February 18, 2023

Actinium Announces Positive Full Data Results From the Pivotal Phase 3 SIERRA Trial in Patients with Active, Relapsed or Refractory Acute Myeloid Leukemia

- Iomab-B met the primary endpoint of durable Complete Remission (dCR) of 6-months following initial complete remission after BMT with high statistical significance (p-value of <0.0001), 22% of patients achieved dCR in the Iomab-B arm compared to 0% in the control arm

- In patients achieving 6-month dCR with Iomab-b, 1-year survival of 92% and 2-year survival of 60% was achieved; median overall survival (OS) has not been reached in these patients

- Iomab-B demonstrated significant improvement in Event Free Survival (EFS) with a Hazard Ratio = 0.22, p<0.0001

- Iomab-B doubled 1-year survival and median overall survival compared to control arm patients who did not crossover

- Iomab-B was well tolerated with a favorable safety profile – 4 times lower rate of sepsis than control arm

- Company to host conference call and webcast on Saturday, February 18, 2023 at 6:00 PM EST to highlight full SIERRA results

NEW YORK, Feb. 18, 2023 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) (Actinium or the Company), a leader in the development of targeted radiotherapies, today announced positive results for the primary and secondary endpoints from its pivotal Phase 3 SIERRA trial of Iomab-B in patients age 55 and above with active relapsed or refractory acute myeloid leukemia (r/r AML). Iomab-B met the primary endpoint of durable Complete Remission (dCR) of 6-months following initial complete remission following BMT with a high degree of statistical significance (p<0.0001). Additionally, Iomab-B produced a significant and clinically meaningful improvement in the secondary endpoint of Event-Free Survival (EFS), with a 78% reduction in the probability of an event (Hazard Ratio=0.22, p<0.0001). Iomab-B doubled 1-year survival compared to the control arm excluding cross over patients (26.1% vs 13.1%) as well as median overall survival (6.4 months vs. 3.2 months). Iomab-B was well tolerated with four times lower rates of sepsis (6.1% vs 28.6%) and lower rates of febrile neutropenia, mucositis and acute graph versus host disease (aGVHD). Iomab-B enabled unprecedented access to BMT with 100%

engraftment in patients receiving a therapeutic dose of Iomab-B compared to 18% of patients in the control arm and Iomab-B produced a 75% post-BMT Complete Remission (CR) rate compared to 6.3% post-BMT CR in the control arm. These high rates of access and post-BMT CR enabled the highly significant primary endpoint results. The full SIERRA results were presented in the late-breaker session 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).

Investor Conference Call and Webcast Details:

Time / Date:	6:00 PM EST on Saturday, February 18, 2023
Presenters:	Sandesh Seth, Chairman & CEO
	Madhuri Vusirikala M.D., VP, Clinical Development – BMT & Cellular Therapy
	Avinash Desai, M.D., Chief Medical Officer
	Caroline Yarbrough, Chief Commercial Officer
Dial-in:	1-877-407-0784 (toll-free domestic) or 1-201-689-8560 (international) or by clicking on this link and requesting a return call
Live webcast:	To access the live webcast of the call with slides please visit the Investors section of Actinium's website https://ir.actiniumpharma.com/presentations-webinars or https://viavid.webcasts.com/starthere.jsp?ei=1590226&tp_key=580722640c

An archived webcast will be available on the Actinium's website (click here) after the event.

Dr. Sergio Giralt, Deputy Head, Division of Hematologic Malignancies, Attending Physician, Adult BMT Service at Memorial Sloan Kettering Cancer Center, stated, "The SIERRA trial results are an exciting advancement for older patients with active r/r AML and will be practice changing in how we treat these patients. I am thrilled to see a high percentage of Iomab-B patients who achieved durable remissions reaching the critical 2-year survival mark. Significant improvement in event-free survival and overall survival, with an excellent safety profile in the SIERRA trial, demonstrate the potential of Iomab-B becoming a new standard of care for active, r/r AML."

