October 21, 2020

Actinium Pharmaceuticals, Inc. Awarded Grant by National Institutes of Health to Study Novel Iomab-ACT Targeted Conditioning with a CD19 CAR T-Cell Therapy

-- NIH grant to support first of its kind clinical trial to use Antibody Radio-Conjugate for targeted conditioning prior to CAR T-cell therapy in patients with acute lymphoblastic leukemia and diffuse large B-cell lymphoma

-- ARC-based targeted lymphodepletion is intended to improve CAR T-cell patient outcomes by selectively depleting immune cells, including those implicated in CAR T-cell toxicities

-- Actinium to host Iomab-ACT program update call on October 22, 2020 at 8:00 AM EDT

NEW YORK, Oct. 21, 2020 /PRNewswire/ --**Actinium Pharmaceuticals, Inc.** (NYSE AMERICAN: ATNM) ("Actinium" or the "Company") today announced that the National Institutes of Health has awarded Actinium a Small Business Technology Transfer grant to support a clinical collaboration with Memorial Sloan Kettering Cancer Center ("MSK") to study Iomab-ACT, Actinium's CD45-targeting Antibody Radio-Conjugate, for targeted conditioning to achieve lymphodepletion prior to administration of a CD19-targeted CAR T-cell therapy developed at MSK. The CD19 CAR-T has been previously studied by MSK in a Phase 2 trial with chemotherapy conditioning in patients with relapsed or refractory B-cell acute lymphoblastic leukemia (R/R B-ALL) or diffuse large B-cell lymphoma (DLBCL). MSK will lead this first of its kind study to utilize targeted radiopharmaceutical ARC-based lymphodepletion to replace chemotherapy-based conditioning prior to CAR T-cell therapy. The study will assess the feasibility of using Iomab-ACT targeted lymphodepletion prior to MSK's 19-28z CAR-T and assess safety and efficacy outcomes relative to results with MSK's CAR-T 19-28z in patients who had received chemotherapy-based lymphodepletion prior to CAR-T administration.

Actinium Pharmaceuticals, Inc.

Results published in the New England Journal of Medicine with MSK's 19-28z CD19 CAR-T in 53 patients with R/R B-ALL reported complete remissions in 83% (44/53) of patients. Median event-free survival (EFS) was 6.1 months and median overall survival (OS) was 12.9 months at a median follow up period of 29 months (range 1 – 65 months) for all patients. Patients with low disease burden, defined as less than 5% blasts in the bone marrow, had markedly enhanced outcomes with increased median EFS of 10.6 months and median OS of 20.1 months. There was a 26% (14/53) rate of Grade 3 of greater cytokine release syndrome (CRS), with 1 patient death as a result, and 42% of patients experienced Grade 3-4 immune effector cell-associated neurotoxicity syndrome (ICANS). In addition to improved duration of response and survival, patients with low disease burden prior to receiving CAR T-cell therapy had lower rates of CRS and neurotoxicity.[1]

"We are excited to be collaborating with MSK on this trial as they are a leader in the field of cellular therapies. We selected MSK's 19-28z CAR T-cell therapy for this NIH grant funded collaboration because it has produced high response rates in patients with relapsed or refractory B-ALL who have previously undergone several lines of standard therapy. However, toxicities such as cytokine release syndrome and neurologic toxicity, as well as durability of response, remain a challenge as is the case with many other CAR T-cell therapies" commented Dr. Mark Berger, Actinium's Chief Medical Officer. "Iomab-ACT enables the delivery of targeted radiation that selectively and specifically targets immune cells, including those implicated in the CAR-T-associated toxicities of cytokine release syndrome and neurotoxicity. We are hopeful that this study will demonstrate improvements in safety and outcomes with MSK's CAR 19-28z as a result of Iomab-ACT targeted lymphodepletion and that this will allow clinicians to make important improvements in patients' ability to receive CAR T-cell therapies."

CAR-T is a type of cellular therapy in which a patient's own (autologous) T-cells are genetically engineered outside of the body to target the patient's cancer cells and which are then reinfused back into the patient to seek out and kill cancer cells. Currently there are 2 approved CD19 targeted CAR-T therapies, which both require chemotherapy-based conditioning to deplete the patient's lymphocytes, known as lymphodepletion, and many other CAR-T constructs in development that also use chemotherapy conditioning for lymphodepletion.

Iomab-ACT targets cells that express CD45, an antigen found on immune cells such as lymphocytes and macrophages as well as leukemia and lymphoma cancer cells and delivers the radioisotope warhead iodine-131 to achieve cell depletion. Iomab-ACT is intended to deplete CD45+ immune cells such as macrophages that are implicated in CAR-T related toxicities and may also have an anti-tumor effect on chemo-refractory cancers. Iomab-ACT is a low dose extension of Actinium's lead program, Iomab-B, which is being studied in a pivotal Phase 3 trial for targeted conditioning prior to a bone marrow transplant. Preclinical data supporting Iomab-ACT's application in targeted lymphodepletion prior to ACT such as CAR-T was recently published in the journal *Oncotarget*

(https://www.oncotarget.com/archive/v11/i39/). In addition, clinical data with trace doses of Iomab-B has shown transient, reversible lymphodepletion in patients and drug clearance pharmacokinetics that fit within the vein to vein time of CAR-T manufacturing and administration.

Sandesh Seth, Actinium's Chairman and CEO, said, "This clinical trial collaboration with MSK is a strong step forward for Actinium and our targeted conditioning program. The 19-28z CAR-T has already produced promising data and we look forward to working with MSK to explore Iomab-ACT's potential to reduce toxicities and improve patient outcomes. As we advance towards the SIERRA interim analysis in the fourth quarter, we are focused on the continued expansion of our ARC-based targeted conditioning program for bone marrow transplant and cell and gene therapies with the goal of providing targeted conditioning regimens that are less toxic and more effective than current chemotherapy-based conditioning. With these therapies being administered in a select number of concentrated centers, we see a large and growing market opportunity where our ARC-based targeted conditioning can improve outcomes and increase access to these important curative treatment options."

Iomab-ACT Program Update Call Details
Webcast link: https://ir.actiniumpharma.com/presentations-webinars
Date: October 22, 2020
Time: 8:00 AM EDT

Source:

1) Park et al. Long-Term Follow-up of CD19 CAR Therapy in Acute Lymphoblastic Leukemia. N Engl J Med 2018;378:449-59. DOI: 10.1056/NEJMoa1709919

About Actinium Pharmaceuticals, Inc.

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 kill patient's cancer cells and certain immune cells prior to a BMT or Bone Marrow Transplant, CAR-T and other cell therapies or gene therapy 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, Iomab-B is being studied in the ongoing pivotal Phase 3 **S**tudy of **I**omab-B in **E**lderly **R**elapsed or **R**efractory **A**cute Myeloid Leukemia (SIERRA) trial for BMT conditioning. The SIERRA trial is over fifty percent enrolled and promising single-agent, feasibility and safety data has been highlighted at ASH, TCT, ASCO and SOHO annual meetings. Beyond Iomab-B, 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. Underpinning our clinical programs is our proprietary AWE (Antibody Warhead Enabling) technology platform. This is where our intellectual property portfolio of over 120 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.

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, including but not limited to, statements relating to the Company's expectations regarding the intended use of proceeds of the public offering. 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 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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