Agios Presents Updated Data for Mitapivat from Extension Phase of the DRIVE PK Study in Patients with Pyruvate Kinase Deficiency

December 9, 2019

– Robust Hemoglobin Increases Maintained in 18 Patients in the Extension Phase of the Study with Median Treatment Duration of Three Years –

– Cumulative Safety Profile (Core Period plus Extension Phase) Continues to Support Long-term Twice Daily Dosing of Mitapivat –

– Data from the Natural History Study Demonstrate that PK Deficiency Patients, Regardless of Transfusion Status, Have Higher Rates of Select Comorbidities and Complications –

– Company to Host Investor Event and Webcast Today at 8:00 p.m. ET –

ORLANDO, Fla., Dec. 09, 2019 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today reported new data from the extension phase of the DRIVE PK Phase 2 study of mitapivat (AG-348) in adults with pyruvate kinase (PK) deficiency at the 2019 American Society of Hematology (ASH) Annual Meeting. Mitapivat is an investigational, first-in-class, oral, small molecule allosteric activator of wild-type and a variety of mutated pyruvate kinase-R (PKR) enzymes that directly targets the underlying metabolic defect in PK deficiency, a rare, potentially debilitating, hemolytic anemia. In addition, data was shared from the Agios-sponsored Natural History Study of PK deficiency that detailed the comorbidities and complications associated with the disease and the impact of transfusion history.

“DRIVE PK was the first clinical trial aimed at addressing the metabolic defect in PK deficiency, and demonstrated that clinically meaningful and robust increases in hemoglobin can be achieved with an oral PKR activator,” said Eduard J. van Beers, M.D., Ph.D., University Medical Center Utrecht and an investigator in the study. “These new data demonstrate that chronic treatment with mitapivat is well tolerated and can lead to a reduction in hemolysis as demonstrated by sustained improvements in hemoglobin and other markers for more than three years.”

“As a rare hemolytic anemia, PK deficiency has historically been under diagnosed and not well characterized. The new and emerging data from the Natural History Study demonstrate that adults with PK deficiency are at increased risk of comorbidities and complications resulting from chronic hemolysis and iron overload, regardless of transfusion history,” said Chris Bowden, M.D., chief medical officer at Agios. “We are committed to advancing the first potential disease-modifying therapy for these patients and are on track to complete enrollment in both of our pivotal Phase 3 trials of mitapivat in PK deficiency by the end of the year. In addition, we are exploring the utility of wildtype PKR activation in other hemolytic anemias, such as thalassemia and sickle cell disease.”

Data from the Extension Phase of the DRIVE PK Study of Mitapivat

DRIVE PK is an ongoing global, open-label, Phase 2, safety and efficacy study evaluating mitapivat in adults with PK deficiency who do not receive regular transfusions. Patients were randomly assigned to receive either 50 mg or 300 mg of mitapivat twice daily for a 24-week core period and eligible patients could continue treatment in an ongoing extension phase. In the extension phase, patients treated with mitapivat doses >25 mg twice daily in the core period undergo a dose taper and continue on a dose that maintained their Hb level at no lower than 1.0 g/dL below their pre-taper level. As of the March 27, 2019 data cutoff, 18 of the 36 patients remain in the extension phase with a median treatment duration of 35.6 months (range 28.7-41.9).

For the 18 patients in the extension phase, improvements in hemoglobin and other markers of hemolysis including reticulocytes, indirect bilirubin and haptoglobin achieved during the core period were sustained during the extension period up to 42 months, as of the data cutoff.

Adverse events (AEs) for patients who continued in the study (n=18) were comparable in the core and extension periods. In the extension, the most common AEs were headache (39%), insomnia (28%), fatigue (28%) and nasopharyngitis (28%). No new safety signals were identified in the extension period.

Data from the Natural History Study Evaluating Comorbidities and Complications in Adults with PK Deficiency

The ongoing PK Deficiency Natural History Study (NHS) evaluated 254 patients (131 adults) at 31 centers in six countries who enrolled from June 2014 through April 2017[2]. Data reported at ASH compare baseline rates of comorbidities and complications in adult patients from the NHS with the general population (U.S.-based IBM MarketScan® claims database), and assess the impact of transfusion frequency on the prevalence of these comorbidities and complications. Individuals from the general population were matched 10:1 to patients with PK deficiency based on age, gender and year of enrollment in the NHS. The analysis showed that patients with PK deficiency, regardless of current or prior transfusion status, have higher rates of the following comorbidities and complications than observed in the general population.

