Nature Publication from Agios Scientists and Co-founder Reinforces Link Between Key Metabolic Enzyme IDH and Cancer

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Cambridge, Mass. – July 5, 2012 – Agios Pharmaceuticals, the leading biopharmaceutical company focused on discovering and developing novel drugs in cancer metabolism, announced today the publication of a new study that provides further evidence of the link between a mutated metabolic enzyme and acute myeloid leukemia (AML), one of the most common types of leukemia in adults. Called an "oncometabolite" for its role in cancer metabolism, the 2-hydroxyglutarate (2HG) metabolite is produced at high levels by cancer-associated mutations in an enzyme known as isocitrate dehydrogenase (IDH). The article, "Idh1-R132H mutation increases murine hematopoietic progenitors and alters epigenetics," was published in the July 4, 2012 online edition of the journal *Nature*.

Lead author and Agios co-founder Tak Mak, Ph.D., director, The Campbell Family Institute for Breast Cancer Research at Princess Margaret Hospital, and professor, University of Toronto, in the Departments of Medical Biophysics and Immunology, said, "This is the first preclinical model to demonstrate the direct oncogenic effects of an IDH1 mutation in vivo. This preclinical research sets the stage for the work of companies like Agios that focus on developing inhibitors to block the mutated enzyme and prevent the production of this disease-initiating metabolite."

"This study provides an important step forward in our understanding of the mechanism of IDH mediated disease," commented David Schenkein, M.D., chief executive officer, Agios. "Several years ago, groundbreaking research by Agios' scientists first established that the mutated metabolic enzyme IDH1 has acquired a novel activity which produces extremely high levels of the metabolite 2HG. Today's study provides important new evidence of the causative link and potential impact of 2HG on acute leukemia. At Agios, our goal is to develop first-in-class anticancer drugs that will help patients with cancers driven by these metabolites. This new research enhances our ability to successfully develop these medicines."

In the lab, Dr. Mak's team genetically engineered a mouse model carrying the IDH1 mutation in its blood system. They discovered that the gene mutation launches a perfect storm – high levels of the oncometabolite 2HG reprograms the blood system to increase the stem cell pool, impairs the normal bone marrow environment and leads to epigenetic changes commonly seen in AML. The resulting condition creates a situation clinically similar to myelodysplastic syndrome – one of the precursors to this type of leukemia.

The connection between cancer and metabolism has been the focus of scientists at Agios, who were the first to identify the oncometabolite in research published in *Nature* in 2009. The IDH gene mutation was initially discovered in brain cancers in 2008 by researchers at Johns Hopkins and subsequently also linked to leukemia.

About Agios Pharmaceuticals

Agios is the leading biopharmaceutical company focused on discovering and developing novel drugs in the fields of cancer metabolism and rare metabolic genetic diseases. Agios has multiple first-in-class programs in cancer metabolism and inborn errors of metabolism advancing toward the clinic, in addition to an active research and discovery pipeline across both therapeutic areas. The company has a significant collaboration with Celgene focused on developing new treatments for cancer leveraging Agios' capabilities and insights into cancer metabolism. For more information, please visit our website at www.agios.com.