Epizyme identifies novel opportunity for treatment of genetically defined human B-cell lymphomas

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Epizyme, Inc., a company leading the discovery and development of first-in-class, targeted cancer therapeutics against epigenetic targets, today announced the publication of breakthrough new research in the *Proceedings of the National Academy of Sciences* (USA). The discovery, centered on the epigenetic enzyme EZH2, illuminates a clear path for the translation of basic science into targeted therapies for the safe and effective treatment of specific forms of human lymphomas. EZH2 is a histone methyltransferase (HMT), a class of enzymes that play an important role in regulating the activity of particular groups of genes that are involved in serious diseases, including cancer.

The paper describes how the development of two non-Hodgkin lymphomas - follicular lymphoma and germinal center B-cell like subtype of diffuse large B-cell lymphoma - requires the combined activities of both the wild-type and Tyr641 mutants of EZH2. This novel insight reinforces the development of targeted therapeutics for these patients, as it repudiates the previous supposition that the Tyr641 mutation resulted in a loss of EZH2 function.

Dr. Robert A. Copeland, EVP of R&D and CSO, said, "We believe this is the first example of a human disease that is reliant on the combined catalytic activity of both normal and disease-associated mutant enzymes. By targeting HMTs with clear genetic disease associations, such as EZH2, Epizyme takes a hypothesis-driven approach to development of

personalized therapeutics for specific patient populations with high unmet needs. Our product platform enables the creation of novel, potent and selective small molecule HMT inhibitors."

"This paper is a novel, important and representative example of the rapidly growing understanding of the oncogenic role played by HMTs in many cancers. It highlights the promise of HMT inhibitors as novel therapeutics against these targets," said Professor Christopher T. Walsh, the Hamilton Kuhn Professor of Biological Chemistry and Molecular Pharmacology (BCMP) at Harvard Medical School and a member of Epizyme's Scientific Advisory Board.

More information: The paper, entitled "Coordinated activities of wild-type plus mutant EZH2 drive tumor-associated hypertrimethylation of lysine 27 on histone H3 (H3K27) in human B-cell lymphomas" by Christopher J. Sneeringer, Margaret Porter Scott, Kevin W. Kuntz, Sarah K. Knutson, Roy M. Pollock, Victoria M. Richon, and Robert A. Copeland, will appear in the *Proceedings of the National Academy of Sciences* during the week of November 15.

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