- Adults with PK deficiency had higher lifetime rates of pulmonary hypertension (4.6% compared to 0.3% in the general population), osteoporosis (15.6% compared to 0%) and liver cirrhosis (5.6% compared to 0.4%).
- Adults with PK deficiency had higher rates of splenectomy (4.9% compared to 0.2% in the general population), cholecystectomy (13.1% compared to 3.6%) and gallstones (16.9% compared to 4.3%) over the preceding eight years.
- Rates of current prophylactic antibiotic and anticoagulant use were significantly higher among patients with PK deficiency.
- It was observed that for some conditions, a gradient is seen across PK deficiency transfusion cohorts, with the highest rates observed in patients who receive regular transfusions (≥ 6 per year). However, even patients with PK deficiency who have never received blood transfusion are at increased risk of complications of the disease and its treatment.

Mitapivat Clinical Development

Agios has two ongoing global, pivotal trials in adults with PK deficiency that are on track to complete enrollment by year-end 2019. Learn more at activatetrials.com.

- ACTIVATE: A placebo-controlled trial with a 1:1 randomization, 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 of ≥1.5 g/dL.
- ACTIVATE-T: A single arm trial of up to 40 regularly transfused patients with a primary endpoint of reduction in transfusion burden over six months compared to individual historical transfusion burden over prior 12 months.

In addition, Agios is conducting a Phase 2 study evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of treatment with mitapivat in adults with non-transfusion-dependent β- and α-thalassemia (NTDT). The primary endpoint is hemoglobin response, and approximately 17 participants with NTDT will be enrolled. Mitapivat is also being studied in sickle cell disease under a Cooperative Research and Development Agreement (CRADA) with the U.S. National Institutes of Health.

Mitapivat is not approved for use by any regulatory authority.

About Pyruvate Kinase Deficiency and Genetic Background
Pyruvate kinase (PK) deficiency is a rare, inherited disease that presents as chronic hemolytic anemia, which is the accelerated destruction of red blood cells. The inherited mutations in PKR genes cause a deficit in cellular energy within the red blood cell, as evidenced by lower PK enzyme activity, a decline in adenosine triphosphate levels and a build-up of upstream metabolites, including 2,3-DPG (2,3-diphosphoglycerate).

PK deficiency is associated with chronic hemolysis leading to complications including gallstones, pulmonary hypertension, extramedullary hematopoiesis, cirrhosis, osteoporosis, and iron overload and its sequelae, which occur regardless of transfusion burden. Current management strategies for PK deficiency, including blood transfusion and splenectomy, are associated with both short- and long-term risks.

More than 300 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]. For more information about PK deficiency, including the signs and symptoms, how to test for it (including a free testing option), and how it is currently managed, visit knowpkdeficiency.com.

The Peak Registry, a global, longitudinal study of children and adults with PK deficiency, has been established to better understand the full spectrum of disease variability, including impact on quality of life. The Registry is open and recruiting patients. Learn more at www.peakregistry.com.

Investor Event and Webcast Information
Agios will host an investor event today at 8:00 p.m. ET in Orlando, Fla. to review the IDH and PKR data presented at ASH. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors section of the company's website at www.agios.com. The archived webcast will be available on the company's website beginning approximately two hours after the event.

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 and adjacent areas of biology. In addition to an active research and discovery pipeline across both therapeutic areas, Agios has two approved oncology precision medicines and multiple first-in-class investigational therapies 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 mitapivat; Agios' plans for the further clinical development of mitapivat; 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; 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.

---

[1] Bianchi P et al. poster, 2017 ASH Annual Meeting

[2] Grace RF et al. Blood 2018;131:2183-92

Investor & Media Contact:
Holly Manning, 617-844-6630

Associate Director, Investor Relations
Holly.Manning@agios.com

Source: Agios Pharmaceuticals, Inc.