Agios Presents New Clinical Data Supporting the Benefits of PYRUKYND® (mitapivat) Treatment in Adults with PK Deficiency at European Hematology Association Annual Congress

June 10, 2022

– Treatment with PYRUKYND® Associated with Early and Robust Hemoglobin Responses in Phase 3 ACTIVATE and Extension Studies; Approximately One-Third of Patients Achieved Normal Hemoglobin Levels at Least Once –

– PYRUKYND®-Treated Patients Reported Significant Improvements in PK Deficiency Signs, Symptoms and Impacts, with Greater Improvements Evident in Hemoglobin Responders –

– New Analysis from Peak Registry Demonstrates Wide Range of Comorbidities and Complications in PK Deficiency Patients Regardless of Genotype –

– Agios to Host Investor Event on Monday, June 13 at 8 a.m. ET –

CAMBRIDGE, Mass., June 10, 2022 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism pioneering therapies for genetically defined diseases, today reported new data further underscoring the significant burden of disease in adults with pyruvate kinase (PK) deficiency regardless of genotype and supporting the potential benefits of treatment with PYRUKYND® for these patients. Data are being presented at the European Hematology Association (EHA) Annual Congress, hosted virtually and in person in Vienna on June 9-12, 2022.

"Following the FDA approval of PYRUKYND ® for the treatment of hemolytic anemia in adults with PK deficiency in February of this year, the data presented at EHA add to the growing body of evidence underscoring the potential of PYRUKYND® to provide real-world benefits for patients with this rare blood disorder," said Sarah Gheuens, M.D., Ph.D., chief medical officer at Agios. "Patients treated with PYRUKYND ® had early and robust hemoglobin responses and improvements in hallmark signs and symptoms of PK deficiency, including jaundice, tiredness and shortness of breath. In addition, new data from the Peak Registry highlight the importance of appropriate disease management for all patients with PK deficiency, regardless of genotype. Agios continues to focus on maximizing the impact of PYRUKYND® as the first approved disease-modifying treatment for this community."

PYRUKYND® was approved in February 2022 by the U.S. Food and Drug Administration (FDA) for the treatment of hemolytic anemia in adults with PK deficiency. PYRUKYND® is also under review by the European Medicines Agency (EMA) as a potential treatment for adults with PK deficiency, and Agios expects a regulatory decision in the EU by the end of 2022. Both the FDA and EMA have granted orphan drug designation to PYRUKYND® in PK deficiency. Learn more at www.PYRUKYND.com.

Long-term Treatment with Oral Mitapivat Is Associated with Normalization of Hemoglobin Levels in Patients with Pyruvate Kinase Deficiency (Abstract P1548)
This analysis of data from the Phase 3 ACTIVATE study and the ongoing long-term extension study assessed the proportion of patients who achieved normal hemoglobin levels, as defined by central and local laboratory manuals, at least once while receiving PYRUKYND® without requiring any transfusions. Data demonstrate that treatment with PYRUKYND® was associated with normalization of hemoglobin levels. A greater proportion of patients achieved normalization of hemoglobin levels among the subset who met the primary endpoint as hemoglobin responders, defined as a hemoglobin increase of ≥1.5 g/dL at ≥2 scheduled assessments at weeks 16, 20 and 24 during the fixed-dose period.

As of the September 21, 2021 data cut-off, 40/40 patients in the mitapivat arm and 38/40 patients in the placebo crossover arm continued treatment in the extension study. Results were as follows:

- Across the ACTIVATE and extension studies, 28/78 (35.9%) of all patients achieved a normal hemoglobin level at least once during treatment with PYRUKYND®
- Among hemoglobin endpoint responders, 26/31 (83.9%) achieved a normal hemoglobin level at least once while receiving treatment with mitapivat
- The majority of patients who achieved a normal hemoglobin level at least once in the ACTIVATE and extension studies achieved their first normal hemoglobin level within four months of treatment with PYRUKYND®

Improvements in Patient-Reported Outcomes in Mitapivat-treated Patients with Pyruvate Kinase Deficiency: A Descriptive Analysis from the Phase 3 ACTIVATE Trial (Abstract P1735)
The purpose of this post-hoc analysis of the ACTIVATE Phase 3 study was to describe the changes in patient-reported outcomes (PROs) for the subset of patients who achieved the primary endpoint of hemoglobin response. Measurements were taken using two disease-specific PRO instruments: the PK deficiency diary (PKDD) and the PK deficiency impact assessment (PKDIA).

