

September 15, 2021



# Actinium Completes Enrollment in the Pivotal Phase 3 SIERRA Trial of lomab-B

- Data updates expected in 4Q:2021 with topline data in mid-2022
- 100% of patients receiving lomab-B accessed bone marrow transplant and engrafted without delay compared to 18% of patients receiving salvage therapy on the control arm of the study through 75% of enrollment
- Lower rates of serious adverse events including febrile neutropenia, sepsis and mucositis in patients receiving lomab-B versus control arm
- SIERRA is the only randomized Phase 3 trial to offer bone marrow transplant as an option for patients with active, relapsed/refractory AML age 55 and above

NEW YORK, Sept. 15, 2021 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium" or the "Company") today announced that it has completed enrollment of the pivotal Phase 3 SIERRA trial for lomab-B, an Antibody Radiation Conjugate (ARC) comprised of apamistamab, a CD45 targeting antibody, and the radioisotope iodine-131. The SIERRA trial is a 150-patient, randomized and controlled study conducted at 24 leading bone marrow transplant centers in the United States and Canada. SIERRA is the only randomized Phase 3 trial to offer bone marrow transplant (BMT) to patients with active, relapsed or refractory acute myeloid leukemia (AML) age 55 and above, which is the only curative treatment option for this patient population.



Actinium expects to present data updates from the SIERRA trial in the fourth quarter of 2021 and to announce topline data for the primary endpoint of six-month durable Complete Remission (dCR) in mid-2022. These data are expected to support registration of a Biologics License Application (BLA) for lomab-B.

Dr. Sergio Giralt, Deputy Division Head, Division of Hematologic Malignancies; Melvin Berlin Family Chair in Multiple Myeloma, said, "As an investigator in the SIERRA trial, I believe it is an important trial in the field of bone marrow transplant, as lomab-B represents a potentially

significant advancement for BMT conditioning. Having spent my career working to expand the use of transplant and improve patient outcomes, I know firsthand the value a targeted conditioning agent like lomab-B can offer patients and transplant physicians. Given lomab-B's targeted nature, it has demonstrated the ability to produce effective myeloablation, even in patients with high disease burden, while also being well tolerated. This has shown to enable more patients, including those with significant comorbidities, to access bone marrow transplant and successfully engraft."

Dr. Avinash Desai, Actinium's Executive Vice President, Clinical Development, Operations, stated, "We are thrilled that the SIERRA trial is now fully enrolled. Since joining Actinium last November, I have ensured our clinical, CMC and supply chain teams have been entirely focused on execution and on achieving this important milestone. lomab-B was developed to address the significant unmet need of patients who could benefit and possibly be cured of their blood cancer with a bone marrow transplant but could not receive a transplant because non-targeted conditioning regimens could not produce a remission or are too toxic in this patient population. We are confident that lomab-B will squarely addresses this unmet need given its targeted nature and ability to deliver high amounts of radiation directly to the bone marrow resulting in myeloablation while sparing healthy organs. The SIERRA trial was designed to evaluate the rate of dCR of at least six months in patients receiving lomab-B and a BMT to those receiving salvage chemotherapy. With enrollment complete, we will turn our focus towards preparing a BLA submission with the goal of making lomab-B available to the patients as soon as possible after receiving the topline results from the SIERRA trial. We sincerely thank the patients, their families, caregivers, staff and investigators that participated in this important study."

Sandesh Seth, Actinium's Chairman and CEO, said, "Completion of SIERRA enrollment is a major milestone for Actinium. It has been exciting seeing the trial conclude with strong momentum under Dr. Desai's leadership. Through strong interactions with our sites, our revitalized clinical team has been able to successfully surmount obstacles that arose from the third wave of the COVID-19 pandemic and recruit the last 25% of patients faster than any previous cohort of patients. Their performance is a testament that our execution has never been stronger. We are eager to present additional data from SIERRA later this year and look forward to reporting topline data next year. As we look ahead, our team will be actively preparing a BLA to support regulatory approval of lomab-B in patients with active r/r AML and executing market access and pre-commercial activities to support a potential U.S. launch."

