



Epizyme Initiates Phase 1 Trial of EPZ-5676, a DOT1L Inhibitor

Personalized Therapeutic for Patients with MLL-r Leukemia, a Genetically Defined Type of Acute Leukemia

Cambridge, MA, September 5, 2012 - [Epizyme, Inc.](#), a company leading the creation of a new class of personalized therapeutics for patients with genetically defined cancers, announced today that it has initiated a Phase 1 Study of [EPZ-5676](#). EPZ-5676 is a novel small molecule inhibitor of DOT1L, a [histone methyltransferase](#) (HMT) that is critical to the development of a specific type of acute leukemia defined by rearrangement of the MLL gene (MLL-r leukemia). The Phase 1 study will evaluate the safety, pharmacokinetics, and pharmacodynamics of escalating doses of EPZ-5676 and will also provide a preliminary assessment of efficacy in a cohort of patients with MLL-r leukemia. Epizyme anticipates that approximately 40 patients will be accrued to this Phase 1 study.

“Acute leukemia with MLL rearrangement can occur in both adults and children, usually with devastating outcomes,” said Dr. Eric Hedrick, Chief Medical Officer at Epizyme. “Patients with this type of leukemia are already identified using existing diagnostics. The medical community has a high level of awareness about this disease and the need to develop more specific and effective treatments for these patients. We are very excited to begin the clinical evaluation of EPZ-5676, which has been designed to block the specific abnormality that causes this genetically defined type of leukemia.”

“EPZ-5676 is the first histone methyltransferase inhibitor (HMTi) to enter human clinical development. It is an important potential therapeutic for MLL-r patients and a significant milestone for the entire field. It is also an example of Epizyme’s approach to creating personalized therapeutics for patients with genetically defined cancers,” said Dr. Robert Gould, Chief Executive Officer and President at Epizyme.

Epizyme retains all US development and commercialization rights to its DOT1L inhibitor program, including EPZ-5676. The program is partnered with Celgene outside of the United States.

About EPZ-5676

EPZ-5676 is being developed as a personalized therapeutic for patients with MLL-r leukemia, a genetically defined type of acute leukemia. EPZ-5676 is a novel, potent and selective small molecule inhibitor of DOT1L. DOT1L is a HMT that leads to the development of acute leukemia associated with rearrangements of the MLL gene on chromosome 11. Rearrangements of MLL result in the recruitment of DOT1L activity to aberrant gene locations, leading to the expression of the leukemia-causing genes HOXA9 and MEIS1. EPZ-5676 was developed internally using Epizyme’s proprietary product platform. Data published by Epizyme in [Cancer Cell](#) demonstrate that a DOT1L inhibitor selectively kills MLL-r cells while sparing cells that do not contain the



MLL-r genetic alteration, significantly extending survival in animal models of MLL-r. EPZ-5676 is the first HMTi to enter human clinical development.

About MLL-r Leukemia

MLL-r leukemia is a group of acute leukemias (either of myeloid, lymphoid, or mixed lineage) that affects adults, infants, and children. They share a common causative abnormality: rearrangements of the MLL gene, located on chromosome 11. These rearrangements are detected by current standard diagnostic tests. The DOT1L HMT, as described above, is directly implicated in the development of these leukemias, by promoting the expression of leukemia-causing genes. Though representing a range of clinical presentations, the prognosis of this group of leukemias is uniformly poor. Current standard chemotherapy is non-specific and toxic, rather than being targeted specifically towards the aberrant DOT1L activity that drives this group of leukemias. More specific and effective therapies are needed for patients with MLL-r leukemia.

About Epizyme

Epizyme is leading the creation of small molecule histone methyltransferase inhibitors (HMTi), a new class of personalized therapeutics for patients with genetically defined cancers. Genetic alterations in HMTs, a family of epigenetic enzymes, drive multiple human diseases. This approach represents the future of healthcare by matching better medicines with the right patients.

Epizyme has benchmark partnerships with Celgene, GSK and Eisai and receives funding and strategic support from the Multiple Myeloma Research Foundation (MMRF) and the Leukemia & Lymphoma Society (LLS). www.epizyme.com

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