August 10, 2016

With Impressive Data in Tow, Actinium Pharma An Overlooked Leader in New AML Therapies

By Elliot Schleicher, Senior Staff Writer, Online Media Group, Inc.

NEW YORK, NY, Aug. 10, 2016 /PRNewswire/ - Acute myeloid leukemia (AML) goes by many names, acute myelogenous leukemia and acute myeloblastic leukemia for example, and comes in eight different subtypes, making it unique from other forms of leukemia. Regardless of name or type, there's one common denominator; it's lethal. There is no standard of care and the prognosis for survival time is often measured in months, if not weeks.

As one of only a handful of companies using alpha particle linked antibodies to treat cancer, Actinium Pharmaceuticals (NYSE MKT: ATNM) is moving its novel products down the clinical path to address this great unmet medical need. Actinium's APIT, an acronym for "Alpha Particle Immunotherapy," technology is a platform initially aimed at AML, with the potential to expand into different cancer indications in the future. The company's most advance therapy is Iomab-B, which is the subject of a pivotal Phase 3 trial initiated in June to evaluate its efficacy as an induction and conditioning agent used to prepare patients 55 and older with relapsed or refractory AML for a hematopoietic stem cell transplant (HSCT), commonly referred to as bone marrow transplant (BMT). Iomab-B is being developed under an FDA Orphan Drug designation for this indication, making it eligible for expedited review, additional market exclusivity and other incentives.

A common approach to treat AML is a cocktail of strong chemotherapy drugs to put the cancer into remission. Oncologists frequently use the "7+3" regimen of seven days of cytarabine combined with three days of an anthracycline drug, often daunorubicin or idarubicin. Another approach to induce remission is total body irradiation. These treatments are intended to kill all detectable cancer cells, but they're not selective and end up destroying many healthy normal cells developing in the bone marrow too. Once in remission, an allogeneic BMT is performed in a bid to eradicate any cancer cells lingering in the bone marrow or blood and normalize critical blood components.

One of the main problems is, though, that the median age of AML patients at diagnosis is 68 and many of these critically ill older patients cannot survive the aggressive chemotherapy or total body irradiation regimens. A process of reduced-intensity conditioning (lower, less toxic levels of chemo) is sometimes used to try and prepare older patients for a BMT.

Sadly, about half of AML patients requiring a BMT die before ever making it to the transplant. For patients over 55 ineligible for high-intensity chemo, survival is a meager one to four months.

Actinium's Iomab-B is a radioimmunotherapy consisting of BC8, a novel murine monoclonal antibody developed by the Fred Hutchinson Cancer Research Center (FHCRC), and iodine-131 radioisotope. BC8 targets CD-45, a pan-leukocytic (and pan-lymphomic) antigen widely expressed on white blood cells. Once cells expressing CD-45 are selectively targeted, the radiation energy payload from iodine-131 destroys the cancer and bone marrow cells with little collateral damage to other cells.

Across several Phase 1 and Phase 2 trials evaluating Iomab-B in almost 300 patients, strong safety and efficacy profiles have been established. A Proof-of-Concept study was conducted at FHCRC, which is widely regarded as the "Transplant Temple" due to all the pioneering work in BMT for leukemia. Data from relapse/refractory patients over 50 years of age showed 100% engraftment (meaning the transplant took) at day 28 and a 100% complete response rate. The one-year survival rate was an impressive 30% compared to the current rate of 10% for patients receiving chemo or BMT. From a two-year view, Iomab-B showed a 20% survival rate compared to 0% (zero) with today's chemo and BMT treatments.

Actinium recently completed a successful investigator meeting regarding the Phase 3 SIERRA (Study of Iomab-B in Elderly Relapsed or Refractory AML) trial, bringing together more than 85 attendees, including the Clinical Research Organization for the trial, principal investigators, bone marrow transplant physicians, care providers and clinical research coordinators from current and prospective clinical trial sites from across the country.

"The investigator meeting furthers our confidence in our ability to successfully execute the pivotal Phase 3 trial for Iomab-B. It was clear from the meeting that there is great enthusiasm from transplant, nuclear medicine and hematology physicians for Iomab-B," commented Dr. Felix Garzon, Actinium's Senior VP and Head of Clinical Development.

The company anticipates top-line data from the trial in the second half of 2018. Investors will surely be looking for clues from independent data monitoring committee reports that will be coming before the trial is completed, as they could be catalytic moments for the company.

In addition, Actinium is targeting patients newly diagnosed with AML with its Actimab-A drug candidate. Actimab-A utilizes a similar approach to Iomab-B, only it targets CD-33 as opposed to CD-45 and uses the isotope Actinium-225. Actimab-A, a second-generation therapy of the company's HuM195-alpha program, was licensed from Memorial Sloan-Kettering Cancer Center (MSK). Only July 12, Actinium was issued two additional provisional patent applications from MSK, adding to the company's intellectual property portfolio. Actinium has also received an Orphan Drug designation from the FDA for Actimab-A for AML.

CD-33 is a molecule expressed on 90% of AML cells, making it a target for companies like Johnson & Johnson, Amgen (both in very early research) and Seattle Genetics. With respect to drugs targeting CD-33, Actimab-A trails only Seattle Genetics' SGN-CD33A in stage of clinical development and could have an advantage due to the properties of Actinium-225, which has intense energy that causes double-stranded breaks, making it arguably one of the most powerful killing agents known to man. At the same time, the energy only travels a minimal distance (about four cell diameters) from where it is released, so its toxicity profile is benign. The safety of Actimab-A has been validated across four

clinical trials enrolling almost 90 patients.

Wyeth (acquired by Pfizer in 2009 for $68 billion) garnered FDA approval of their CD-33 targeting drug Mylotarg for AML in 2000, making it the only drug approved for AML in the last 30 years. The FDA approved the drug on Phase 2 data showing a complete response rate of 26% in patients over the age of 60. However, Pfizer removed Mylotarg from the market in 2010 due to toxicity issues.

In a completed Phase 1 dose-escalation trial of Actimab-A, a 28% complete response rate was shown, similar to that of Mylotarg, albeit an early study. The complete response rate increased to 33% by excluding the lowest dose (0.5 µCi/kg), meaning that early data is very favorable for Actinium as it works through an ongoing Phase 1/2 study. A single 0.5 µCi/kg dose was not even included in the current study.

In the Phase 2 portion, Actinium is also incorporating a peripheral burden threshold as part of inclusion criteria, which should further improve results, considering Actinium said, "[The] complete response rate at the dose level which the Company intends to progress into the Phase 2 trial was 50% in patients with low peripheral blast burden." It's impressive that a 50% complete response rate can be achieved, especially without any serious adverse events being attributed to Actimab-A.

Demonstrating the value that markets are putting to a new AML drug, Jazz Pharma in May agreed to buy Celator Pharma for $1.5 billion, representing a 71% premium to the price of CPXX, to take control of the late-stage experimental drug Vyxeos (cytarabine: daunorubicin) for AML. In a Phase 3 study, Vyxeos outperformed the 7+3 therapy of cytarabine and daunorubicin and met its primary endpoint of improvement in overall survival.

With these things in mind, it seems an anomaly that Actinium only has a market capitalization of only $84 million and likely that it's just a matter of time before the markets catch on. This is with consideration that it is a wide open space and Actinium is targeting patients that do not qualify for Celator therapy with Actimab-A, while carving out a new market segment for the some 7,000 patients that undergo AML procedures annually with Iomab-B.

full disclosure, we call the reader's attention to the fact that Online Media Group, Inc. may have received compensation from the companies mentioned in this release.

SOURCE Actinium Pharmaceuticals, Inc.