December 29, 2020

Actinium Announces Successful Pre-Planned Ad Hoc Interim Analysis of Phase 3 SIERRA trial

- 100% rate of BMT and engraftment in patients receiving therapeutic dose of Iomab-B and lower rates of sepsis and sepsis related Grade ≥3 adverse events compared to patients receiving salvage therapies at 75% enrollment recently highlighted in oral presentations at ASH 2020 Annual Meeting

- Independent Data Monitoring Committee recommends SIERRA continue as planned to full enrollment of 150 patients; trial is currently over 75% enrolled

- SIERRA trial remains the only randomized Phase 3 trial to offer potentially curative bone marrow transplant as an option for patients with active relapsed or refractory AML

NEW YORK, Dec. 29, 2020 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium" or the "Company") today announced that the independent Data Monitoring Committee (DMC) has completed the single ad hoc interim analysis of the pivotal Phase 3 SIERRA study of Iomab-B for bone marrow transplant (BMT) conditioning in patients over the age of 55 with active relapsed or refractory Acute Myeloid Leukemia (R/R AML). The SIERRA trial is a randomized, controlled study evaluating outcomes of patients receiving Iomab-B and a BMT compared to outcomes of patients on the control arm who receive physician's choice of salvage therapies, including recently approved targeting agents such as venetoclax, who may proceed to BMT if they achieve a required complete remission (CR). Based on the DMC's review of unblinded data, including the study's primary endpoint of durable Complete Remission (dCR) of at least 180 days, it was recommended that the study continue as planned to full enrollment of 150 patients. Actinium did not receive the unblinded primary and secondary endpoint efficacy data from SIERRA.

A single ad hoc analysis was exercised by Actinium in April 2020 consistent with the study's design that allowed for up to two ad hoc analyses between 70 to 110 patients. This ad hoc

analysis was exercised for a number of patients representing less than two thirds of anticipated final enrollment which required a higher success threshold compared to 100% of trial enrollment. With Actinium exercising only a single analysis, there was a minimal alpha spend resulting in a p-value threshold of 0.046 for the primary endpoint evaluation at full enrollment of 150 patients. The SIERRA trial is currently over 75% enrolled. Data from the first 75% of patients showing that 100% of patients receiving a therapeutic dose of Iomab-B proceeded to transplant and achieved engraftment compared to 16% of patients on the control arm was recently highlighted in an oral presentation at the American Society of Hematology Annual Meeting. A second oral presentation evaluated safety data showing lower rates of serious adverse events categories including sepsis, febrile neutropenia, mucositis and 100-day non-relapse transplant related mortality (TRM) in patients receiving Iomab-B and BMT compared to those on the control arm.

"We are encouraged by the DMC's recommendation to continue the SIERRA trial as planned and that there continues to be no safety concerns from the Iomab-B arm. All of us at Actinium are intensely focused on completing the final portion of patient enrollment in the SIERRA trial," said Dr. Mark Berger, Actinium's Chief Medical Officer. "The recent presentations at ASH highlight Iomab-B's value proposition to universally enable older patients with active relapsed or refractory AML to proceed to a potentially curative bone marrow transplant via a well-tolerated targeted conditioning regimen, which we believe will be a paradigm shift compared to current non-targeted chemotherapy regimens that restrict patient access to BMT. While we believed there was potential for early stoppage of the trial as a result of this ad hoc analysis, we note that the hurdle rate for early stoppage, given the smaller number of patients representing less than two thirds of full enrollment, was much higher for the ad hoc than what is now required at the final analysis of 150 total patients. With the large difference in the number of patients advancing to BMT with Iomab-B and those potentially evaluable for dCR compared to the control arm through seventy-five percent of enrollment, we remain strongly optimistic about the ultimate success of SIERRA. We look forward to capitalizing on the positive momentum resulting from ASH and from our recent senior personnel additions in medical affairs and clinical development in order to complete enrollment as quickly as possible in 2021."

SIERRA Safety and Feasibility at 75% Enrollment

Detailed safety and feasibility data from 75% of patient enrollment presented at the ASH 2020 Annual Meeting highlighted that 100% (49/49) of patients receiving a therapeutic dose of Iomab-B in SIERRA have successfully proceeded to BMT and achieved engraftment, the first sign of BMT success, without delay compared to 16% (9/56) of patients in the control arm who received physician's choice of salvage therapies. The control arm includes a wide range of salvage therapies, including targeted agents like venetoclax, as there is no standard of care in this setting. Of the 84% (47/56) of patients that did not achieve complete remission on the control arm, 64% (30/47) of patients crossed over to receive Iomab-B with 100% (30/30) of those patients successfully engrafting after BMT. In total, 78% (88/113) of patients enrolled on the SIERRA trial were able to receive a BMT despite this being a patient population not typically considered for BMT. At the 100-day post BMT time point, on an ITT basis, there were 43 patients from the Iomab-B study arm potentially evaluable for the primary endpoint of (dCR) at 180 days compared to 7 patients in the control arm. By this measure, 77 percent of patients in the Iomab-B arm are potentially eligible for the dCR primary endpoint compared to 12 percent of patients in the control arm, a greater than 6-

times difference, which is consistent with results at the 25% and 50% interim feasibility and safety analyses.

