# Agios Announces Data from Ongoing Phase 1 Trial of AG-120 Showing Durable Responses in Patients with Advanced Hematologic Malignancies

December 5, 2015

*- Patients on Study for up to 14.1 Months with a Median Response Duration of 5.6 Months -*

*- Four Phase 1 Expansion Cohorts Enrolling; Planned Global Registration-enabling Phase 3 Study On Track -*

*- Company to Host Investor Event and Webcast Monday, December 7, 2015 -*

CAMBRIDGE, Mass., Dec. 5, 2015 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO), a leader in the fields of cancer metabolism and rare genetic metabolic disorders, today announced new data from the ongoing Phase 1 study evaluating single agent AG-120, a first-in-class, oral, selective, potent inhibitor of mutant isocitrate dehydrogenase-1 (IDH1), in advanced hematologic malignancies. The data are being presented at the 2015 American Society of Hematology Annual Meeting and Exposition (ASH) taking place December 5-8, 2015 in Orlando. AG-120 is being developed in collaboration with Celgene.

Data as of October 1, 2015 from 87 patients with advanced IDH1 mutant positive hematologic malignancies confirmed a favorable safety profile consistent with previously reported data and showed durable clinical activity in 78 dose-escalation patients. Twenty-nine patients remain on study as of the analysis. Efficacy data is provided from the dose-escalation phase of the study only, where an overall response rate of 35 percent (27 of 78 response-evaluable patients) and a complete remission rate of 15 percent (12 of 78 response-evaluable patients) were observed. Patients were on study treatment for up to 14.1 months with a median duration of treatment of 2.9 months (ranging from 0.1 to 14.1 months). Data continue to show durable clinical activity for AG-120, with responses maintained for up to 12.5 months and a median duration of response of 5.6 months (previously unreported).

"With the addition of 30 new patients to the study, AG-120 has maintained durable responses and continues to demonstrate an impressive single-agent overall response rate of 35 percent," said Courtney DiNardo, M.D., lead investigator and assistant professor, department of leukemia at the University of Texas MD Anderson Cancer Center. "These data further validate AG-120's potential to provide clinical benefit for IDH1 mutant relapsed/refractory AML patients with few, if any effective therapeutic options."

"These data increase our confidence in the favorable safety and efficacy profile of AG-120," said Chris Bowden, M.D., chief medical officer of Agios. "Our focus remains on bringing AG-120 to patients with IDH1 mutant cancers as quickly as possible, and we look forward to continuing to enroll our 125-patient expansion arm in relapsed/refractory AML and initiating two frontline studies to reach additional IDH1 mutant AML patients in need of better options."

**About the Ongoing Phase 1 Trial for AG-120 in Advanced Hematologic Malignancies**

AG-120 is being evaluated in an ongoing Phase 1 trial that includes a dose escalation phase and four expansion cohorts, including:

- Arm 1: 125 IDH1 mutant positive AML patients who relapsed after bone marrow transplantation, are in second or later relapse, refractory to second line induction or reinduction treatment
- Arm 2: 25 untreated IDH1 mutant positive AML patients who are not candidates for standard-of-care chemotherapy
- Arm 3: 25 patients with other non-AML IDH1 mutant, relapsed or refractory advanced hematologic malignancies
- Arm 4: 25 patients with relapsed IDH1 mutant positive AML not eligible for arm 1 or standard of care

Data reported are from patients treated with AG-120 administered from 200 mg to 1,200 mg total daily doses as of October 1, 2015. The median age of these patients is 68 (ranging from 36-89). Patients received a median of two prior lines of therapy (ranging from zero to five). A safety analysis was conducted for all 87 treated patients and an efficacy analysis was conducted in the evaluable population of 78 dose-escalation patients, which includes all patients with a pre-AG-120 screening assessment and day 28 or later response assessment or an earlier discontinuation for any reason.

**Safety Data**

Of the 87 treated patients, 78 were from the dose-escalation phase and nine from the expansion.

