Epizyme and Collaborators Publish Paper in *Cancer Cell* Supporting Use of DOT1L Histone Methyltransferase Inhibitors as Personalized Therapeutics for Genetically-Defined MLL-rearranged Leukemia Patients

-Survival Benefit Demonstrated in Mouse MLL Model with Epizyme's Selective DOT1L Inhibitor-

Cambridge, Massachusetts, July 11, 2011– Epizyme, Inc., a company leading the discovery and development of personalized therapeutics for genetically-defined cancer and rare disease patients, and its collaborators announced the publication in *Cancer Cell* of breakthrough research in the treatment of MLL-rearranged leukemia (MLL), a genetically-defined subset of acute lymphoblastic leukemia (ALL) and acute myelogenous leukemia (AML).

This seminal research demonstrates for the first time that a small molecule histone methyltransferase inhibitor (HMTi) can:

- selectively kill genetically-defined MLL tumors *in vitro*, with little effect on non-MLL leukemia cells, and
- drive a statistically significant anti-tumor survival benefit in an *in vivo* model.

HMTs are a class of epigenetic enzymes that regulate entire pathways of gene expression. Many members of this 100-member target class have strong genetic associations with the underlying causes of human diseases, including cancer and orphan diseases. In MLL, chromosomal rearrangements of the MLL gene result in aberrant recruitment of the DOT1L HMT, which drives the expression of genes that are leukemogenic in the affected patients. Researchers exposed leukemic cells *in vitro* to Epizyme's potent and DOT1L-targeted HMTi, selectively killing genetically-defined cells bearing the MLL rearrangement. When Epizyme's compound was administered *in vivo* in an aggressive disseminated mouse model of MLL, the treatment led to statistically significant extension of survival at every dose tested.

"MLL is a devastating disease that affects both pediatric and adult patients. Inhibiting DOT1L with potent, targeted small molecules like Epizyme's HMTi represents a promising new therapeutic avenue for the treatment of this specific and genetically-defined subset of leukemia," said Bruce Chabner, M.D., the Director for Clinical Research at the Massachusetts General Hospital Cancer Center, former head of the Division of Cancer Treatment at the National Cancer Institute, and Epizyme SAB member.

"Our ability to create targeted small molecules that selectively inhibit the enzymatic activity of DOT1L *in vitro* and *in vivo* is a breakthrough for the field of epigenetic

drug discovery," said Roy Pollock, Ph.D., Director of Biological Sciences at Epizyme and corresponding author on the paper.

Dr. Robert A. Copeland, EVP of R&D and CSO, said, "The findings published today are a giant step forward in the translation of HMT science to the development of targeted epigenetic therapies through the demonstration of anti-tumor activity in an *in vivo* model. Our DOT1L program's progress is an example of the power of Epizyme's approach to creating personalized therapeutics for patients with genetically-defined diseases. In addition to DOT1L, Epizyme is pursuing a rich pipeline of proprietary and partnered HMTi therapeutic programs, all of which are directed to patient-defined targets."

The paper titled, "Selective Killing of Mixed Lineage Leukemia Cells by a Potent Small-Molecule DOT1L Inhibitor," was authored by Roy M. Pollock and colleagues from Epizyme in collaboration with researchers from the Dana-Farber Cancer Institute, Children's Hospital Boston, Harvard Medical School and the Harvard Stem Cell Institute. The paper is available online today by clicking here and will be published in print in the July issue on July 12, 2011.

About Epizyme
Epizyme is leading the discovery and development of small molecule histone methyltransferase (HMT) inhibitors, a new class of targeted therapeutics for the treatment of genetically-defined cancer patients based on breakthroughs in the field of epigenetics. Genetic alterations in the HMTs are strongly associated with the underlying causes of multiple human diseases, including cancer. Epizyme's patient--driven approach represents the future of personalized therapeutics by creating better medicines for the right patients more quickly and at lower cost than traditional approaches. www.epizyme.com

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