Agios Presents Updated PYRUKYND® (mitapivat) Long-term Extension Data Demonstrating Sustained Clinical Benefits in Adults with Pyruvate Kinase (PK) Deficiency at 64th ASH Annual Meeting and Exposition

December 12, 2022

– Data Suggest Long-term Treatment with PYRUKYND® in Adults with PK Deficiency is Associated with Improvements in Hemoglobin, Iron Overload, Transfusion Burden and Patient-reported Outcomes, Regardless of Transfusion Status –

– Additional Data Presented at ASH Characterize Disease Complications and Co-morbidities of PK Deficiency in Pediatric Populations, Supporting Ongoing Pivotal ACTIVATE-Kids and ACTIVATE-KidsT Studies of PYRUKYND® –

– Agios to Host Live and Webcast Investor Event on Dec. 12, 2022, at 7 a.m. CT –

CAMBRIDGE, Mass., Dec. 11, 2022 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism pioneering therapies for rare diseases, today reported new data from the ongoing extension study assessing the long-term efficacy and safety of PYRUKYND® (mitapivat) in adults with pyruvate kinase (PK) deficiency who had participated in one of the pivotal studies, ACTIVATE and ACTIVATE-T, conducted in not regularly transfused and regularly transfused adults with PK deficiency, respectively. Data from the studies were featured in multiple presentations at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition, hosted Dec. 10-13, 2022, in New Orleans. PYRUKYND® is a first-in-class, oral PK activator and the first approved disease-modifying therapy for patients in the U.S. and EU with this rare, debilitating, lifelong hemolytic anemia.

Long-term extension data (abstract # 2328) show that previously reported effects of PYRUKYND® on hemoglobin and transfusion burden were maintained over time. As of the March 27, 2022 data cut-off, the median duration of hemoglobin response among the 31 hemoglobin responders from ACTIVATE and the long-term extension study was 18.3 months, with responses ongoing up to 32.9 months. Hemoglobin response rate among patients who switched from placebo in ACTIVATE to PYRUKYND® in the extension study (39.5 percent Hb response rate) was similar to that observed in patients treated with PYRUKYND® in ACTIVATE. All regularly transfused patients who achieved transfusion-free status in ACTIVATE-T with PYRUKYND® treatment maintained transfusion-free status through the extension study for up to 38.3 months. PYRUKYND® was well tolerated, and the safety profile was consistent with that in ACTIVATE and ACTIVATE-T, as well as previous studies.

“PYRUKYND® is the first oral agent that has the potential to improve symptoms and long-term complications of PK deficiency in adult patients,” said Rachael Grace, M.D., MMSc, director of hematology clinical research at Boston Children’s Hospital and investigator on the long-term extension study. “People living with PK deficiency experience a wide range of complications throughout their lives, including osteopenia, iron overload and pulmonary hypertension, many of which occur at earlier ages than would be expected. We are encouraged by the long-term extension data reported today and look forward to researching the efficacy and safety of PYRUKYND® in the ACTIVATE-Kids and ACTIVATE-KidsT studies in pediatric PK deficiency patients who are not regularly transfused and are regularly transfused, respectively.”

“Collectively, the data we have presented at ASH continue to demonstrate the benefits of long-term treatment with PYRUKYND® for adults with PK deficiency, including improvements in hemoglobin, transfusion burden, iron overload and patient-reported outcomes,” said Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. “In addition to progressing our pivotal trials in pediatric patients, we are encouraged by the results from the long-term extension study of our Phase 2 study of PYRUKYND® in both alpha- and beta-thalassemia, which we also presented at ASH, and believe the consistency of the data between indications further supports the potential of PYRUKYND® to make a positive impact across rare blood disorders with similar underlying pathophysiology.”

Agios also presented data at ASH further supporting the potential of PYRUKYND® to address hallmark symptoms and complications of PK deficiency. More details on the presentations are provided below and on the ASH 2022 page on Agios.com.

Long-term Improvements in Patient-reported Outcomes in Patients with Pyruvate Kinase Deficiency Treated with Mitapivat (Abstract #506)
In an oral presentation, data from ACTIVATE, ACTIVATE-T and the long-term extension study were reported, showing that treatment with PYRUKYND® was associated with long-term, durable and clinically meaningful improvements in signs, symptoms and functional impacts, irrespective of transfusion status. Patient-reported outcome (PRO) improvements among patients treated with PYRUKYND® were sustained over time in the long-term extension (LTE) study through Week 84. At Week 84 of the LTE study, clinically meaningful improvements in PROs mean scores were achieved in more than half of patients. These results suggest that by improving health-related quality of life, treatment with PYRUKYND® may provide meaningful patient-centric benefits.

Mitapivat Improves Iron Overload in Patients with Pyruvate Kinase Deficiency (Abstract #1021)
In a poster presentation, data from ACTIVATE and the long-term extension study were reported that showed meaningful long-term improvements in key systemic regulators of iron homeostasis and measures of iron overload – including erythroferrone, soluble transferrin receptor (sTfR) and hepcidin – continued up to 96 weeks in patients treated with PYRUKYND®. Additionally, patients treated with PYRUKYND® who had evidence of iron overload at baseline showed clinically meaningful and continued improvements in iron overload over time as measured by liver iron concentration (median [Q1, Q3] decrease from baseline to Week 96 of PYRUKYND® treatment of –1.95 [–4.85, –0.70] mg Fe/g dw). Ferritin levels remained stable across both patient groups treated with PYRUKYND® or placebo.

Mitapivat Improves Markers of Hemolysis and Erythropoiesis in Patients with Pyruvate Kinase Deficiency Irrespective of Hemoglobin

Response (Abstract #3644)
In a separate poster presentation, data from the ACTIVATE study were reported showing that treatment with PYRUKYND® improved markers of hemolysis and ineffective erythropoiesis in adults with PK deficiency. The analysis also shows that directional improvements occur even in patients who did not achieve the clinical trial definition of hemoglobin response.

PYRUKYND® was approved in February 2022 by the U.S. Food and Drug Administration (FDA) and received marketing authorization in November 2022 by the European Medicines Agency (EMA) for adults with PK deficiency. Both the FDA and EMA have granted orphan drug designation to PYRUKYND® in PK deficiency. In addition, PYRUKYND® has been granted FDA orphan drug designation for the treatment of thalassemia and sickle cell disease, for which enrollment for ongoing pivotal studies is underway.

Conference Call Information
Agios will host a live investor event on Dec. 12, 2022, at 7:00 a.m. CT in New Orleans to review the key clinical oral and poster presentations from this year's ASH meeting. 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 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 www.knowpkdeficiency.com.

About PYRUKYND® (mitapivat)
PYRUKYND is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency in the United States, and for the treatment of PK deficiency in adult patients in the European Union.

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 and Summary of Product Characteristics for PYRUKYND.

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 rare 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 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 the potential benefits of PYRUKYND® (mitapivat); Agios' plans regarding future data presentations; and the potential benefit of its strategic plans and focus. The words "anticipate," "expect," "intend," "potential," "milestone," "goal," "will," "on track," "upcoming," 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 or its collaborators 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. Moreover, there can be no guarantee that any medicines ultimately commercialized by Agios will receive commercial acceptance. 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, without limitation: risks and uncertainties related to 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 of current or future approved products, and launching, marketing and selling current or 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; 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 with Servier; 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, except as required by law.

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