Phase 3 SIERRA – 75% Enrollment Results			
Baseline Characteristics	**Iomab-B Arm (N=56)**	**Conventional Care (CC) Arm (N=57)[1]**	
Age (yrs, median, range)	63 (55-77)	65 (55-77)	
Cytogenetic and Molecular Risk[2,3]	Favorable: 4% Intermediate: 33% Adverse: 63%	Favorable: 5% Intermediate: 30% Adverse: 64%	
% Transplanted Intent-to-Treat Group	88% (49/56)	16% (9/56)	64% (30/47)
Results	**Underwent Iomab-B based Conditioning and HCT (N=49)[4]**	**Achieved CR and received standard of care HCT (N=9)**	**Randomized to Conventional Care and Crossed Over to Iomab-B with HSCT (N=30)[5]**
Cross-over Rate	n/a	n/a	Received Therapeutic Dose of Iomab-B (N=30) Transplanted (N=30) 64% (30/47)
% Transplanted	100% (49/49)	16% (9/56)	100% (30/30)
BM Blast % @ randomization (median, range)	30% (5-95)[6]	20% (5-97)	22% (6-87)
Days to ANC Engraftment	14 (9-22)[7]	17 (13-83)[8]	14 (10-37)[9]
Days to Platelet Engraftment	18 (4-39)[7]	22 (8-35)[8]	19 (1-38)[9]
Days to HCT (Post Randomization)	30 (23-60)	66 (51-86)	64 (36-100)[10]
Myeloablative Dose Delivered to Bone Marrow	14.8 (4.6-32) Gv 641 (354-1027) mCi	n/a	15.5 (6.3-42) Gv 607 (313-1013) mCi
100-day non-Relapse Transplant-Related Mortality[11]	4% (2/45 Evaluable)	22% (2/9 Evaluable)	12% (3/26 Evaluable)

1) Data unavailable for one (1) patient.
2) Iomab-B arm: data unavailable (4) and patient was excluded (1), conventional care arm: data unavailable (1)
3) Per NCCN guidelines version 3. 2020
4) No therapy dose (7) due to: declining KPS (4), Infusion reaction (1), unfavorable biodistribution (1), post-randomization eligibility (1). Two (2) did not receive DI and five (5) received DI without proceeding to TI.
5) Thirteen (13) patients ineligible for crossover due to: hospice care/progression (4), declined/ineligible for HCT (5), died pre-crossover (4). Additionally, four (4) patients were eligible for crossover and did not receive Iomab-B due to declining KPS.
6) One (1) patient with 4% blasts in the marrow had circulating AML blasts
7) ANC engraftment data not available (3), platelet engraftment data not available (6)
8) ANC engraftment data not available (2), platelet engraftment data not available (1)
9) ANC engraftment data not available (3), platelet engraftment data not available (4)
10) One (1) patient at 161 days had delayed transplant due to infection & respiratory failure, received Iomab & transplant when stable, not included in range
11) Iomab-B arm: Four (4) patients unevaluable; Conventional Care arm: Four (4) patients unevaluable (4). Rates of NRM were not significantly different between any 2 groups

Detailed SIERRA Safety Analysis

It was also highlighted in an oral presentation at the ASH 2020 Annual Meeting that high amounts of radiation are able to be targeted to the bone marrow compared to non-targeted organs with Iomab-B resulting in lower rates of sepsis and sepsis related Grade ≥3 adverse events. A median of 14.9 Gy (Range: 4.6 – 32) of radiation was delivered to the marrow compared to 2.8 Gy (Range: 1.6 – 6.7) of radiation to the gastrointestinal tract. In comparing rates of adverse events in patients receiving Iomab-B and a BMT (N=47) to patients receiving salvage therapy and a BMT (N=9), lower rates of sepsis 4.3% (2/47) vs. 33% (3/9), Grade 3 – 4 febrile neutropenia 34.8% (16/47) vs. 55.6% (5/9) and Grade 3 – 4 mucositis 10.9% (5/47) vs. 33% (3/9) were observed in patients receiving Iomab-B. This is consistent

with the targeted nature of Iomab-B. Unlike chemotherapy, which harms the GI tract and leads to infection with enteric bacteria, Iomab-B therapy is associated with minimal damage to the GI tract leading to lower rates of serious infections.