As previously reported, PYRUKYND®-treated patients in the ACTIVATE study demonstrated significant improvements in signs, symptoms and impacts based on these PRO instruments compared with patients receiving placebo. This analysis further revealed that improvements were greater in the patients who met the primary endpoint of hemoglobin response (n=16) and sustained over time.

Comorbidities and Complications Across Genotypes in Adult Patients with Pyruvate Kinase Deficiency: Analysis from the Peak Registry

(Abstract P1542)
This analysis of the Peak Registry, a global retrospective and prospective observational study of adult and pediatric patients diagnosed with PK deficiency, was designed to characterize comorbidities and complications across genotypes in adult patients. The analysis demonstrates that adult patients experienced a wide range of serious comorbidities and complications across multiple systems, regardless of *PKLR* genotype. In addition, these data highlight the existence of multiple complications in individual patients with PK deficiency and the need for appropriate monitoring and management of these patients, regardless of genotype.

Additional PK Deficiency Data
Agios is also presenting encore data supporting the benefits of treatment with PYRUKYND® in adults with PK deficiency, regardless of transfusion status. Key abstracts include:

- Durability of Hemoglobin Response and Reduction in Transfusion Burden Is Maintained Over Time in Patients With Pyruvate Kinase Deficiency Treated With Mitapivat in a Long-term Extension Study (Abstract 1545)
- Mitapivat Decreases the Need for Transfusions Secondary to Poorly Tolerated Anemia and Acute Events Compared to Placebo in Patients With Pyruvate Kinase Deficiency Who Are Not Regularly Transfused (Abstract P1543)
- Bone Mineral Density Remains Stable in Pyruvate Kinase Deficiency Patients Receiving Long-term Treatment With Mitapivat (Abstract P1544)
- Mitapivat Improves Ineffective Erythropoiesis and Reduces Iron Overload in Patients With Pyruvate Kinase Deficiency (Abstract P1565)

In addition, the company is presenting trials-in-progress posters for ACTIVATE-kids (Abstract P1547) and ACTIVATE-kidsT (Abstract P1546), its pivotal clinical trials for pediatric PK deficiency patients who do not receive regular transfusions and who do receive regular transfusions, respectively.

About ACTIVATE
ACTIVATE is a Phase 3 global, double-blind, placebo-controlled study with a 1:1 randomization evaluating the efficacy and safety of PYRUKYND® in adults with PK deficiency who do not receive regular transfusions. Patients were required to have a hemoglobin concentration less than or equal to 10.0g/dL. The trial randomized 80 patients.

The study was designed with two parts. Part 1 was a dose escalation period in which patients started at 5 mg of PYRUKYND® or placebo twice daily, with two potential dose escalations to 20 mg twice daily and 50 mg twice daily over a 12-week period. After the dose escalation period, patients received a fixed dose for an additional 12 weeks in Part 2.

The primary endpoint of the study was hemoglobin response, defined as a ≥1.5 g/dL increase in hemoglobin concentration from baseline that is sustained at two or more scheduled assessments at Weeks 16, 20 and 24 during Part 2 of the trial.

Agios conducted an additional pivotal Phase 3 study, ACTIVATE-T, in adults with PK deficiency who receive regular transfusions. The company is conducting an ongoing extension study designed to evaluate the long-term safety, tolerability and efficacy of treatment with PYRUKYND® in adults with PK deficiency previously enrolled in ACTIVATE or ACTIVATE-T.

Data from ACTIVATE and ACTIVATE-T studies were presented at the European Hematology Association (EHA) Annual Congress in June 2021.

About Peak Registry
The Peak Registry is a global, longitudinal study of children and adults with PK deficiency and 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.

About PK Deficiency
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 mutation in the *PKLR* gene can cause a deficit in energy within the red blood cell, as evidenced by lower PK enzyme activity, a decline in adenosine triphosphate (ATP) levels and a build-up of upstream metabolites, including 2,3-DPG (2,3-diphosphoglycerate).

PK deficiency is associated with serious complications, including gallstones, pulmonary hypertension, extramedullary hematopoiesis, osteoporosis and iron overload and its sequelae, which can occur regardless of the degree of anemia or transfusion burden. PK deficiency can also cause quality of life problems, including challenges with work and school activities, social life and emotional health. Current management strategies for PK deficiency, including red blood cell transfusions and splenectomy, are associated with both short- and long-term risks. For more information, please visit the websites of two U.S.-based independent patient advocacy groups dedicated to PK deficiency: PK Deficiency Foundation and Thrive with PK Deficiency.

