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Actinium Announces Positive Pivotal Phase 3 SIERRA Trial Results of lomab-B Showcased to the European Transplant Community in Oral Presentation at the European Society for Blood and Marrow Transplantation (EBMT) Annual Meeting

- *EBMT oral presentation builds awareness for lomab-B and the SIERRA trial results with the European transplant community that performs twice as many transplants compared to the U.S.*
- *lomab-B enabled unprecedented 100% bone marrow transplant access and engraftment with 75% post-BMT CR rate in patients with active, relapsed or refractory acute myeloid leukemia who are considered unfit and transplant ineligible in routine clinical practice*
- *lomab-B met the SIERRA trial primary endpoint of durable Complete Remission (dCR) with high statistical significance ($p < 0.0001$) and had a favorable safety profile compared to the control arm*
- *92% 1-year survival and 60% 2-year survival in patients achieving dCR, median overall survival has not been reached in these patients*

NEW YORK, April 27, 2023 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium" or the "Company"), a leader in the development of targeted radiotherapies, today announced that the positive results from the pivotal Phase 3 SIERRA Trial of lomab-B were presented in an oral presentation at the European Society for Blood and Marrow Transplantation (EBMT) 49th Annual Meeting that was held in Paris, France April 23 – 26, 2023. Europe represents a large market opportunity with approximately twice as many transplants performed in Europe compared to the United States. The SIERRA trial is the first randomized Phase 3 trial to take unfit, transplant ineligible patients with active relapsed or refractory (r/r) acute myeloid leukemia (AML) age 55 and above to bone marrow transplant (BMT), which was feasible due to lomab-B's novel targeted radiotherapy approach that allows patients to receive a BMT without achieving a Complete Remission (CR).



As previously presented at the 2023 Tandem Meetings: Transplantation & Cellular Therapy Meetings of the American Society for Transplantation and Cellular Therapy (ASTCT) and the Center for International Blood & Marrow Transplant Research (CIBMTR) in February 2023, lomab-B enabled unprecedented 100% access to BMT in half the time, 29 days vs. 66.5 days, with 100% of lomab-B patients achieving engraftment, the first sign of BMT success. lomab-B met the study's primary endpoint of dCR of 6-months following initial complete remission after BMT with high statistical significance (p-value of <0.0001) with only patients receiving lomab-B achieving dCR. The lomab-B patients achieving dCR had a 92% 1-year survival rate and a 60% 2-year survival rate, which represents a potential cure, and median overall survival (OS) has not been reached in the patients achieving dCR.

Sandesh Seth, Actinium's Chairman and CEO, said, "lomab-B and the SIERRA trial represent a paradigm change for patients with r/r AML by making a BMT and its curative potential a reality for the significant number of patients who cannot achieve a CR or tolerate current induction and conditioning therapies. We're thrilled the SIERRA results were showcased to the European transplant community, as Europe represents a large commercial market with twice as many BMTs performed in Europe compared to the US each year. With our efforts fully underway to complete and submit our BLA for lomab-B with the FDA by the end of 2023, we are committed to bringing lomab-B to r/r AML patients globally and look forward to working with Immedica, our European, Middle East and North African (EUMENA) partner for their subsequent marketing authorization application (MAA) with the European Medicines Agency. With these positive results in hand, we're eager to continue to build awareness for lomab-B globally and to launch an early access program for lomab-B in the U.S. as well as launch life cycle planning initiatives in the second half of this year to leverage lomab-B's potential across blood cancers."

Dr. Avinash Desai, Actinium's Chief Medical Officer, added, "The efficacy and tolerability of lomab-B in these heavily pre-treated patients with active, high-risk r/r AML enrolled in the SIERRA trial is unprecedented. Despite 10 drug approvals for AML since 2017, approximately 30% of patients never achieve a remission and over 50% develop relapsed or refractory disease, which is associated with dismal survival outcomes of 2-4 months. BMT remains the only potential curative treatment option for r/r AML patients, but current clinical practice precludes the overwhelming majority of r/r AML patients from BMT due to the need to first achieve a remission and the use of highly toxic, non-targeted chemotherapies for conditioning. Based on the reaction to the SIERRA results from BMT physicians in the U.S. and now Europe, if approved, lomab-B can be practice changing by enabling r/r AML patients with active disease, one of the largest segments of AML, to access BMT in days, via a single therapeutic infusion, without having to first achieve a remission."

