Agios Pharmaceuticals Announces Initiation of a Phase 1/2 Clinical Trial of AG-221 in Patients with Advanced Solid Tumors with an IDH2 Mutation

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AG-221 Now Being Evaluated in Broad Range of Cancers

CAMBRIDGE, Mass., Oct. 21, 2014 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO), a leader in the fields of cancer metabolism and rare genetic disorders of metabolism, today announced the initiation of a Phase 1/2 multicenter study of AG-221 in patients with advanced solid tumors, including gliomas, as well as angioimmunoblastic T-cell lymphoma (AITL) that carry an isocitrate dehydrogenase-2 (IDH2) mutation. The study will enroll patients who have recurred or progressed following standard therapy or have not responded to prior standard therapy. This is the second trial to be initiated in patients with cancer as part of AG-221's clinical development program, which includes the ongoing Phase 1 trial with four expansion cohorts in patients with hematologic malignancies.

Preclinical evidence shows that mutant IDH2 enzyme, the target of AG-221, produces 2-hydroxyglutarate (2HG), which blocks the normal maturation of progenitor cells. In solid tumor cells expressing the IDH2 mutation, AG-221 inhibited the production of 2HG, which has the potential to affect differentiation and cell proliferation in patients with solid tumors. In addition, AG-221 has demonstrated an acceptable safety profile and evidence of antitumor activity in the ongoing Phase I trial of AG-221 in patients with advanced hematologic malignancies that carry an IDH2 mutation.

"Evaluating AG-221 in patients with advanced solid tumors is an important next step in our efforts to understand the potential of this investigational medicine to treat a broad range of cancers with the IDH2 mutation," said Chris Bowden M.D., chief medical officer at Agios. "The safety, pharmacokinetics, clinical activity, and effect on the biomarker 2HG we have observed from the different dose levels studied in the Phase 1 trial for advanced hematologic malignancies give us insights into the potential to fight cancer in patients with advanced solid tumors. AG-221 will only be evaluated in prospectively defined patients whose cancers carry an IDH2 mutation, and who we believe have the greatest potential to benefit from treatment."

About the Phase 1/2 Trial

The Phase 1/2 multicenter, open-label, dose-escalation clinical trial of AG-221, which is being conducted by Agios, is designed to assess the clinical activity, safety and tolerability of AG-221 among patients who have an IDH2-mutant advanced solid tumor. AG-221 will be given as a single agent and will be administered orally at an initial dose of 100 mg once daily, in 28-day cycles. Key objectives of the trial include describing the dose-limiting toxicities and determining the maximum tolerated dose, evaluating the pharmacokinetic and pharmacodynamics, and characterizing the clinical activity of AG-221. The Phase 1/2 trial is expected to include a dose expansion phase where three cohorts of patients with gliomas, AITL and other solid tumors that are IDH2 mutant-positive will receive AG-221 to further evaluate safety, tolerability and clinical activity.

AG-221 and IDH2

IDH1 and IDH2 are metabolic enzymes that are mutated in a wide range of hematologic and solid tumor malignancies, including AML. Normally, IDH enzymes help to break down nutrients and generate energy for cells. When mutated, IDH creates a molecule that alters the cells' genetic programming, and instead of maturing, the cells remain primitive and proliferate quickly. Agios believes that inhibition of these mutated proteins may lead to clinical benefit for the subset of cancer patients whose tumors carry them. AG-221 was developed by Agios as a selective, potent inhibitor of the mutated IDH2 protein. While most cancer treatments attempt to destroy the cancerous cells, AG-221 uniquely attacks its target – mutated IDH2 – and aids the maturation of the cells into functioning blood cells. AG-221 has received orphan drug designation for AML and fast track designation for patients with IDH2-mutant AML.

About Agios/Celgene Collaboration

AG-221 is a part of Agios' global strategic collaboration with Celgene Corporation, a leading biotechnology company. In June 2014, Celgene exercised its exclusive option to license AG-221. Under the terms of the agreement, Celgene gained worldwide development and commercialization rights for AG-221. Agios continues to conduct early clinical development and regulatory activities within the AG-221 development program in collaboration with Celgene. The companies are also collaborating on the development of AG-120, which is being studied in two Phase 1 trials in patients whose hematologic malignancies and solid tumors carry an IDH1 mutation. Agios retains U.S. development and commercialization rights for AG-120, and Celgene has an exclusive option to the ex-U.S. rights.

About Agios Pharmaceuticals, Inc.

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and rare genetic disorders of metabolism 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 investigational medicines in cancer metabolism and rare genetic disorders of metabolism in clinical and/or preclinical development. All Agios programs focus on genetically identified patient populations, leveraging the company's knowledge of metabolism, biology and genomics. For more information, please visit Agios' 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 the potential of IDH2 mutations as therapeutic targets; the potential benefits of Agios' drug candidate AG-221 targeting IDH2 mutations; its plans and timelines for the clinical development of AG-221; and the benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "could," "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' Quarterly Report on Form 10-Q for the quarter ended June 30, 2014, 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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