SIERRA Trial Results

The pivotal Phase 3 SIERRA trial is a 153-patient, randomized, multi-center, controlled trial, where Iomab-B is compared to the control arm that allowed physician's choice of over 20 available agents including chemotherapies and/or targeted therapies such as Venetoclax

(Bcl-2), FLT3 inhibitors, IDH inhibitors and Mylotarg. The control arm reflects current best practices for the treatment of r/r AML patients. SIERRA was conducted at 24 of the leading BMT centers in the United States and Canada. SIERRA enrolled older, heavily pre-treated patients with active disease and high-risk characteristics who would not be offered BMT in standard practice outside of a clinical trial and therefore have dismal survival outcomes of two to three months.

Iomab-B Patient Characteristics:

- Patients with active, r/r disease
- 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%
- Median blast count: 30%
- Prior lines of treatment: 3 (1-8)

BMT Access and Engraftment:

All patients receiving the therapeutic dose of Iomab-B were able to access BMT with 100% engraftment. Patients in the Iomab-B arm were able to access a BMT without having to first attain a CR, consequently they were able to access BMT in half the time compared to the control arm as those patients need to attain a CR prior to BMT, which is the norm per current practice.

- Iomab-B treatment provided unprecedented access to BMT and engraftment without delay (less than 20 days for platelets and neutrophils) in all patients who received the therapeutic dose of Iomab-B (66/66), (59/59 for per protocol analysis)
- Iomab-B enabled more than a 6x increase in BMT access compared to the control arm where 17% of patients (11/64) were able to access a BMT per protocol analysis
- Of the 82% of patients (62/76) in the control arm who failed to achieve a CR and access BMT, 67% of patients (40/62) were able to crossover. Crossover patients are counted as failures for the primary endpoint analysis. Of the 40 crossover patients, 100% (40/40) were able to receive Iomab-B and accessed BMT also achieving engraftment without delay
- Iomab-B enabled access to BMT in approximately half the time (median of 29 days) compared to control arm patients (median 66.5 days)

Post-BMT CR:

- 75% of patients (44/59) receiving Iomab-B achieved an initial remission after their BMT compared to 6.3% of patients (4/64) in the control arm which represents a 12x increase in post-BMT CR rates in favor of Iomab-B

Primary Endpoint – dCR 6-months After Initial CR:

- Iomab-B met the primary endpoint of 6 months dCR with a high degree of statistical significance ($p<0.0001$)
- 22% of patients (13/59) achieved dCR on the SIERRA arm compared to 0% of patients on the control arm
- Patients who achieved 6-month dCR had 92% 1-year survival and 60% 2-year survival.

Median OS has not been reached in these patients

Secondary Endpoints – Event Free Survival and Overall Survival

- Iomab-B demonstrated significant improvement in EFS with a Hazard Ratio = 0.22, p<0.0001, which means Iomab-B reduced the probability of an event by 78%. EFS is not confounded by the SIERRA crossover arm and allows for direct comparison of survival outcomes between Iomab-B and the control arm
    - Event is defined as not achieving CR/CRp, crossover, not receiving BMT, relapse or death
- Iomab-B doubled 1-year survival and median overall OS of Iomab-B compared to patients who did not crossover in the control arm was 26.1% vs 13.1% and Median OS was 6.4 months vs 3.2 months
- In the crossover arm, 1-year overall survival was 35.8% in patients who received Iomab-Band median overall survival was 7.1 months

Safety Information:

- Iomab-B was well-tolerated with a favorable safety profile
- In transplanted patients, incidence of sepsis was four times lower in the Iomab-B arm then the control arm (6.1% vs 28.6%)
- Rates of other treatment related adverse events were lower in favor of Iomab-B, including febrile neutropenia (43.9% vs. 50%), mucositis (15.2% vs 21.4%) and aGVHD (26.1% vs 35.7%)