SIERRA Trial Results:

- 100% BMT access and engraftment with lomab-B vs only 17% in the control arm, where patients received current AML best practice treatment comprised of 20 available agents including venetoclax (Bcl-2 inhibitor), FLT3 inhibitors, IDH inhibitors, Mylotarg and multiple cytotoxic chemotherapies
- Time to BMT was half in lomab-B patients compared to control arm patients – 29 days versus 66.5 days

- 75% of lomab-B patients achieved Complete Remission (CR/CRp) within 30 days following their BMT versus only 6.3% of patients on the control arm
- 22% of lomab-B treated patients achieved a dCR, the primary endpoint of SIERRA versus 0% of control arm patients ($p < 0.0001$)
- Patients achieving dCR with lomab-B had a 92% 1-year survival rate and 60% 2-year survival rate; longer-term follow-up is ongoing as median overall survival (OS) has not been reached in these patients.
- Event-free survival, a secondary endpoint, was 26% versus 0.2% in favor of lomab-B with a Hazard Ratio of 0.22 ($p < 0.0001$)
- Median OS was doubled in lomab-B patients - 6.4 months versus 3.2 months in control arm patients who did not cross over – as was 1-year survival – 26.1% versus 13.1%
- lomab-B had a favorable safety profile with more than 4-times lower rates of sepsis (6.1% versus 28.6%) along with lower rates of febrile neutropenia, mucositis and acute Graft Versus Host Disease compared to control arm.

SIERRA Trial lomab-B Patient Characteristics:

- Median blast count: 30%
- Prior lines of treatment: 3 (1-8)
- Median age: 64 (55-77)
- Intermediate and adverse cytogenetics and molecular risk: >90%
- Majority of patients had primary induction failure or first early relapse: 78%

EBMT Presentation Details:

Title: A Randomized Phase 3 Study of Allogeneic HCT with lomab-B Versus Conventional Care in Older Patients with Active, Relapsed/Refractory AML: Pivotal SIERRA Trial Results

About lomab-B and the Pivotal Phase 3 SIERRA Trial

lomab-B is a first-in-class targeted radiotherapy intended to improve patient access to potentially curative BMT by simultaneously and rapidly depleting blood cancer, immune and bone marrow stem cells that uniquely express CD45. Multiple studies have demonstrated increased survival in patients receiving BMT, however, an overwhelming majority of patients with blood cancers do not receive BMT as current approaches do not produce a remission, which is needed to advance to BMT, or are too toxic. Studied in over 400 patients, prior studies with lomab-B have demonstrated nearly universal access to BMT, increased survival and tolerability in multiple clinical trials including the recently completed pivotal Phase 3 SIERRA trial in patients with active (leukemic blasts >5%), relapsed or refractory acute myeloid leukemia (r/r AML) age 55 and above.

lomab-B met the primary endpoint of durable Complete Remission (dCR) of 6 months after initial remission post-BMT in the pivotal Phase 3 SIERRA trial with high statistical significance ($p < 0.0001$). lomab-B produced a 75% post-BMT CR rate (44/59 patients), which is 12-times greater than the post-BMT rate of 6.3% (4/64 patients) in the control arm. Event

Free Survival was 26%, compared to 0.02% in control arm with a Hazard Ratio of 0.22 ($p < 0.0001$), in other words patients receiving lomab-B had a 78% lower probability of an event compared to control arm where event is defined as not achieving a CR/CRp, crossing over to be rescued by lomab-B, not receiving a BMT, disease relapse or death. lomab-B doubled 1-year overall survival with 26.1% compared to 13.1% in the control arm for patients who did not crossover as well as median overall survival with 6.4 months vs 3.2 months. Overall survival statistics are confounded by the very early crossover of 60% patients from control arm to be rescued with lomab-B. Crossover patients had a 35.8% 1-year overall survival rate. Due to its targeted nature, lomab-B was well tolerated with more than four times lower rates of sepsis compared to the control arm (6.1% vs. 28.6%) along with febrile neutropenia, mucositis and graft versus host disease (GVHD). Actinium intends to submit a Biologics License Application (BLA) seeking approval for lomab-B in 2023 based on the SIERRA data. lomab-B has been granted Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) and has various patent protection into 2037.

