# Agios Pharmaceuticals Enrolls First Patient in Phase 1 Study of AG-221 in Advanced Hematologic Malignancies with an IDH2 Mutation

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*-- First-in-class Clinical Program Targets Cancer Metabolism in Genetically Defined Patient Population --*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 23, 2013-- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), today announced dose administration for the first patient in a Phase 1 study of AG-221 in patients with advanced hematologic malignancies with an isocitrate dehydrogenase-2 (IDH2) mutation. AG-221 is an oral, selective, potent inhibitor of the mutated IDH2 protein, making it the first targeted therapeutic candidate to treat patients with cancers that harbor IDH2 mutations.

“IDH2 represents one of the most promising targets in cancer biology today,” said David Schenkein, M.D., chief executive officer at Agios. “Agios is a first mover in targeting dysregulated cellular metabolism to develop potentially transformative medicines. With AG-221, we are combining our deep understanding of metabolism and cancer genetics in an effort to bring a precisely targeted new treatment option to patients with IDH2-mutant hematological cancers.”

“Cancer drug development is advancing at a remarkable pace, and we think that patients will benefit as our therapies evolve to target specific genetic abnormalities,” said Eytan Stein, M.D., lead investigator at Memorial Sloan-Kettering Cancer Center. “By enrolling patients with the appropriate genetic background, we hope to expedite our understanding of the safety, tolerability and efficacy of AG-221."

AG-221 is part of Agios' global strategic collaboration with Celgene, a leading biotechnology company. Established in 2010, the goal of the partnership is to discover, develop and deliver novel disease-altering oncology therapies based on Agios’ cancer metabolism research platform.

**About the Study**

The Phase 1 multicenter, open-label, dose escalation clinical trial of AG-221 is designed to assess the safety and tolerability of AG-221 as a single agent administered orally twice daily in a 28-day cycle. The study is expected to only enroll subjects who have an IDH2-mutant hematologic malignancy, including acute myelogenous leukemia (AML) and myelodysplastic syndrome. Key objectives in the study include determining maximum tolerated dose, pharmacokinetics, pharmacodynamics (including inhibition of the oncometabolite 2-hydroxyglutarate, or 2-HG) and preliminary anti-tumor activity of AG-221. Disease-specific expansion cohorts will be enrolled at the maximally tolerated or biologically relevant dose. Please refer to www.clinicaltrials.gov for additional clinical trial details.

**About IDH Mutations**

The IDH protein is a critical metabolic enzyme in the citric acid cycle, also known as the tricarboxylic acid (TCA), or Krebs cycle. Agios' scientists first established that the mutated forms of IDH produce a metabolite, 2-HG, which may contribute to the formation and malignant progression of various forms of cancer. Agios and its collaborators recently demonstrated that IDH1 and IDH2 mutations initiate and drive cancer growth by blocking differentiation, also referred to as maturation, of primitive cells. Agios believes that inhibition of these mutated proteins may lead to clinical benefit for the subset of cancer patients whose tumors carry these mutations.

The connection between cancer and metabolism has been the central focus of scientists at Agios, who were the first to identify the neo-activity of IDH1 mutations to produce the oncometabolite 2-HG in research published in *Nature* in 2009. These insights revealed the potential of IDH1 and IDH2 mutations as novel therapeutic targets in cancer. The IDH1 gene mutation was initially discovered in brain cancers in 2008 by researchers at Johns Hopkins. More recently, mutations in both IDH1 and IDH2 have been linked to hematologic malignancies including AML, one of the most common types of leukemia in adults, as well as several other cancers.

**About Agios Pharmaceuticals, Inc.**

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and rare metabolic genetic diseases (known as inborn errors of metabolism or IEMs) through scientific leadership in the field of cellular metabolism. In addition to an active research and discovery pipeline across both therapeutic areas, Agios has multiple first-in-class lead product candidates in cancer metabolism and IEMs in clinical and preclinical development. All Agios programs focus on genetically identified patient populations leveraging our knowledge of metabolism, biology and genomics. For more information, please visit our website at www.agios.com.

**Cautionary Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Such forward-looking statements include those regarding Agios’ expectations and beliefs about: the potential of IDH1 and IDH2 mutants as therapeutic targets; the potential benefits of Agios’ product candidates targeting IDH1 and IDH2 mutations, including AG-221; its plans and timelines for the clinical development of AG-221; the benefit of its strategic plans and focus. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Such statements are subject to numerous important factors, risks and uncertainties that may cause actual events or results to differ materially from Agios’ current expectations and beliefs. For example, there can be no guarantee that any product candidate Agios is developing will successfully commence or complete necessary preclinical and clinical development phases, or that development of any of Agios’ product candidates will successfully continue. There can be no guarantee that any positive developments in Agios’ business will result in stock price appreciation. Management’s expectations and, therefore, any forward-looking statements in this press release could also be affected by risks and uncertainties relating to a number of other important factors, including: Agios’ results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; the content and timing of decisions made by the U.S. FDA and other

regulatory authorities, investigational review boards at clinical trial sites and publication review bodies; Agios' ability to obtain and maintain requisite regulatory approvals and to enroll patients in its planned clinical trials; unplanned cash requirements and expenditures; competitive factors; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' Registration Statement on Form S-1 which was declared effective by the Securities and Exchange Commission (SEC) on July 23, 2013, and other filings that Agios may make with the SEC in the future.

**Any forward-looking statements contained in this press release speak only as of the date hereof, and Agios expressly disclaims any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise.**

Source: Agios Pharmaceuticals, Inc.

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