Agios Announces Enrollment of First Patient in Phase 1 Study of AG-120 in Advanced Hematologic Malignancies with an IDH1 Mutation

March 19, 2014

Second Agios Clinical Program in the New Field of Cancer Metabolism

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 19, 2014-- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the fields of cancer metabolism and inborn errors of metabolism, today announced that the first patient has been dosed in a Phase 1 study of AG-120 in patients with advanced hematologic malignancies with an isocitrate dehydrogenase-1 (IDH1) mutation. AG-120 is an orally available, selective, potent inhibitor of the mutated IDH1 protein, making it the first targeted therapeutic candidate to treat patients with cancers that harbor the IDH1 mutation.

“Today’s announcement marks the second cancer metabolism clinical program that we’ve initiated in less than six months, both of which utilize a precision medicine approach that could potentially set up a rapid clinical development pathway,” said David Schenkein, M.D., chief executive officer of Agios. “Initiation of this study also represents a significant milestone for Agios, as we have exclusive U.S. rights for the IDH1 program, as well as for our partner Celgene, who has an option on IDH1 program rights in the rest of the world. Most importantly, we believe this program has the potential to change the treatment of cancer and help patients.”

Groundbreaking research by Agios' scientists (published in the November 22, 2009 edition of the journal *Nature*) established for the first time that the mutated metabolic gene IDH1 has novel enzyme activity consistent with a cancer-causing gene or oncogene. This discovery shows that the mutated form of IDH1 produces a metabolite, 2-hydroxyglutarate (2HG), which may contribute to the formation and malignant progression of many forms of cancer, including hematologic malignancies such as acute myeloid leukemia and solid tumors such as gliomas (the most common type of brain cancer), chondrosarcomas and cholangiocarcinomas.

“We expect that this study will generate important insights about the utility of AG-120 among this genetically defined patient population, for whom there are very few treatment options available,” said Richard Stone, M.D., Dana-Farber Cancer Institute. “This research furthers the field of cancer metabolism and advances potential treatment options for patients whose cancers harbor genetic abnormalities.”

AG-120 is a part of Agios’ global strategic collaboration with Celgene Corporation, a leading biotechnology company. Established in 2010, the goal of the collaboration is to discover, develop and deliver novel, disease-altering oncology therapies based on Agios’ cancer metabolism research platform. The parties are also collaborating on the development of AG-221, an oral, selective, potent inhibitor of the mutated IDH2 protein.

About the Study

The Phase 1, multicenter, open-label, dose-escalation clinical trial of AG-120 is designed to assess the safety and tolerability of AG-120 as a single agent. The study is expected to only enroll subjects with an IDH1-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 2HG) and preliminary anti-tumor activity. Disease-specific expansion cohorts will be enrolled at the maximally tolerated or biologically relevant dose. Please refer to www.clinialtrials.gov for additional clinical trial details.

About IDH Mutations and Cancer

The connection between cancer and metabolism has been the central focus for scientists at Agios, who were the first to identify the neo-activity of IDH1 mutations to produce 2HG in research published in *Nature* in 2009. These insights revealed the potential of IDH1 and IDH2 mutations as novel therapeutic targets in cancer. Mutations in both IDH1 and IDH2 have been linked to numerous hematologic and solid tumor malignancies.

Agios and its collaborators recently demonstrated that IDH1 and IDH2 mutations initiate and drive cancer growth by blocking differentiation, or 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 them.

Agios is also conducting a Phase 1 study of AG-221, evaluating its safety, pharmacokinetics, pharmacodynamics and clinical activity in patients with advanced hematologic malignancies that harbor an IDH2 mutation.

About Agios Pharmaceuticals, Inc.

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and inborn errors of metabolism (IEMs), which are rare genetic metabolic diseases, 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/IDH2 as therapeutic targets; the potential benefits of Agios’ product candidates AG-120 and AG-221; its plans and timelines for the clinical development of AG-120 and AG-221; and 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; Agios' ability to maintain key collaborations, such as its agreement with Celgene; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' Annual Report on Form 10-K for the year ended December 31, 2013, and other filings that Agios may make with the Securities and Exchange Commission (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.

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