Adverse Event	Received Iomab-B/HCT (N=47)[1] % (N)	Achieved CR and received Std HCT (N=9) % (N)	No CR Crossed over to Iomab-B/HCT (N=30)[2] % (N)
Sepsis	4.3 (2)	33.3 (3)	22.2 (6)
Febrile Neutropenia Gr 3-4	34.8 (16)	55.6 (5)	40.7 (11)
Mucositis Gr 3-4	10.9 (5)	33.3 (3)	18.5 (5)

Day +100 Non-Relapse Mortality[3]	2/45 (4.4%)	2/9 (22.2%)	3/26 (11.5%)

1 Adverse Event data available for 46 of 47 evaluable patients
2 Adverse Event data available for 27 of 30 evaluable patients
3 Iomab-B arm: 4 patients unevaluable. Conventional Care Arm: 4 patients unevaluable

Patient Group	No. of Patients	Radiation dose delivered to the Marrow. Median (range)	Radiation dose to GI tract. Median (range)
Iomab-B	47	14.9 Gy (4.6-32)	2.8 Gy (1.6-6.7)

The SIERRA trial is the only randomized Phase 3 trial to offer BMT as an option for patients over the age of 55 with active R/R AML. BMT remains the only therapeutic option with curative potential for this patient population. Iomab-B is intended to simultaneously be a targeted induction and conditioning agent that allows patients to proceed to BMT in days after receiving Iomab-B compared to current chemotherapy-based approaches that require a patient to first achieve a complete remission before proceeding to additional conditioning and a BMT.

Sandesh Seth, Actinium's Chairman and CEO said, "With more than 75% of patients for the SIERRA trial enrolled and positive data presented at ASH earlier this month, interest in the trial has never been stronger. We were excited to report a consistent 100% engraftment rate for patients receiving a therapeutic dose of Iomab-B in SIERRA compared to 16% of patients in the control arm who received physician's choice of salvage therapies. We remain confident in the value added by Iomab-B in getting patients to BMT and look forward to the completion of the trial. In addition to the promising results from Iomab-B, we are excited by the data emerging from across our pipeline including the Actimab-A CLAG-M and Actimab-A venetoclax combination trials in fit and unfit relapsed and refractory AML. The results of these combinations demonstrate the power of targeted radiotherapy and its potentiating and synergistic effects and we are excited to be developing two promising programs for indications that are not well addressed with current standard treatment options despite several recently approved therapies. With our strong balance sheet and growing team, we are excited and confident in our ability to execute on our vision and look forward to the several milestones expected for both these programs next year."

About Iomab-B

Iomab-B (I-131 apamistamab) via the monoclonal antibody apamistamab, targets CD45, an

antigen widely expressed on leukemia and lymphoma cancer cells, B cells, and stem cells. Apamistamab is linked to the radioisotope iodine-131 (I-131) and once attached to its target cells emits energy that travels about 100 cell lengths, destroying a patient's cancer cells and ablating their bone marrow. By carrying iodine-131 directly to the bone marrow in a targeted manner, Actinium believes Iomab-B will avoid the side effects of radiation on most healthy tissues, such as the heart, lungs, and GI tract, while effectively killing the patient's cancer and marrow cells.

Iomab-B is currently being studied in the pivotal Phase 3 SIERRA (Study of Iomab-B in Relapsed or Refractory AML) trial, a 150-patient, randomized controlled clinical trial in patients with relapsed or refractory Acute Myeloid Leukemia (AML) who are age 55 and above. The SIERRA trial is being conducted at preeminent transplant centers in the U.S. with the primary endpoint of durable Complete Remission (dCR) at six months and a secondary endpoint of overall survival. Upon approval, Iomab-B is intended to prepare and condition patients for a bone marrow transplant, also referred to as a hematopoietic stem cell transplant, in a potentially safer and more efficacious manner than the non-targeted intensive chemotherapy conditioning that is the current standard of care in bone marrow transplant conditioning. A bone marrow transplant is often considered the only potential cure for patients with certain blood-borne cancers and blood disorders. Additional information on the Company's Phase 3 clinical trial in R/R can be found at www.sierratrial.com.

About Actinium Pharmaceuticals, Inc. (NYSE: ATNM)

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 deplete a patient's disease or cancer cells and certain immune cells prior to a BMT or Bone Marrow Transplant, Gene Therapy or Adoptive Cell Therapy (ACT) such as CAR-T to enable engraftment of these transplanted cells with minimal toxicities. 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, I-131 apamistamab (Iomab-B) is being studied in the ongoing pivotal Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. The SIERRA trial is over seventy-five percent enrolled and positive single-agent, feasibility and safety data has been highlighted at ASH, TCT, ASCO and SOHO annual meetings. More information on this Phase 3 clinical trial can be found at www.sierratrial.com. I-131 apamistamab will also be studied as a targeted conditioning agent in a Phase 1 study with a CD19 CAR T-cell therapy and in a Phase 1/2 anti-HIV stem cell gene therapy with UC Davis. In addition, 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 acute myeloid leukemia, myelodysplastic syndrome and multiple myeloma. Ongoing combination trials include our CD33 ARC, Actimab-A, in combination with the salvage chemotherapy CLAG-M and the Bcl-2 targeted therapy venetoclax. Underpinning our clinical programs is our proprietary AWE (Antibody Warhead Enabling) technology platform. This is where our intellectual property portfolio of over 130 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. Website: https://www.actiniumpharma.com/

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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