About PYRUKYND® (mitapivat)
PYRUKYND is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

IMPORTANT SAFETY INFORMATION
Acute Hemolysis: Acute hemolysis with subsequent anemia has been observed following abrupt interruption or discontinuation of PYRUKYND in a dose-ranging study. Avoid abruptly discontinuing PYRUKYND. Gradually taper the dose of PYRUKYND to discontinue treatment if possible. When discontinuing treatment, monitor patients for signs of acute hemolysis and anemia including jaundice, scleral icterus, dark urine, dizziness, confusion, fatigue, or shortness of breath.

Adverse Reactions: Serious adverse reactions occurred in 10% of patients receiving PYRUKYND in the ACTIVATE trial, including atrial fibrillation, gastroenteritis, rib fracture, and musculoskeletal pain, each of which occurred in 1 patient. In the ACTIVATE trial, the most common adverse reactions including laboratory abnormalities (≥10%) in patients with PK deficiency were estrone decreased (males), increased urate, back pain, estradiol decreased (males), and arthralgia.

Drug Interactions:

- Strong CYP3A Inhibitors and Inducers: Avoid concomitant use.
- Moderate CYP3A Inhibitors: Do not titrate PYRUKYND beyond 20 mg twice daily.
- Moderate CYP3A Inducers: Consider alternatives that are not moderate inducers. If there are no alternatives, adjust PYRUKYND dosage.
- Sensitive CYP3A, CYP2B6, CYP2C Substrates Including Hormonal Contraceptives: Avoid concomitant use with substrates that have narrow therapeutic index.
- UGT1A1 Substrates: Avoid concomitant use with substrates that have narrow therapeutic index.
- P-gp Substrates: Avoid concomitant use with substrates that have narrow therapeutic index.

Hepatic Impairment: Avoid use of PYRUKYND in patients with moderate and severe hepatic impairment.
Please see full Prescribing Information for PYRUKYND.

Conference Call Information
Agios will host a virtual investor event on June 13, 2022, at 8 a.m. ET to review select data from the EHA presentations. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors and Media 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 a biopharmaceutical company that is fueled by connections. The Agios team cultivates strong bonds with patient communities, healthcare professionals, partners and colleagues to discover, develop and deliver therapies for genetically defined diseases. In the U.S., Agios markets a first-in-class pyruvate kinase (PK) activator for adults with PK deficiency, the first disease-modifying therapy for this rare, lifelong, debilitating hemolytic anemia. Building on the company's leadership in the field of cellular metabolism, Agios is advancing a robust clinical pipeline of investigational medicines with active and planned programs in alpha- and beta-thalassemia, sickle cell disease, pediatric PK deficiency and MDS-associated anemia. In addition to its clinical pipeline, Agios has multiple investigational therapies in preclinical development and an industry-leading research team with unmatched expertise in cellular metabolism and genetics. 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 preclinical, clinical and commercial advancement of its drug development programs, including PYRUKYND® (mitapivat); the potential benefits of Agios' products and product candidates, including PYRUKYND®; and the potential benefits of Agios' strategic plans and focus. The words "anticipate," "expect," "goal," "hope," "milestone," "plan," "potential," "possible," "strategy," "will," "vision," 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. 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, without limitation risks and uncertainties related to: the failure of Agios to receive milestone or royalty payments related to the sale of its oncology business, the uncertainty of the timing of any receipt of any such payments, and the uncertainty of the results and effectiveness of the use of proceeds from the transaction; the impact of the COVID-19 pandemic to Agios' business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply and launching, marketing and selling of current and future approved products; 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, the EMA or 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 and 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 establish and maintain 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, or SEC, including the risks and uncertainties set forth under the heading Risk Factors in our filings with the SEC. While the list of factors presented here is considered representative, this list should not be considered to be a complete statement of all potential risks and uncertainties. Any forward-looking statements contained in this press release are made only as of the date hereof, and we undertake no obligation to update forward-looking statements to reflect developments or information obtained after the date hereof and disclaim any obligation to do so other than as may be required by law.

Contacts

Investors:
Holly Manning, 617-844-6630
Senior Director, Investor Relations
Holly.Manning@agios.com

Media:
Jessica Rennekamp, 857-209-3286
Director, Corporate Communications
Jessica.Rennekamp@agios.com

Source: Agios Pharmaceuticals, Inc.