- The majority of adverse events reported by investigators were mild to moderate, with the most common being fatigue, diarrhea, pyrexia and nausea.
- 51 patients experienced at least one serious adverse event (SAE), the majority being disease related.
- A maximum tolerated dose (MTD) has not been reached.
- 19 patients discontinued from the study due to death, and all were considered unrelated to AG-120.
- All cause mortality at 30 and 60 days was 10.3 percent and 18.4 percent, respectively.

**Efficacy Data**

Twenty-seven out of 78 response-evaluable patients from the dose-escalation achieved investigator-assessed objective responses for an overall response rate of 35 percent.

- Of the 27 patients who achieved an objective response, there were 12 complete remissions (CR), seven CRs with incomplete platelet recovery (CRp), six marrow CRs (mCR), one CR with incomplete hematologic recovery (CRi) and one partial remission (PR).
- Patients were on study treatment for up to 14.1 months with a median duration of treatment of 2.9 months (ranging from 0.1 to 14.1 months).
- Data continue to show durable clinical activity for AG-120, with responses maintained for up to 12.5 months and a median duration of response of 5.6 months.

**2015 Milestones for AG-120 in Hematologic Malignancies**

Remaining milestones for AG-120 in 2015 include:

- Continue to enroll patients in the expansion cohort of 125 patients with IDH1 mutant positive AML who relapsed after bone marrow transplantation, are in second or later relapse, refractory to second line induction or reinduction treatment.
- Initiate a Phase 1b combination study of either AG-221 or AG-120 with standard induction (7+3, Ara-C and idarubicin/daunorubicin) and consolidation (Ara-C, or mitoxantrone with etoposide) chemotherapy in newly diagnosed AML patients eligible for intensive chemotherapy by the end of 2015.

**Investor Event and Webcast Information**

Agios will host an investor event on Monday, December 7, 2015 beginning at 12:00 p.m. ET in Orlando to review data presented at ASH, including new data from the ongoing studies of AG-221 and AG-120. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors and Media section of the company's website at www.agios.com.

**About IDH Mutations and Cancer**

IDH1 and IDH2 are two metabolic enzymes that are mutated in a wide range of hematologic and solid tumor malignancies. Normally, IDH enzymes help to break down nutrients and generate energy for cells. When mutated, IDH increases production of an oncometabolite 2-hydroxyglutarate (2HG) that alters the cells' epigenetic programming, thereby promoting cancer. 2HG has been found to be elevated in several tumor types. Agios believes that inhibition of the mutated IDH proteins may lead to clinical benefit for the subset of cancer patients whose tumors carry them.

**About Acute Myelogenous Leukemia (AML)**

AML, a cancer of blood and bone marrow characterized by rapid disease progression, is the most common acute leukemia affecting adults. Undifferentiated blast cells proliferate in the bone marrow rather than mature into normal blood cells. AML incidence significantly increases with age, and according to the American Cancer Society, the median age of onset is 66. Less than 10 percent of U.S. AML patients are eligible for bone marrow transplant and the vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory AML. The five-year survival rate for AML is approximately 20 to 25 percent. IDH1 and IDH2 mutations are present in about 15 to 23 percent of AML cases.

**About Agios/Celgene Collaboration**

AG-221, AG-120 and AG-881 are part of Agios' global strategic collaboration with Celgene Corporation. Under the terms of the collaboration, Celgene has worldwide development and commercialization rights for AG-221 (CC-90007). Agios continues to conduct clinical development activities within the AG-221 development program and is eligible to receive up to $120 million in payments on achievement of certain milestones and royalties on net sales. For AG-120, Agios retains U.S. development and commercialization rights and Celgene retains development and commercialization rights outside the United States. Celgene is eligible to receive royalties on net sales in the U.S. Agios is eligible to receive royalties on net sales outside the U.S. and up to $120 million in payments on achievement of certain milestones. For AG-881, the companies have a joint worldwide development and 50/50 profit share collaboration, and Agios is eligible to receive regulatory milestone payments of up to $70 million.

**About Agios**

Agios is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic metabolic disorders 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 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 the company's 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 benefits of Agios' product candidates targeting IDH mutations, including AG-120; its plans for the clinical development of AG-120; its plans regarding future data presentations; and the benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "hope," "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 September 30, 2015, 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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