Agios Announces Initial Phase 1 Data Demonstrating Clinical Activity of AG-221, First-in-Class Inhibitor of IDH2 Mutations, in Patients with Advanced Blood Cancers

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- Significant Clinical Responses and Reduction of 2HG Biomarker in Early Cohorts -

- Data Presented at AACR Corroborate Company's Precision Medicine Approach in Targeting Cancer Metabolism; Company to Host Investor Webcast on April 6 -

CAMBRIDGE, Mass. & SAN DIEGO--(BUSINESS WIRE)--Apr. 6, 2014-- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the fields of cancer metabolism and inborn errors of metabolism, announced that data from its lead, first-in-class program AG-221 will be presented today at a Clinical Trials Symposium titled "Novel Immune and Targeted Therapies for Hematological Malignancies and Solid Tumors" at the American Association for Cancer Research (AACR) Annual Meeting 2014. These preliminary data demonstrate the clinical activity, tolerability and unique mechanism of action of AG-221 in patients with advanced hematologic malignancies with an isocitrate dehydrogenase-2 (IDH2) mutation.

"This is the first clinical trial of an inhibitor of mutant IDH, and while the primary objectives of this study are to determine the safety and tolerability of AG-221, we were also able to demonstrate promising clinical activity, including multiple complete remissions, in patients whose blood cancers carried an IDH2 mutation, even at the lowest tested dose," said Eytan Stein, M.D., lead investigator and assistant attending physician in the leukemia service at Memorial Sloan-Kettering Cancer Center. "The treatment has been well tolerated to date, and as we have not yet achieved the maximum tolerated dose, the study continues to enroll patients."

The preliminary data to be presented by Dr. Stein show that in the first two cohorts of the Phase 1 trial of AG-221, six of seven evaluable patients had objective responses, including three complete remissions (CR) and two complete remissions with incomplete platelet recovery (CRp). AG-221 also substantially lowered plasma levels of the oncometabolite 2-hydroxyglutarate (2HG) with a favorable exposure profile and good tolerability to date.

"We are very encouraged by these early data," said David Schenkein, M.D., chief executive officer of Agios. "The observation of complete remissions, reduction of 2HG, preliminary favorable safety profile and effects on cellular differentiation provide proof-of-principle for AG-221's novel mechanism of action. These findings corroborate the use of precision medicine in genetically defined patient populations and demonstrate the potential of targeting cancer metabolism to develop transformative medicines for patients."

AG-221 is an orally available, selective, potent inhibitor of the mutated IDH2 protein. As of March 20, 2014, this ongoing Phase 1 dose-escalation study had enrolled 22 patients with acute myeloid leukemia (AML) or myelodysplastic syndrome, all of whose cancers harbored an IDH2 mutation. Patient cohorts received AG-221 administered at 30 mg twice a day, 50 mg twice a day, 75 mg twice a day or 100 mg once a day.

In today's presentation, efficacy data will be presented for patients from the first two cohorts (30 mg and 50 mg twice a day). These cohorts enrolled 10 patients with relapsed or refractory AML whose disease had progressed after or was refractory to between one and four prior therapeutic regimens. Median age of these patients was 62.5 years, and all 10 patients had documented mutations in IDH2. Of these patients, seven were evaluable for efficacy (three patients did not complete a full 28-day cycle of therapy and died due to complications of disease-related infection, all in the first dose cohort).

Of the seven evaluable patients, six patients had investigator-assessed objective responses, including three patients who achieved complete remission (CR), two patients who achieved complete remission with incomplete platelet recovery (CRp) and one patient with a partial response (PR). One patient with a CR was removed from the study to undergo a bone marrow transplant; all other responses are ongoing with patients continuing to receive drug.

Treatment with AG-221 has been well tolerated to date, with no dose-limiting toxicities reported. Possible drug-related severe adverse events were reported in two patients, including one patient with an abnormally elevated white blood count and one patient with confusion and respiratory failure in the setting of disease-related infection.

The mechanism of response is consistent with preclinical studies, including substantial reduction of plasma 2HG levels, as well as evidence of cellular differentiation and normalization of cell counts in the bone marrow and blood. This differentiation effect is distinct from that seen with traditional chemotherapeutics used as standard of care for AML regimens.

Preliminary analysis of pharmacokinetics (PK) at the 30 mg and 50 mg dose levels demonstrated excellent oral AG-221 exposure and a mean plasma half-life of greater than 40 hours. Based on this PK profile, AG-221 is now being evaluated on a once-a-day and twice daily schedule in parallel. Dose escalation continues on both schedules, as the maximum tolerated dose has not been achieved.

AG-221 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 companies are also collaborating on the development of AG-120, an oral, selective, potent inhibitor of the mutated IDH1 protein, which recently began Phase 1 trials in IDH1m positive hematologic malignancies and solid tumors.

Investor Event and Webcast

Agios will host a live event with a webcast on Sunday, April 6, 2014, at 7:00 p.m. PDT (10:00 p.m. EDT) to review the clinical data from the ongoing Phase 1 study of AG-221 presented at the AACR Annual Meeting. The webcast can be accessed live or in archived form under "Events & Presentations" in the Investors and Media section of the company's website at www.agios.com.

About the Study

The ongoing 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 once or twice daily in a 28-day cycle. The study is only enrolling subjects who have an IDH2-mutant hematologic malignancy, including AML and myelodysplastic syndrome. Key objectives in the study include determining maximum tolerated dose, PK, pharmacodynamics or PD (including inhibition of 2HG), and preliminary clinical activity of AG-221. Disease-specific expansion cohorts are being enrolled at the maximally tolerated or biologically relevant dose. Please refer to www.clinicaltrials.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-morphic activity of isocitrate dehydrogenase (IDH) mutations to produce high levels of the oncometabolite 2-hydroxyglutarate (2HG) in research first published in *Nature* in 2009. IDH1 and IDH2 are metabolic enzymes that are mutated in a wide range of hematologic and solid tumor malignancies. Agios research revealed the potential of IDH1 and IDH2 mutations as novel therapeutic targets in cancer.

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.

About Agios Pharmaceuticals, Inc.

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and inborn errors of metabolism, or 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/or 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-221 and AG-120; its plans and timelines for the clinical development of AG-221 and AG-120; 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 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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