Dr. Avinash Desai, Chief Medical Officer of Actinium, said, "We are excited that Iomab-B met the primary endpoint and produced positive results across all SIERRA trial endpoints with improved safety compared to control arm in such a difficult patient population. In routine clinical BMT practice, patients enrolled on SIERRA would never be considered for transplant and often have dismal outcomes. Iomab-B provides unprecedented BMT access and improved outcomes with better tolerability – opening the promise of better transplant outcomes for the entire universe of relapsed and refractory AML patients. These results clearly demonstrate Iomab-B's practice expanding opportunity as more patients will be able to access transplant and upon reaching the 100-day post-transplant mark they can return to their referring hematologist for long-term care. We look forward to launching an early access program, completing our BLA submission and initiating life cycle management activities to bring Iomab-B to as broad a patient population as possible."

Sandesh Seth, Actinium's Chairman and CEO, added, "These positive SIERRA results will help to establish Iomab-B as a new standard of care for r/r AML. Iomab-B is a very attractive option for patients due to its excellent safety and strong efficacy profile. It will enable physicians to provide a treatment intervention with potential long-term survival outcomes and will help bring more patients to curative BMTs. We truly believe that Iomab-B enables potentially better value to be unlocked by getting more patients safely to an effective BMT and by increasing the length and quality of life for patients who otherwise would have dismal outcomes using currently available options. The commercial opportunity for Iomab-B is attractive as the majority of relapsed/refractory patients cannot be treated with a BMT today and Iomab-B can enable them to access this potentially curative treatment. These patients comprise of over half of all AML patients. In addition, the lack of current or visible competition for Iomab-B and the concentration of BMT centers imply that successful

commercialization of this high-value treatment can be achieved with a streamlined, efficient organization that is sparing to the balance sheet. We look forward to establishing this practice expanding treatment as the standard of care and to updating on our plans to file the BLA and progress toward this goal."

About Iomab-B and the Pivotal Phase 3 SIERRA Trial

Iomab-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 Iomab-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.

Iomab-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 ($p<0.0001$). Iomab-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. Patients receiving Iomab-B had a 78% lower probability of an event, defined as not achieving a CR/CRp, crossover, not receiving a BMT, relapse or death, with a Hazard Ratio of 0.22 ($p<0.0001$). Iomab-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 crossover arm. Crossover patients had a 35.8% 1-year overall survival rate. Due to its targeted nature, Iomab-B was well tolerated with four times lower rates of sepsis compared to the control arm (6.1% vs. 28.6%) and lower rates of BMT associated adverse events including febrile neutropenia, mucositis and graft versus host disease (GVHD). Actinium intends to submit a Biologics License Application (BLA) seeking approval for Iomab-B in 2023 to address patients age 55+ with r/r AML who cannot access BMT with currently available therapies. Iomab-B has been granted Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) and has patent protection into 2037.

The pivotal Phase 3 SIERRA (Study of Iomab-B in Elderly relapsed or refractory AML) is a 153-patient, randomized, multi-center clinical trial, studying Iomab-B compared to the control arm of physician's choice of salvage therapy. Control arm options included chemotherapies like cytarabine and daunorubicin and 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 over 30% of AML BMTs.

Developed at the Fred Hutchinson Cancer Research Center, a pioneer in the field of BMT, Iomab-B is supported by data in six disease indications including leukemias, lymphomas and multiple myeloma, which afflict over 100,000 patients annually. Actinium intends to pursue additional indications for Iomab-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 Iomab-B to Immedica AB, a fully-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. Iomab-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, Iomab-B (I-131 apamistamab) has been studied in over four hundred patients, including the pivotal Phase 3 Study of Iomab-B in Elderly Relapsed or Refractory Acute Myeloid Leukemia (SIERRA) trial for BMT conditioning. The SIERRA trial was positive with Iomab-B meeting the primary endpoint of durable Complete Remission of 6-months with high statistical significance ($p<0.0001$). Iomab-B enabled 100% of patients to access a BMT and produced higher rates of post-BMT CR. Iomab-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. Iomab-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-SIRPα inhibitor. More information is available on Actinium's website: https://www.actiniumpharma.com/.

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