"In addition, we will explore opportunities to expand the use of lomab-B in other indications to support our targeted conditioning strategic business unit vision. Given that lomab-B is the only CD45 targeting agent in clinical development, and that CD45 is expressed in all blood cancers, we believe there is a significant market opportunity. This multi-indication opportunity excites us as our commercial efforts would target a concentrated number of transplant centers and physicians that we believe will result in significant operating leverage. Beyond targeted conditioning, we will continue to leverage our targeted radiotherapy expertise, particularly in the field in the field of Actinium-225 based alpha therapies, to be at the forefront of innovation focused on bringing value to patients and investors," concluded Mr. Seth.

### **lomab-B SIERRA Engraftment and Safety Data and Highlights Through 75%**

## Enrollment

(presented at the 2021 Transplantation and Cellular Therapy Annual Meeting)

- 100% (49/49) BMT access and engraftment rate for patients receiving a therapeutic dose of lomab-B compared to 18% (10/57) of patients receiving physician's choice of salvage therapy on the control arm

- 79% (89/113) of all patients enrolled on SIERRA were able to proceed to BMT despite being a patient population not considered eligible for BMT with standard approaches due to cross over

- lomab-B delivers high amounts of targeted radiation to the bone marrow with minimal impact on other organs resulting in lower rates and severity of adverse events

Phase 3 SIERRA – 75% Enrollment Results			
Baseline Characteristics	lomab-B Arm (N=56)	Conventional Care (CC) Arm (N=57)	
Age (years) Median (Range)	63 (55-77)	65 (55-77)	
Cytogenetic and Molecular Risk <sup>1, 2</sup>	Favorable: 4% Intermediate: 35% Adverse: 61%	Favorable: 5% Intermediate: 32% Adverse: 63%	
% Transplanted Intent-to-Treat Group	88% (49/56)	18% (10/57)	64% (30/47)
Results	Underwent lomab-B based Conditioning and BMT (N=49) <sup>3</sup>	Achieved CR and received standard of care BMT (N=10)	Randomized to Conventional Care and Crossed Over to lomab-B with BMT (N=30) <sup>4</sup>
Crossover Rate	n/a	n/a	64% (30/47)
% Transplanted	100% (49/49)	18% (10/57)	100% (30/30)
% Marrow Blast @ Randomization Median (Range)	29% (4-95) <sup>5</sup>	20% (5-97)	28% (6-87)
Days to ANC Engraftment	14 (9-22) <sup>6</sup>	17 (13-83) <sup>7</sup>	14 (10-37) <sup>8</sup>
Days to Platelet Engraftment	18 (4-39) <sup>6</sup>	22 (8-35) <sup>7</sup>	19 (1-38) <sup>8</sup>
Days to BMT (Post Randomization)	30 (23-60)	67 (52-104)	62 (36-100) <sup>9</sup>
Myeloablative Dose Delivered to Bone Marrow	14.7 (4.6-32) Gv	n/a	15.5 (6.3-42) Gv
	646 (354-1027) mCi		592 (313-1013) mCi
100-day Non-Relapse Transplant-Related Mortality	4% (2/45 Evaluable)	20% (2/10 Evaluable)	10.7% (3/28 Evaluable)

1) lomab-B arm: data unavailable (4) and patient was excluded (1)

2) Per NCCN guidelines version 3. 2020

3) 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.

4) Thirteen (13) patients ineligible for crossover due to: hospice care/progression (4), declined/ineligible for BMT (5), died pre-crossover (4). Additionally, four (4) patients were eligible for crossover and did not receive lomab-B due to declining KPS.

