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Actinium Announces Actimab-A Plus 7+3 Combination Trial for Newly Diagnosed Acute Myeloid Leukemia Patients

- Study builds on recent Actimab-A plus CLAG-M combination trial results showing an 86% remission rate with 71% MRD negative rate in CD33 positive patients with relapsed or refractory AML**
- Combination trial with 7+3 standard of care regimen in intermediate and high-risk patients expands potential of Actimab-A into large segment of AML**
- Trial to be led by Dr. Joseph Jurcic, M.D., Director of Hematologic Malignancies at Columbia University Irving Medical Center**

NEW YORK, Feb. 26, 2020 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium") announced today that it is expanding its CD33 program studying Actimab-A into a combination trial with the chemotherapy regimen 7+3 in patients with newly diagnosed acute myeloid leukemia (AML) who have intermediate or high-risk cytogenetic or molecular markers. The intent of this Phase 1 dose escalation study is to determine whether these patients can benefit from a combination of the 7+3 standard of care chemotherapy regimen, which causes DNA damage and has radiation sensitizing properties via inhibition of DNA replication and repair, with an ARC or Antibody Radiation Conjugate such as Actimab-A that delivers targeted, highly potent alpha particle radiation directly to tumor cells. This study builds upon results of an ongoing study with a similar rationale wherein a sub-therapeutic dose of Actimab-A when added to a chemotherapy regimen called CLAG-M was shown to improve responses by nearly sixty percent compared to CLAG-M given alone in relapsed or refractory AML patients. The planned Phase 1 study, if successful, could make Actimab-A a potential treatment for patients newly diagnosed with AML, which is a larger patient population than patients with refractory AML. The new trial could also support the rationale of combining ARCs with other treatment mechanisms to produce superior clinical results. To that end, Actimab-A is also being studied in a Phase 1 combination with the Bcl-2 inhibitor in patients with relapsed or refractory AML.



Dr. Joseph Jurcic, Professor of Medicine and Director of Hematology Malignancies at Columbia University Herbert Irving Comprehensive Cancer Center, said, "Having studied ARCs extensively, including Actimab-A as the lead investigator in its prior Phase 1/2 trial, I am fully aware of its potential and look forward to leading this combination trial. ARCs may enable us to deliver the validated modality of radiation to cancers at a cellular level without exposing patients to toxicities that would come from delivering radiation via external beam to diffuse hematologic malignancies. While 7+3 chemotherapy can produce high rates of initial complete remission, most patients still relapse, which suggests that this therapy is not potent enough to kill all AML cells and cancer stem cells at the levels that can be safely administered. There is a strong mechanistic rationale for adding Actimab-A to 7+3 that we believe will result in higher response rates and more durable complete remissions without additive toxicities. Indeed, this type of effect has recently been demonstrated with the promising results of combining Actimab-A with the salvage chemotherapy regimen CLAG-M."

Actimab-A is intended to selectively deliver Actinium-225 to cause double stranded DNA breaks in cancer cells, for which there is no known resistance mechanism. This leads to a potent anti-tumor effect. Prior clinical results in over 100 patients treated with Actimab-A, including a Phase 1/2 trial of 58 patients, demonstrated a safety profile with minimal non-hematologic toxicities and an unmatched ability to deliver attenuated doses of radiation internally to CD33 expressing cancer cells. In the Phase 1/2 trial, Actimab-A as a single agent produced a 69% remission rate (CR, CRi, CRp) at high doses in patients with newly diagnosed AML but Actinium elected to pursue low dose combination trials for therapeutic development based on observed myelosuppression. 7+3 is an intensive chemotherapy regimen considered to be the standard of care for patients with newly diagnosed AML who are able to tolerate intensive chemotherapy. The 7+3 regimen intended for this study consists of seven days of the chemotherapeutic cytarabine that inhibits DNA synthesis and replication and 3 days of the cytotoxic anthracycline daunorubicin that inhibits DNA replication and repair as well as RNA synthesis. Chemotherapy, such as 7+3, has shown to sensitize cancer cells to radiation.

The rationale for studying Actimab-A in combination with 7+3 is the potential for a synergistic effect due to the interplay of various mechanisms including DNA damage from alpha radiation, radiation sensitization and prevention of DNA damage repair. Supporting this rationale are results from an ongoing Phase 1 trial studying Actimab-A in combination with the salvage chemotherapy regimen CLAG-M support ARC combinations with chemotherapy were reported at the 2019 American Society of Hematology Annual Meeting. The addition of subtherapeutic doses of Actimab-A to CLAG-M resulted in an 86% complete remission rate, a nearly 60% increase over the 54% complete remission rate that was observed in a study of CLAG-M alone in the same patient population. Notably, 71% of patients receiving Actimab-A with CLAG-M achieved MRD or minimal residual disease negative status. The combination also had a clinically acceptable safety profile. The goal of this study is to evaluate the potential for generating deeper and more durable remissions with a favorable safety profile.

Dr. Mark Berger, Actinium's Chief Medical Officer, said, "The ability of ARCs to deliver radiation at the cellular level to targeted cells provides multiple opportunities for development. The recent results showing that a subtherapeutic dose of Actimab-A is clinically synergistic with chemotherapy supports our low dose ARC development strategy."

Our previously announced trial with Actimab-A in combination with venetoclax is a second example of this strategy, and this trial in front line AML with 7+3 is a further step in establishing Actimab-A as the backbone of combination therapies. We are excited to add this trial to our growing pipeline aimed at establishing our ARC based therapies as treatment options for patients with a wide range of hematologic diseases."

Actimab-A targets CD33, an antigen expressed on nearly all AML cells, as well as on MDS cells. CD33 is a well validated and high-conviction target, with one anti-CD33 drug approved and a number of other antibody-based therapies in development. Mylotarg (gemtuzumab ozogamicin), an antibody drug conjugate targeting CD33, is approved for the treatment of AML in combination with chemotherapy. However, Mylotarg use has been associated with VOD or Veno-Occlusive Disease of the liver, especially in patients who receive an allogeneic hematopoietic cell transplant, and the addition of Mylotarg to 7+3 was most effective in patients with favorable cytogenetic/molecular risk. In fact, treatment of patients with poor cytogenetic/molecular risk with Mylotarg 7+3 was reported to have no benefit above 7+3 alone. Actimab-A by virtue of the radioisotope payload is agnostic to cytogenic or molecular markers and has not been associated with VOD. This dose evaluating, multi-center study will follow a standard 3+3 dose escalation design and would have the flexibility of adding additional cohorts above or in between the planned doses if further optimization required.

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 fifty percent enrolled and positive single-agent, feasibility and safety data has been highlighted at ASH, TCT, ASCO and SOHO annual meetings. I-131 apamistamab will also be studied as a targeted conditioning agent in a Phase 1/2 anti-HIV stem cell gene therapy with UC Davis and is expected to be studied with a CAR-T therapy in 2020. 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 alpha 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 100 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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