Agios Presents Preclinical Data from Lead Programs at American Society of Hematology Annual Meeting

December 10, 2013

Preclinical In Vivo Efficacy Demonstrated for IDH Inhibitors in Patient-Derived Leukemia Models

CAMBRIDGE, Mass. & NEW ORLEANS--(BUSINESS WIRE)--Dec. 9, 2013-- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the fields of cancer metabolism and inborn errors of metabolism, today announced that data from its lead programs were highlighted at the American Society of Hematology (ASH) Annual Meeting this week in New Orleans.

Two presentations featured *in vivo* efficacy data in acute myelogenous leukemia (AML) for the company's lead cancer metabolism programs targeting IDH1 and IDH2 mutations. In AML and other cancers, IDH1 and IDH2 mutations initiate and drive cancer growth by blocking maturation of primitive cells. The data presented at ASH demonstrate preclinical single agent and combination efficacy of Agios' IDH mutant inhibitors in patient-derived primary models of AML. Agios also presented data on AG-348, its lead inborn errors of metabolism (IEM) program candidate focused on pyruvate kinase deficiency (PK deficiency), a rare, inherited hemolytic anemia with no approved therapeutic options.

"We are excited to present data highlighting our IDH and PKR programs, which focus on genetically identified patient populations with limited or no therapeutic options," said Scott Biller, Ph.D., chief scientific officer at Agios. "These results highlight the potential for all three programs to provide significant clinical benefit to patients in the future."

Agios Presentations

- *"AG-221 offers a survival advantage in a primary human IDH2 mutant AML xenograft model,"* an oral presentation, provides strong preclinical *in vivo* evidence of AG-221's potential clinical benefit for patients with tumors that harbor an IDH2 mutation. AG-221 is a potent, selective, orally available IDH2 mutant inhibitor currently in clinical trials for patients with hematologic malignancies. In this study, Agios scientists evaluated the efficacy of AG-221 as a single agent in a primary human model of aggressive AML carrying an IDH2 mutation. AG-221 caused a potent reduction in 2HG, the oncometabolite produced by the mutant IDH2 protein, found in the bone marrow, plasma and urine of engrafted mice. Treatment also induced a dose-dependent, statistically significant survival benefit in which all mice in the high-dose treatment group survived to the end of the study.
- *"IDH1 mutant inhibitor induces cellular differentiation and offers a combination benefit with Ara-C in a primary human IDH1 mutant AML xenograft model,"* a poster, evaluates the use of AGI-14100, a potent, selective, orally available IDH1 mutant inhibitor. Agios scientists treated a primary human mutant AML model with AGI-14100, either alone or in combination with low-dose chemotherapy (Ara-C). Researchers observed a significant decrease in tumor burden in peripheral blood in the model treated with AGI-14100 alone, and a more pronounced response, as measured by a simultaneous decrease in the bone marrow tumor burden, in the model that received combination therapy. The duration of response continued for three weeks after dosing of both drugs had been terminated. These data suggest that this combination therapeutic approach could be an important option for patients, to be explored in future clinical trials.
- *"Small Molecule Activation of Pyruvate Kinase Normalizes Metabolic Activity in Red Cells From Patients With Pyruvate Kinase Deficiency-associated Hemolytic Anemia,"* a poster, presents preclinical data supporting Agios' lead IEM clinical candidate, AG-348, as a potentially effective approach to correcting the underlying pathology of PK deficiency. The results demonstrate that AG-348 potently activates a spectrum of PKR mutant proteins, the isoform of pyruvate kinase that is present in red blood cells, leading to a normalization of metabolic balance in patient-derived blood samples. These data support the hypothesis that drug intervention with AG-348 may restore glycolytic pathway activity and normalize red cell metabolism *in vivo*.

About IDH Mutations and Cancer

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, 2HG, 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 the 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 2HG 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 PK Deficiency

Pyruvate kinase, or PK, is a key enzyme in glycolysis – the conversion of glucose into lactic acid – and is critical for the survival of red blood cells. PK deficiency is a rare genetic disorder caused by a deficiency of the R isoform of pyruvate kinase (PKR) that results in accelerated destruction of red blood cells. It has a wide phenotypic spectrum of disease presentation and progressions. In infants and children, it presents with severe hemolytic anemia, and an attenuated disease presents in other patients later in life. Infantile cases might require immediate life-saving intervention via replacement of their entire blood system with a donor's blood, referred to as an exchange transfusion. Treatment of PK deficiency is supportive, including blood transfusions, splenectomy, chelation therapy to address iron overload and interventions for other disease-related morbidity. Currently, there is no approved therapy to address the underlying etiology of life-long hemolytic anemia.

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 and pyruvate kinase R mutations as therapeutic targets; and the potential benefits of Agios' product candidates targeting IDH1/IDH2 or pyruvate kinase R mutations, including AG-221, AG-120 and AG-348. 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, including risks and uncertainties relating to: Agios' ability to successfully commence and complete necessary preclinical and clinical development of its product candidates; Agios' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; Agios' ability to maintain its collaboration with third parties on acceptable terms; 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; 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 obtain the substantial additional capital required to execute its plans and strategies; and general economic and market conditions. These and other risks are described in greater detail in filings that Agios makes with the SEC from time to time including risks described under the caption "Risk Factors" included in Agios' Quarterly Report on Form 10-Q for the quarter ended September 30, 2013. 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.

Agios Pharmaceuticals, Inc.
Media Contact:
Dan Budwick, 973-271-6085
dan@purecommunicationsinc.com
or
Investor Contact:
Glenn Goddard
investors@agios.com