5) One (1) patient with 4% blasts in the marrow had circulating AML blasts

6) ANC engraftment data not available (4), platelet engraftment data not available (7)

7) ANC and platelet engraftment data not available (1)

8) ANC engraftment data not available (1), platelet engraftment data not available (2)

9) One (1) patient at 161 days had delayed transplant due to infection & respiratory failure, received lomab & transplant when stable, included in range

Adverse Event	Underwent lomab-B based Conditioning and BMT (N=49) <sup>1</sup> % (N)	Achieved CR and received standard of care BMT (N=10) % (N)	Randomized to Conventional Care and Crossed Over to lomab-B with BMT (N=30) <sup>2</sup> % (N)
Sepsis	4 (2)	30 (3)	23 (7)
Febrile Neutropenia Gr 3-4	42 (20)	50 (5)	40 (12)

Mucositis Gr 3-4	10 (5)	30 (3)	17 (5)
Day +100 Non-Relapse Mortality <sup>3</sup>	2/45 (4.4)	2/10 (20.0)	3/28 (10.7)
1) Adverse Event data available for 46 of 47 evaluable patients 2) Adverse Event data available for 27 of 30 evaluable patients 3) lomab-B arm: 4 patients unevaluable. Conventional Care Arm: 4 patients unevaluable			

Patient Group	No. of Patients	Radiation dose delivered to the Marrow. Median	Radiation dose to GI tract. Median
lomab-B	49	14.6 Gy	2.8 Gy

## About the SIERRA Phase 3 Trial

The SIERRA trial is a 150-patient, randomized clinical trial, studying lomab-B compared to physician's choice of salvage therapy in patients with active, relapsed or refractory acute myeloid leukemia (r/r AML) age 55 and above. In SIERRA, patients receiving lomab-B, those achieving a remission after salvage therapy or those patients not achieving remission after salvage therapy that crossed over to receive lomab-B were offered a bone marrow transplant (BMT), which is the only treatment option with curative potential for patients with active r/r AML. The SIERRA trial is the only randomized Phase 3 trial to offer BMT to this patient population. The control arm of SIERRA included over 20 single agents or combination treatment options based on physician's choice which include salvage chemotherapy and recently approved targeted agents including Bcl-2 inhibitor (Venetoclax), FLT3 inhibitors and IDH 1/2 inhibitors as there is no standard of care for this patient population. The SIERRA trial was conducted at 24 sites in the United States and Canada.

## About lomab-B

lomab-B (I-131 apamistamab) via the monoclonal antibody apamistamab, targets CD45, an antigen widely expressed on leukemia and lymphoma cancer cells, immune cells and bone marrow 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 lomab-B may avoid the side effects of radiation on most healthy tissues while effectively killing the patient's cancer (induction) and marrow cells (myeloablation) including those in bone marrow niches due to the "crossfire" effect enabled by the I-131 radioisotope.

lomab-B was licensed from the Fred Hutchinson Cancer Research Center where it was studied in nearly 300 patients, in multiple clinical trials in 6 blood cancer indications. lomab-B is being studied in the pivotal Phase 3 SIERRA (Study of lomab-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 was conducted at 24 preeminent transplant centers in the U.S. and Canada. The primary endpoint of durable Complete Remission (dCR) at six months and a secondary endpoint of overall survival. Upon approval, lomab-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 lomab-B and the Phase 3 SIERRA clinical trial can be found at [www.sierratrial.com](http://www.sierratrial.com).

### **About Actinium Pharmaceuticals, Inc.**

Actinium Pharmaceuticals, Inc. is a clinical-stage biopharmaceutical company developing targeted radiotherapies to deliver cancer-killing radiation with cellular level precision to treat patients with high unmet needs not addressed by traditional cancer therapies. Actinium's current clinical pipeline is led by ARCs or Antibody Radiation-Conjugates that are being applied to 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. Actinium's targeted conditioning ARCs 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 (lomab-B) has been studied in several hundred patients including in the recently completed, 150-patient, pivotal Phase 3 Study of lomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. lomab-ACT, low dose I-131 apamistamab is being studied as a targeted conditioning agent in a Phase 1 study with a CD19 CAR T-cell Therapy with Memorial Sloan Kettering Cancer Center. In addition, we are leaders in the field of Actinium-225 alpha therapies. Actimab-A, our clinical stage CD33 targeting ARC alpha therapy has been studied in nearly 150 patients including our ongoing combination trials 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 160 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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