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Actinium Announces Iomab-B Produces High Response Rates and Significant Improvement in Overall Survival in Relapsed Refractory AML Patients with Active Disease Overcoming TP53 Mutation

- Relapsed or refractory AML patients with TP53 mutation known to have dismal outcomes due to limited effective treatment options
- Median Overall Survival of 5.49 months observed in patients with a TP53 mutation receiving an Iomab-B led allogeneic bone marrow transplant compared to 1.66 months in patients that did not receive Iomab-B (hazard ratio=0.23, p=0.0002)
- Eighth oral presentation of Iomab-B data since announcement of positive Phase 3 SIERRA Results

NEW YORK, Dec. 11, 2023 /PRNewswire/ -- **Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) (Actinium or the Company), a leader in the development of targeted radiotherapies, today announced that results from the Phase 3 SIERRA trial of Iomab-B were presented in an oral presentation at the 65th Annual American Society of Hematology Meeting & Exposition (ASH). The oral presentation highlighted significantly improved survival in patients with a TP53 mutation receiving Iomab-B.

Iomab-B is a targeted radiotherapeutic comprised of an anti-CD45 monoclonal antibody with the Iodine-131 radioisotope payload. The Phase 3 SIERRA trial enrolled 153 patients with active relapsed or refractory acute myeloid leukemia (AML) and compared outcomes of patients receiving Iomab-B and a bone marrow transplant (BMT) to those of patients receiving physician's choice of care in the control arm, which was intended to reflect current best practices. Patients not achieving a Complete Remission (CR) in the control arm who were unable to proceed to a BMT were offered to crossover to receive an Iomab-B led BMT.

Iomab-B achieved the primary endpoint in the SIERRA trial of durable Complete Remission

(dCR) of at least 6 months with high statistical significance (p<0.0001), with 22% of patients randomized to the Iomab-B arm achieving dCR and 0% of patients in the control arm achieving dCR, irrespective of TP53 mutational status. In addition, Iomab-B significantly improved event-free survival, a secondary endpoint, with a hazard ratio of 0.22 and median overall survival (mOS) was doubled.

Data highlighted in the ASH oral presentation, which can be accessed on the investor relations page of Actinium's website, included:

Overall Survival in Patients with a TP53 Mutation:

	Iomab-B & Crossover	**Control Arm**
Median OS	5.49 months	1.66 months
Number of Patients	27	10
Hazard Ratio	**0.23**	
p-value	**0.0002**	

Median OS was 6.37 months in TP53 negative patients receiving Iomab-B and 5.72 months for TP53 positive patients demonstrating Iomab-B's ability to overcome TP53 gene mutations.

Response rates by TP53 Mutation Status:

	Iomab-B & Crossover	**Control Arm**
TP53 Positive	**N=27**	**N=10**
CR	**55.56% (15/27)**	**0 %**
dCR	**14.81% (4/27)**	**0 %**
TP53 Wildtype	**N=93**	**N=23**
CR	**58.06% (54/93)**	**17.39% (4/23)**
dCR	**16.13% (15/93)**	**0 %**

Dr. Hannah Choe, Assistant Professor of Medicine at Ohio State University and SIERRA trial investigator, commented, "Patients with a TP53 mutation have notoriously poor outcomes due to resistance to anti-leukemic therapies and are rarely offered access to potentially curative transplantation. Iomab-B can grant patients increased access to transplant and induces high complete remission rates despite active, relapsed/refractory disease and even in those with a TP53 mutation. This speaks to the novelty and safety of a CD45-directed radiotherapy. More importantly, we see that these response rates translated into improved overall survival, overcoming the increased risk associated with TP53 mutation while no other viable treatment options exist. We are excited to present these results that further support the use and safety of Iomab for disease control."

Overall, twenty-four percent (37/153) of patients enrolled on SIERRA had a TP53 mutation. In total, 27 patients with a TP53 mutation received Iomab-B and accessed BMT on the SIERRA trial either after initial randomization or following crossover after not being able to access a BMT on the control arm. Only 1 patient with a TP53 mutation was able to access a BMT on the control arm via conventional care.

Dr. Avinash Desai, Actinium's Chief Medical Officer, added, "The SIERRA trial data support that regardless of advanced age, prior therapy, or high-risk cytogenetics including a TP53 mutation, Iomab-B provides unprecedented access to a potentially curative BMT. The results also show that on a population basis and across subgroups, an Iomab-B led BMT may result in improved survival. We are incredibly excited for the potential of Iomab-B and what it represents for patients with relapsed or refractory AML. The international enthusiasm for the SIERRA data amongst key medical and scientific communities is evidenced by the eight oral presentations at some of the most prestigious medical conferences held this year including TCT, EBMT, ONS, EHA, SNMMI, EANM, SOHO and now ASH is highly motivating, and we are committed to bringing Iomab-B to transplant physicians and their patients globally."

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 2024 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 Pharma 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 approximately 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 develops targeted radiotherapies to meaningfully improve survival for people who have failed existing oncology therapies. Advanced pipeline candidates Iomab-B (pre-BLA), an induction and conditioning agent prior to bone marrow transplant, and Actimab-A (National Cancer Institute CRADA pivotal development path), a therapeutic, have demonstrated potential to extend survival outcomes for people with relapsed and refractory acute myeloid leukemia. Actinium plans to advance Iomab-B for other blood cancers and next generation conditioning candidate Iomab-ACT to improve cell and gene therapy outcomes. Actinium's technology platform is the basis for collaborations with Astellas Pharma for solid tumors, AVEO Oncology/LG Chem Life Sciences for HER3 solid tumors, and several internal programs in solid tumors. Actinium holds more than 220 patents and patent applications.

For more information, please visit: https://www.actiniumpharma.com/

Forward-Looking Statements

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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Sources: Granowicz EM, Jonas BA. Targeting *TP53*-Mutated Acute Myeloid Leukemia: Research and Clinical Developments. Onco Targets Ther. 2022 Apr 21;15:423-436. doi: 10.2147/OTT.S265637. PMID: 35479302; PMCID: PMC9037178.

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