The pivotal Phase 3 SIERRA (Study of lomab-B in Elderly relapsed or refractory AML) is a 153-patient, randomized, multi-center clinical trial, studying lomab-B compared to the control arm of physician's choice of salvage therapy. Control arm options included chemotherapies like cytarabine and daunorubicin and various targeted agents such as a Bcl-2 inhibitor (Venetoclax), FLT3 inhibitors and IDH 1/2 inhibitors. The SIERRA control arm reflects real-world treatment of r/r AML patients with over 20 agents used alone or in combination as no standard of care exists for this patient population. The SIERRA trial enrolled patients at 24 leading transplant centers in the United States and Canada that perform approximately over 30% of current AML BMTs.

Developed at the Fred Hutchinson Cancer Research Center, a pioneer in the field of BMT, lomab-B is supported by data in six other disease indications including leukemias, lymphomas and multiple myeloma, which afflict over 100,000 patients annually. Actinium intends to pursue additional indications for lomab-B beyond AML. Actinium also intends to pursue international regulatory approvals independently and through partnerships. In April 2022, Actinium licensed the European, Middle East and North African commercial rights for lomab-B to Immedica AB, a full-fledged independent pharmaceutical company headquartered in Sweden. In exchange, Actinium received an upfront payment of \$35 million USD with the potential for an additional \$417 million USD in regulatory and sales milestones and mid-twenty percent royalties. Europe represents a commercial opportunity double the size of the United States by number of patients with AML receiving BMT. lomab-B has been granted Orphan Drug Designation by the European Medicines Agency (EMA) and has received positive Scientific Advice from the Committee for Medicinal Products for Human Use (CHMP) of the EMA indicating that the Phase 3 SIERRA trial design, primary endpoint and planned statistical analysis are acceptable as the basis for a Marketing Authorization Application.


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. Actinium's clinical pipeline is led by targeted radiotherapies 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 bone marrow transplant

(BMT), gene therapy or adoptive cell therapy, such as CAR-T, to enable engraftment of these transplanted cells with minimal toxicities. Our lead product candidate, lomab-B (I-131 apamistamab) has been studied in over four hundred patients, including the pivotal Phase 3 Study of lomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. The SIERRA trial was positive with lomab-B meeting the primary endpoint of durable Complete Remission of 6-months with high statistical significance ($p < 0.0001$). Lomab-B enabled 100% of patients to access a BMT and produced higher rates of post-BMT CR. Lomab-B produced positive results for the secondary endpoints of the SIERRA trial including reducing the probability of an event by 78% resulting in an Event-Free Survival (EFS) Hazard Ratio of 0.22 ($p < 0.0001$), doubled 1-year overall survival and median overall survival. 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 with NIH funding. Actimab-A, our second most advanced product candidate has been studied in approximately 150 patients with Acute Myeloid Leukemia or AML, including in combination trials with the chemotherapy regimen CLAG-M and with venetoclax, a targeted therapy. Actimab-A or lintuzumab-Ac225 is an Actinium-225 based antibody radiation conjugate targeting CD33, a validated target in AML. Actinium has entered into a Cooperative Research and Development Agreement (CRADA) with the National Cancer Institute (NCI) to develop Actimab-A as a single agent or combination with chemotherapy, targeted agents or immunotherapy in Phase 1, 2 or 3 trials. The NCI will fund clinical trial expenses under the CRADA while Actinium will supply Actimab-A. The NCI is currently accepting proposals for non-clinical and clinical studies with Actimab-A. Actinium is a pioneer and leader in the field of Actinium-225 alpha therapies with an industry leading technology platform comprising over 190 patents and patent applications including methods of producing the radioisotope AC-225. Our technology and expertise have enabled collaborative research partnerships with Astellas Pharma, Inc. for solid tumor theranostics, with AVEO Oncology Inc. to create an Actinium-225 HER3 targeting radiotherapy for solid tumors, and with EpicentRx, Inc. to create targeted radiotherapy combinations with their novel, clinical stage small molecule CD47-SIRP α inhibitor. More information is available on Actinium's 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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