AG-348 Achieves Proof-of-Concept in Ongoing Phase 2 DRIVE-PK Study and Demonstrates Rapid and Sustained Hemoglobin Increases in Adults with Pyruvate Kinase Deficiency

June 11, 2016

- 9 of 18 Total Patients and 9 of 13 Patients with at Least One Missense Mutation Showed Maximal Hemoglobin Increases Between 2.3 to 4.9 g/dL -

- AG-348 Well Tolerated with Up to Six Months of Daily Dosing -

- Results Validate Agios' Novel Approach to Treatment of Rare Metabolic Disorders -

- Company to Host Conference Call and Webcast Today at 9:30 a.m. ET -

COPENHAGEN, Denmark, June 11, 2016 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO) today announced initial data demonstrating that AG-348 achieved proof-of-concept in an ongoing Phase 2 study (DRIVE-PK) of patients with pyruvate kinase (PK) deficiency, a rare, potentially debilitating, congenital anemia. AG-348 is a novel, first-in-class, oral activator of both wild-type (normal) and mutated pyruvate kinase-R (PKR) enzymes. AG-348 is wholly owned by Agios. Data will be presented today at the 21st Congress of the European Hematology Association (EHA) taking place June 9-12, 2016 in Copenhagen.

DRIVE-PK is the first study to evaluate the safety and efficacy of AG-348 in patients with PK deficiency. As of the March 27, 2016 data cut-off, 18 transfusion-independent patients (13 with at least one missense mutation and five with two non-missense mutations) were treated with twice-daily dosing of AG-348 for up to six months. Treatment resulted in rapid and sustained hemoglobin increases of >1.0 g/dL in nine out of 18 patients (nine of 13 patients with at least one missense mutation), ranging from 2.3–4.9 g/dL with a mean maximum hemoglobin increase of 3.4 g/dL. It is estimated that approximately 80 percent of all PK deficiency patients carry at least one missense mutation. These data support the hypothesis that AG-348 restores metabolic function and has the potential to correct the underlying defect in the red blood cells of patients with PK deficiency.

"People with PK deficiency suffer from chronic anemia and a range of other complications brought on by both their disease and existing supportive therapies, including blood transfusions and splenectomy," 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 data are exciting for the hematology community and patients, as they demonstrate the potential for AG-348 to provide the first disease-modifying treatment with impressive and prolonged increases in hemoglobin levels."

"These data have established proof-of-concept for AG-348, validating our novel approach to the treatment of rare genetic metabolic disorders by correcting the underlying enzymatic defect with a small molecule," said Chris Bowden, M.D., chief medical officer at Agios. "The rapid and sustained hemoglobin increases and well-tolerated safety profile shown in this trial to date support continued study and moving into late-stage development. In addition, these data demonstrate the important potential role that PK activation may have in transforming treatment of PK deficiency."

About the DRIVE-PK Study

DRIVE-PK is a global Phase 2, open-label safety and efficacy trial evaluating AG-348 in adult, transfusion-independent patients with PK deficiency. The study includes two arms of up to 25 patients each, receiving a dose of 50 milligrams (mg) or 300 mg twice daily for at least six months. Hemoglobin levels are assessed in weekly intervals for the first 3 weeks of study and then at weeks 6, 9, 12, 16, 20 and 24. As of the March 27, 2016 data cut-off, 18 patients had been treated with AG-348 for at least three weeks in the DRIVE-PK study. Three of the 18 patients had completed 24 weeks of treatment with either 50 mg or 300 mg twice daily. The mean patient age was 31. The mean baseline hemoglobin was 9.3 g/dL. Thirteen of the 18 patients underwent prior splenectomy.

Safety Data

A safety analysis was conducted based on all 18 treated patients as of the data cut-off.

- AG-348 was well tolerated, and no patients discontinued treatment early.
- The majority of adverse events (AEs) reported by investigators were mild to moderate (Grade 1-2) and transient.
- The most frequent AEs included nausea, headache, hot flush and insomnia.
- One patient received a dose reduction due to rapidly increasing hemoglobin. This patient was dose-reduced from 300 mg to 50 mg and remained on study.
- One Grade 2 AE of osteoporosis has been reported since the cut-off date. This patient had osteopenia at baseline assessment.
- Sex steroids were assessed at baseline, week 12 and week 24. Free testosterone and estradiol were available for four and five male patients, respectively. An upward trend in free testosterone and a downward trend in estradiol were observed. Additional data and longer follow up are needed to determine if hormonal changes are clinically significant.

Efficacy Data

Nine of 18 total patients and nine of 13 patients with at least one missense mutation achieved rapid, robust and sustained hemoglobin increases of >1.0 grams per deciliter (g/dL) as of the data cut-off.

- Both doses of AG-348 demonstrated clinical activity, with four patients in the 50 mg group and five patients in the 300 mg group experiencing increases of >1.0 g/dL.
- In patients who had hemoglobin increases of >1.0 g/dL, the mean maximum hemoglobin increase was 3.4 g/dL (range 2.3–4.9 g/dL).
- The median time to a hemoglobin increase of >1.0 g/dL was 1.9 weeks (range 1.1–9.1 weeks).
- Further data are needed to obtain a greater understanding of the relationship between genotype and response. Preliminary observations show:
    - Of the 13 patients with at least one missense mutation, nine have shown an increase in hemoglobin of >1.0 g/dL.
    - None of the five patients with two non-missense mutations showed increases in hemoglobin of >1.0 g/dL.
- Pharmacokinetics were favorable and consistent with those observed in healthy volunteers.
- Pharmacodynamics data did not demonstrate a correlation with hemoglobin increases and ATP (adenosine triphosphate) elevation. More data are needed to clarify if any correlation exists between 2,3-DPG (2,3-diphosphoglycerate) decreases and Hb increases of >1.0 g/dL.

About Pyruvate Kinase Deficiency and Genetic Background

Pyruvate Kinase Deficiency (PKD) 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 levels and a build-up of upstream metabolites, including 2,3-DPG.

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' PK-R Activators

Agios has discovered and is currently evaluating two orally available, potent, selective small molecule activators of PKR in clinical trials, AG-348 and AG-519. Agios scientists previously reported that AG-348 is a potent activator of the wild-type and mutated PKR enzymes. Agios retains worldwide development and commercialization rights to AG-348 and AG-519.

Conference Call Information

Agios will host a conference call and webcast to review data presented at EHA and corporate milestones on Saturday, June 11, 2016 beginning at 9:30 a.m. ET (3:30 p.m. CEST). To participate in the conference call, please dial (877) 377-7098 (domestic) or (631) 291-4547 (international) and refer to conference ID 18475657. The webcast will be accessible live or in archived form under "Events & Presentations" in the Investors and Media section of the company's website at www.agios.com.

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 pyruvate kinase-R mutations, including AG-348 and AG-519; Agios' plans for the further clinical development of AG-348; and its 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' Quarterly Report on Form 10-Q for the quarter ended March 31, 2016, 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.

[1] Bianchi P et al. poster, 2015 ASH Annual Meeting

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