Agios Announces Initiation of Global Phase 3 Trial (ACTIVATE) of AG-348 in Adults with Pyruvate Kinase Deficiency Who Are Not Regularly Transfused

June 18, 2018

- Broad Late-stage Development Plan in Place with Two Pivotal Trials and Patient Registry Open for Enrollment -

CAMBRIDGE, Mass., June 18, 2018 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ:AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today announced the initiation of the Phase 3 ACTIVATE trial evaluating AG-348, a first-in-class, selective, small molecule activator of the pyruvate kinase-R (PKR) enzyme. ACTIVATE is a randomized, placebo-controlled trial that will enroll approximately 80 adults with pyruvate kinase (PK) deficiency who do not receive regular blood transfusions. The trial is designed to demonstrate that treatment with AG-348 results in a sustained increase in hemoglobin in these patients.

“AG-348 is the first potential treatment for PK deficiency that targets the underlying cause of a patient’s anemia and has demonstrated robust and sustained hemoglobin increases in adults with this disease who are not regularly transfused,” said Chris Bowden, M.D., chief medical officer of Agios. “With the initiation of ACTIVATE, and the ongoing ACTIVATE-T study in patients who are regularly transfused, we are executing a comprehensive pivotal development plan for adults with this lifelong anemia who currently only have access to supportive care.”

ACTIVATE Trial Design

The purpose of this Phase 3, 1:1 randomized, double-blind, placebo-controlled global trial is to evaluate the efficacy and safety of treatment with AG-348 in approximately 80 adults with PK deficiency across approximately 35 sites in 15 countries. Key eligibility criteria include a hemoglobin less than or equal to 10 g/dL and at least one missense mutation. Patients homozygous for the R479H mutation will not be eligible for the trial. The study design has two parts. Part 1 is a dose optimization period where patients start at 5 mg of AG-348 or placebo twice daily, with the flexibility to titrate up to 20 mg or 50 mg twice daily over a three month period to establish their individual optimal dose, as measured by maximum increase in hemoglobin levels. After the dose optimization period, patients will receive their optimal dose for an additional three months in Part 2. The primary endpoint of the study is the proportion of patients who achieve at least a 1.5 g/dL increase in hemoglobin sustained over multiple visits in Part 2 of the trial.

Ongoing ACTIVATE-T Trial and PEAK Registry

- A pivotal trial of AG-348 in adults with pyruvate kinase deficiency who are regularly transfused (ACTIVATE-T) is ongoing. ACTIVATE-T is a global, single-arm trial of approximately 20 adults with PK deficiency designed to demonstrate that treatment with AG-348 reduces transfusion burden.
- A global registry known as PEAK, for adult and pediatric patients with PK deficiency, is open for enrollment. PEAK is designed to develop a greater understanding of the long-term clinical implications of PK deficiency, including natural history of the disease, current treatments and associated outcomes, variability of clinical care and disease burden. The registry will enroll up to 500 patients across approximately 60 global sites and will follow patients for at least two years. Please refer to www.clinicaltrials.gov for additional information on the trials mentioned above.

About Pyruvate Kinase (PK) 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]

About Agios Pharmaceuticals, Inc.
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 an approved oncology precision medicine 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 Agios’ plans, strategies and expectations for the clinical development of its drug development programs, including AG-348; the potential benefits of Agios' product candidates, including AG-348; and the potential benefit of its strategic plans and focus. The words “estimate,” “expect,” “goal”, “intend,” “may,” “on track”, “plan,” “could,” “potential,” “strategy,” “will,” 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, 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, except as required by law.

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

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Source: Agios Pharmaceuticals, Inc.