data establishes that the proposed 75 mCi dosage of Iodine-131 apamistamab would be sufficiently cleared in approximately 147 hours (6.1 days) to allow for CAR-T administration

Dale Ludwig, Ph.D., Actinium's Chief Scientific Officer, said, "CAR-T, adoptive cell therapy, and gene therapy are revolutionary medical advances with great promise. However, despite the innovation in these technologies, they continue to rely on generic chemotherapies for the necessary pre-conditioning prior to their administration, which are non-targeted and toxic. We believe this restricts the true potential of these therapies by hindering their efficacy and durability while increasing toxicities such as cytokine release syndrome and neurotoxicity. With a starting clinical dose and time to clearance defined and supported by clinical results from the SIERRA trial, we look forward to our next step of advancing this program into human clinical testing with a cell therapy while continuing to introduce the lomab-ACT program to cell and gene therapy developers."

### **About the lomab-ACT program**

lomab-ACT is a lower dose of Actinium's lead program lomab-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 Bone Marrow Transplant (BMT). lomab-ACT targets CD45, an antigen expressed on many of the cells that are relevant to CAR-T including lymphocytes, macrophages and regulatory T-cells and that have been associated with CAR-T challenges such as durability of response, cytokine release syndrome (CRS) and neurotoxicity. Actinium has generated preclinical data that targeted lymphodepletion via lomab-ACT has the potential to improve tumor control, selectively deplete necessary cells, and be highly differentiated in terms of tolerability compared to chemotherapy-based lymphodepletion regimens, namely fludarabine/cyclophosphamide (Flu/Cy). The lomab-ACT program may enable 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.

### **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 kill patient's cancer cells and certain immune cells prior to a BMT or Bone Marrow Transplant, CAR-T and other cell therapies. 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, lomab-B is being studied in the ongoing pivotal Phase 3 Study of lomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. Beyond lomab-B, 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 AML (Acute Myeloid Leukemia), MDS (Myelodysplastic Syndrome), MM (Multiple Myeloma). 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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