Agios Presents Updated Data from DRIVE PK Study Demonstrating AG-348 is Well-Tolerated and Results in Clinically Relevant, Rapid and Sustained Hemoglobin Increases in Patients with Pyruvate Kinase Deficiency

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– Safety and Efficacy Profile Consistent with Previously Reported Data –

– Hemoglobin Increases >1.0 g/dL in 26 of 52 Patients Overall; Responses Remain Durable with Completion of Six Month Core Treatment Period –

– Two Global Pivotal Trials in PK Deficiency on Track to Initiate in First Half of 2018 –

ATLANTA, Dec. 10, 2017 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO) presented updated data today from its wholly owned pyruvate kinase-R (PKR) activator, AG-348, demonstrating its potential as the first disease-modifying treatment for patients with pyruvate kinase (PK) deficiency at the 2017 American Society of Hematology (ASH) Annual Meeting and Exposition. 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 52 adult, transfusion-independent patients with PK deficiency. As of the July 14, 2017 data cut-off 43 patients had completed the six-month core dosing period and 9 patients discontinued treatment during the core dosing period. Of the 52 patients enrolled, 26 (50%) experienced a maximum hemoglobin (Hb) increase from baseline of >1.0 gram per deciliter (g/dL) during the six-month core period. For the 42 patients enrolled with at least 1 missense mutation, 25 (60%) experienced a maximum Hb increase from baseline of >1.0 g/dL. AG-348 remains well-tolerated with the majority of adverse events (AEs) being Grade 1 or 2. The median treatment duration was 37.5 weeks, with a maximum of 92.4 weeks.

“With some patients approaching two years of treatment, we are encouraged that AG-348 continues to be well-tolerated and demonstrates clinically relevant, 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. “AG-348 has the potential to be the first therapy for patients with PK deficiency that targets the underlying cause of this chronic anemia and its associated complications.”

Patients in DRIVE PK 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 treatment in an extension period. Enrollment was completed in November 2016 with 52 patients. Nine subjects discontinued during the core treatment period. Thirty-six of 43 patients who completed the six month core treatment period entered the extension period. As of the data cut-off, 29 patients remain on treatment in the extension period.

“DRIVE PK has established a clear signal of activity for AG-348 in PK deficiency and was instrumental in informing the design of the pivotal program we are on track to initiate in the first half of 2018,” said Chris Bowden, M.D., chief medical officer at Agios. “In addition to this clinical work, our planned global PKD patient registry will complement our patient finding efforts and further advance our understanding of the disease burden for this rare anemia.”

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 AEs were Grade 1-2; the most frequent were headache, insomnia and nausea.
- As previously reported, four patients experienced treatment-related AEs leading to discontinuation: pleural effusion (n=1), hypertriglyceridemia (n=1), pharyngitis/nausea (n=1) and anemia (n=1).
- As previously reported, four patients experienced treatment-related serious adverse events: withdrawal hemolysis followed by anemia (n=1), anemia (n=1), osteoporosis (n=1) and hypertriglyceridemia (n=1).
- A previously reported case of drug-related pharyngitis (n=1) was subsequently deemed unrelated to study drug.
- Measurements of hormone levels in men at doses ≤50 mg BID suggest mild aromatase inhibition by AG-348; ongoing follow-up will continue to assess potential clinical significance.

Efficacy Data

In the efficacy analysis 26 of 52 patients (50%) overall and 25 of 42 patients (60%) with at least one missense mutation achieved rapid 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 3.4 g/dL (range 1.1-5.8 g/dL).
- The median time to first Hb increase of >1.0 g/dL was 10 days (range 7–187 days).
- As previously reported, the median baseline Hb in patients who experienced a maximum Hb increase of >1.0 g/dL was 9.7 g/dL (range 7.3–12.3 g/dL) vs. 8.0 g/dL (range 6.5–10.1 g/dL) in patients who did not experience the increase.

Pivotal Development Plan

Agios plans to initiate two global, pivotal trials in adults with PK deficiency in the first half of 2018 based on transfusion status:

- A randomized, placebo-controlled trial with a 1:1 randomization known as ACTIVATE is expected to enroll approximately 80 patients who do not receive regular transfusions. The primary endpoint of the trial is the proportion of patients who achieve a sustained hemoglobin increase ≥1.5 g/dL.
- A single arm trial of approximately 20 regularly transfused patients known as ACTIVATE-T will have a primary endpoint of reduction in transfusion burden over six months.

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 58 percent of patients with PK deficiency have two missense mutations, 27 percent have one missense and one non-missense mutation, and 15 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, 2017 ASH Annual Meeting

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