Agios Announces Updated Data from Fully Enrolled DRIVE PK Study Demonstrating AG-348's Potential as the First Disease-modifying Treatment for Patients with Pyruvate Kinase Deficiency

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– AG-348 Is Well-Tolerated and Demonstrates Clinically Relevant, Rapid and Sustained Hemoglobin Increases in 25 of 52 Patients Overall –

– New Data Show Improvements in Hemolysis Associated Parameters Indicate Positive Impact on Disease Biology –

– Program on Track to Enter Global Pivotal Development in First Half of 2018 –

MADRID, Spain, June 24, 2017 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO) presented updated data from its wholly owned pyruvate kinase-R (PKR) activator demonstrating the potential for the first disease-modifying treatment for patients with pyruvate kinase (PK) deficiency at the 22nd Congress of the European Hematology Association (EHA). PK deficiency is a rare, potentially debilitating, congenital anemia.

DRIVE PK is an ongoing global open-label, Phase 2, safety and efficacy trial evaluating AG-348 in adult, transfusion-independent patients with PK deficiency. As of the March 27, 2017 data cut-off, 48% of all 52 treated patients (n=25/52) and 57% of patients with at least 1 missense mutation (n=24/42) treated with AG-348 experienced a maximum Hb increase from baseline of >1.0 g/dL. Hb increases were rapid with a median time to a Hb increase of >1.0 g/dL of 10 days.

Enrollment in DRIVE PK was completed in November 2016 with 52 patients. Patients were randomized to a starting dose of 50 mg or 300 mg twice daily, treated for six months in a core treatment period and then offered up to two years of treatment in an extension period. As of the data cut-off, 15 patients remain in the core period, 29 patients completed the core treatment period and 21 remain in the extension period. The median baseline hemoglobin (Hb) for all patients was 8.9 gram per deciliter (g/dL) (ranging from 6.5 to 12.3 g/dL). Forty-three of the 52 patients (83%) had been splenectomized prior to study entry and 25 (48%) have received prior iron chelation therapy.

"With data now available from all 52 patients, AG-348 continues to demonstrate clinically relevant and sustained increases in hemoglobin in adults with PK deficiency," said Rachael Grace, M.D., of the Dana-Farber Boston Children's Cancer and Blood Disorder Center and a principal investigator for the study. "These findings offer patients and physicians a well-tolerated, oral therapy as the first potential disease-altering treatment for people suffering from this chronic anemia and its associated complications."

"The rapid and sustained hemoglobin increases shown in DRIVE PK, combined with improvements in hemolysis related parameters, indicate that AG-348 is having a meaningful impact on the biology of PK deficiency," said Chris Bowden, M.D., chief medical officer at Agios. "We look forward to advancing this novel investigational therapy into a planned global pivotal program in the first half of 2018."

Safety Data

A safety analysis conducted for all 52 treated patients as of the data cut-off shows that AG-348 continues to be well tolerated.

- The majority of treatment-related adverse events (AEs) were Grade 1-2; the most frequent were headache, insomnia and nausea.
- Three patients experienced treatment related AEs leading to discontinuation: chest discomfort/pleural effusion (n=1), pharyngitis/nausea (n=1) and anemia (n=1).
- Five patients experienced drug-related serious adverse events: withdrawal hemolysis followed by anemia (n=1), anemia (n=1), osteoporosis (n=1), hypertriglyceridemia (n=1) and pharyngitis (n=1).
  ° Grade 4 hypertriglyceridemia at week 24 resolved upon AG-348 discontinuation (patient had Grade 1 hypertriglyceridemia at baseline).
- Preliminary measurements of testosterone in men suggest aromatase inhibition by AG-348 with the majority of testosterone changes remaining within the normal range. Longer follow-up is required to assess clinical significance.

Efficacy Data

In the efficacy analysis of all 52 treated patients, 25 patients overall and 24 of 42 patients with at least one missense mutation achieved rapid, robust and sustained Hb increases from baseline of >1.0 g/dL as of the data cut-off.

- In patients who had Hb increases of >1.0 g/dL, the mean maximum Hb increase was 3.5 g/dL (range 1.1-5.8 g/dL).
- The median time to a Hb increase of >1.0 g/dL was 10 days (range 7–141 days).
- Median baseline Hb in patients who experienced a maximum Hb increase of >1.0 g/dL was 9.7 g/dL (range 7.5–12.3 g/dL) vs. 8.0 g/dL (range 6.5–10.1 g/dL) in patients who did not experience the increase.
- In patients with a Hb increase of >1.0 g/dL improvements in hemolysis associated parameters were observed:
  ° An increase in haptoglobin and decrease in lactate dehydrogenase (LDH) were observed in the first weeks of dosing.
  ° Rapid decreases in reticulocytes were observed.

About Pyruvate Kinase Deficiency and Genetic Background

PK deficiency is a rare inherited disease that presents as hemolytic anemia, which is the accelerated destruction of red blood cells. The inherited

mutations in PKR enzymes cause a deficit in cellular energy within the red blood cell, as evidenced by lower pyruvate kinase enzyme activity and a decline in ATP (adenosine triphosphate) levels and a build-up of upstream metabolites, including 2,3-DPG (2,3-diphosphoglycerate).

The current standard of care for PK deficiency is supportive, including blood transfusions, splenectomy, chelation therapy to address iron overload and/or interventions for other treatment- and disease-related morbidities. There is no approved therapy to treat the underlying cause of PK deficiency.

PK deficiency is an autosomal recessive disease whereby all patients inherit two mutations, one from each parent. More than 250 different mutations have been identified to date. The mutations observed in PK deficiency patients are classified in two main categories. A missense mutation causes a single amino acid change in the protein, generally resulting in some functional protein. A non-missense mutation is any mutation other than a missense mutation, generally resulting in little functional protein. It is estimated that 53 percent of patients with PK deficiency have two missense mutations, 25 percent have one missense and one non-missense mutation, and 22 percent have two non-missense mutations[1].

Boston Children's Hospital, in collaboration with Agios, is conducting a Natural History Study to better understand the symptoms and complications of PK deficiency, identify patients and treatment centers, and capture other clinical data, including quality of life measures and genetic information.

About Agios

Agios is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic 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 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 AG-348; Agios' plans for the further clinical development of AG-348; and Agios' strategic plans and prospects. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would," "could," "potential," "possible," "hope" 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; that positive safety and efficacy findings observed in early stage clinical trials will be replicated in later stage trials; 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 agreements 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' public filings with the Securities and Exchange Commission. 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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[1] Bianchi P et al. poster, 2015 ASH Annual Meeting

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