Agios Reports New, Final Data from Phase 1 Multiple Ascending Dose (MAD) Study in Healthy Volunteers for AG-348, an Investigational Medicine for Pyruvate Kinase (PK) Deficiency

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Data Support Activation of DRIVE PK, a Global Phase 2 Study of AG-348 in PK Deficiency Patients

First Data from Natural History Study of PK Deficiency Characterize Severity of this Rare Genetic Disease

Company to Host Conference Call and Webcast Today

CAMBRIDGE, Mass. & VIENNA--(BUSINESS WIRE)--Jun. 12, 2015-- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO), a leader in the fields of cancer metabolism and rare genetic disorders of metabolism, presented today new, final data from its Phase 1 multiple ascending dose (MAD) clinical trial of AG-348 in healthy volunteers in an oral presentation at the 20th Congress of the European Hematology Association (EHA) taking place June 11-14, 2015 in Vienna. In addition, the first data from the global natural history study of PK deficiency will be presented by Dana-Farber Boston Children's Cancer and Blood Disorder Center.

The data from the MAD trial establish clear proof-of-mechanism for AG-348, a novel, first-in-class, oral activator of both wild-type (normal) and mutated pyruvate kinase-R (PKR) enzymes that is wholly owned by Agios. These data support the hypothesis that AG-348 enhances PKR activity and has the potential to correct the underlying defect of pyruvate kinase (PK) deficiency, a rare, potentially severe, genetic hemolytic disorder. The sensitivity of the wild-type PKR enzyme to the activating effects of AG-348 allowed the study of enzyme activation in healthy volunteers, and provided an opportunity to understand the safety, dosing and pharmacodynamic activity of AG-348 prior to entering a proof-of-concept study in patients.

“There are currently no approved or disease-modifying treatments for PK deficiency, and to date, there has been little research to address the condition or understand the degrees of severity and prevalence of complications associated with it,” said Chris Bowden, M.D., chief medical officer of Agios. “We are encouraged by the data presented today in healthy volunteers that provide further evidence that AG-348 activates the glycolytic pathway across a range of doses with a favorable safety profile. The final MAD data coupled with the findings from the natural history study represent important new developments as we initiate enrollment for DRIVE PK, our Phase 2 clinical trial of AG-348 in patients with this rare genetic disease.”

Data Summary from Completed Phase 1 MAD Trial for AG-348

Complete results are being reported from the Phase 1 MAD, randomized, double-blind, placebo-controlled study in 48 healthy volunteers who received either placebo or AG-348 for 14 days at 15 mg, 60 mg, 120 mg, 360 mg or 700 mg twice daily or 120 mg once daily in six sequential cohorts. The study showed that AG-348 was well tolerated, with most adverse events (AE) occurring in the highest dose group (700 mg), with all but one being mild to moderate. Thirty-two of 36 healthy volunteers receiving AG-348 completed the study. Two volunteers receiving AG-348 withdrew due to adverse events, including drug eruption (60 mg) and Grade 3 liver function test abnormalities (700 mg), which resolved after treatment discontinuation. Two additional AG-348 volunteers (both 700 mg) withdrew consent due to nausea or vomiting. Serum hormone changes consistent with reversible aromatase inhibition were observed. AG-348 also showed a favorable pharmacokinetic profile with rapid absorption, low to moderate variability and a dose-proportional increase in exposure following multiple doses.

As predicted by the mechanism of action of AG-348, there was a robust activation of the glycolytic pathway as evidenced by a decrease in 2,3-DPG (2,3-diphosphoglycerate) and increase in ATP (adenosine triphosphate) in blood. The decrease in 2,3-DPG was approximately 50 percent for doses 120 mg and higher with levels returning back to baseline approximately 72 hours after AG-348 was discontinued. There was also an approximately 50 percent increase in ATP in blood with AG-348 at doses 60 mg and higher.

Clinical Development Plans for AG-348

Based on these findings and those from the single ascending dose (SAD) portion of the Phase 1 study of AG-348 in healthy volunteers, Agios has opened DRIVE PK, a global Phase 2, first-in-patient, open-label safety and efficacy trial in adult, transfusion-independent patients with PK deficiency. The multi-center, randomized study will include two arms with 25 patients each. The patients in the first arm will receive 50 mg twice daily, and the patients in the second arm will receive 300 mg twice daily. The study will include a six-month dosing period with the opportunity for continued treatment beyond six months based on safety and clinical activity. Please refer to www.clinicaltrials.gov for additional clinical trial information.

Data Summary from the Natural History Study of PK Deficiency

“This natural history study features the largest cohort of patients with PK deficiency assembled to date, giving us a unique opportunity to understand the characteristics of this disorder,” said Rachael Grace, M.D., Dana-Farber Boston Children's Cancer and Blood Disorder Center. “These data show not only the range of severity of the disorder, but also the unifying characteristics such as iron overload, which was common in all age groups regardless of transfusion history. We are hopeful that these findings will lead to improved supportive care and help guide the development of new treatments for these patients.”

The e-poster titled, “The Clinical Features and Treatment of Iron Overload in Pyruvate Kinase Deficiency (PKD): Data from the PKD Natural History Study,” by researchers from the Dana-Farber Boston Children's Cancer and Blood Disorder Center, Agios and other collaborators describe the demographic features, iron monitoring and chelation practices in PK deficiency patients with iron overload. Iron overload is characterized by an excess of iron in the body, which can be acquired by blood transfusions that are often used as supportive care for patients with PK deficiency. The study enrolled 105 PK deficiency patients, including patients who have not received transfusions to date. Findings revealed that iron overload was common in all age groups, regardless of transfusion history, and is likely related to the chronic hemolysis. Despite this finding, iron monitoring is not routinely performed in PK deficiency patients.

The poster titled, “Categorization of Clinical Severity in Pyruvate Kinase Deficiency (PKD) in an International, Observational Cohort,” by researchers from the Dana-Farber Boston Children's Cancer and Blood Disorder Center, Agios and other collaborators categorized PK deficiency clinical severity based on the degree of anemia, transfusion history and splenectomy status and identified predictors and prevalence of complications in the various severity groups. The study enrolled 105 PK deficiency patients. The patients were categorized into four distinct severity groups ranging from never transfused to splenectomized and regularly transfused. The study found that complications such as cholecystectomy and iron overload are correlated with severity of disease, and this classification may be helpful for determining monitoring and treatment practices.

Conference Call Information

Agios will host a conference call and webcast from the congress to review the data on Friday, June 12, 2015 beginning at 8:00 a.m. ET (2:00 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 53010830. 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 AG-348 and Pyruvate Kinase (PK) Deficiency

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 a decline in the energy metabolite ATP and a build-up of the metabolite 2,3-DPG. Agios scientists have previously reported that AG-348 is a potent activator of the wild-type and mutated PKR enzymes, resulting in restoration of ATP levels and a decrease in 2,3-DPG levels in blood sampled from patients with PK deficiency. 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. Currently, there is no approved therapy to treat the underlying cause of PK deficiency. AG-348, a first-in-class orally available, potent, selective small molecule activator of PKR, was discovered in the laboratory of Agios, and the company retains worldwide development and commercialization rights.

About Agios Pharmaceuticals, Inc.

Agios Pharmaceuticals is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic disorders of metabolism 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 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 candidate targeting pyruvate kinase R mutations, including AG-348; its plans and timelines for the clinical development of AG-348; and the benefit of its strategic plans and focus. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “potential,” “possible,” “hope,” “could,” “would” 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 agreement 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, 2015, 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.

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