Agios Presents Updated PYRUKYND® (mitapivat) Data Highlighting Long-term Safety Profile and Durable Improvement in Hemoglobin and Markers of Hemolysis and Ineffective Erythropoiesis in Non-transfusion-dependent α- and β-Thalassemia at 64th ASH Annual Meet

December 10, 2022

– Actively Enrolling Phase 3 ENERGIZE and ENERGIZE-T Studies Evaluating PYRUKYND® in Adults with Non-transfusion-dependent and Transfusion-dependent α- or β-Thalassemia, Respectively –

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

CAMBRIDGE, Mass., Dec. 10, 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 long-term extension period of the Phase 2 open-label study of PYRUKYND® (mitapivat), a first-in-class, oral, small molecule allosteric activator of wild-type and a variety of mutated pyruvate kinase (PK) enzymes, in adults with non-transfusion dependent α- or β-thalassemia. Data from the study were featured in a poster presentation (abstract #1030) at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition, hosted Dec. 10-13, 2022, in New Orleans.

Consistent with previously reported data, durable improvements in hemoglobin concentration and markers of hemolysis and ineffective erythropoiesis were observed for up to 72 weeks of treatment in both α- and β-thalassemia patients. Additionally, markers of iron homeostasis remained stable or improved through Week 72. PYRUKYND® was well tolerated, and the safety profile was consistent with previous studies.

“The data presented today continue to underscore the potential of PK activation to address multiple aspects of the complex underlying pathophysiology of α- and β-thalassemia, including hallmarks of the disease: hemolysis and ineffective erythropoiesis,” said Kevin Kuo, M.D., hematologist at University of Toronto, Toronto General Hospital, and an investigator in the study. “Thalassemia is a rare, debilitating lifelong blood disorder, and there are no currently approved treatment options for those with α-thalassemia and options are limited for those with β-thalassemia. These data, along with long-term extension study data from ongoing studies of the treatment in pyruvate kinase deficiency, demonstrate the potential clinical benefits of PYRUKYND® for a broad spectrum of hemolytic anemias and support its continued investigation in thalassemia.”

“Together, the data presented at ASH continue to highlight the need for new therapies for both α- and β-thalassemia and underscore the potential of PYRUKYND® to serve as a potentially meaningful new option for these patients,” said Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. “We are now laser-focused on enrolling our two global, placebo-controlled pivotal trials of mitapivat – ENERGIZE and ENERGIZE-T – in adults with non-transfusion dependent and transfusion dependent thalassemia, respectively, and expect to enroll a substantial portion of patients in the trials by year-end.”

Agios also presented data at ASH further elucidating the burden of disease and unmet needs in α- and β-thalassemia. More details on the presentations are provided below and on the ASH 2022 page on Agios.com.

Characterizing the Clinical, Health-related Quality of Life and Economic Burden of Alpha-thalassemia: A Systematic Literature Review and Evidence Gaps Assessment (Abstract #1036)
In a first-of-its-kind systemic literature review investigating clinical, health-related quality of life and economic burden associated with α-thalassemia, results underscore the need for further research to fully characterize the burden of disease. Where reported, adult patients with deletional and non-deletional α-thalassemia experience clinical complications across a range of conditions, including moderate-to-severe iron overload (31%), iron overload of unspecified severity (66%) and advanced liver fibrosis (20%). Complications were significantly higher in adults with non-deletional α-thalassemia. Generally, children and adolescents with α-thalassemia experience similar health-related quality of life scores, across psychological, emotional, social and school functioning parameters, as those with β-thalassemia.

Clinical Burden of Alpha- and Beta-thalassemia Compared to Matched Controls in the Real-world Setting (Abstract #2351)
In a poster presentation reviewing claims data for patients and controls from commercial and government databases, an analysis showed that serious comorbidities and unmet needs persist for patients with thalassemia, even in thalassemia types that have historically been considered less severe, such as non-transfusion dependent thalassemia. Both α- and β-non-transfusion dependent thalassemia had significantly higher clinical burden than matched controls including endocrinopathies, cardiovascular disease, liver disease and pulmonary hypertension – conditions associated with considerable morbidity and mortality. Additional therapies are needed to address the underlying cause of the disease and for prevention of these serious complications.

Conference Call Information
Agios will host a live investor event on Dec. 12, 2022, at 7:00 a.m. ET 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 Thalassemia
Thalassemia is a rare, inherited blood disorder caused by mutations in either α- or β-globin genes, resulting in excessive destruction of red blood cells. Globin precipitates in thalassemia cause oxidative damage, leading to hemolytic anemia, ineffective erythropoiesis and iron overload.

Thalassemia is associated with serious complications, including fatigue, jaundice, facial bone deformities, delayed growth and development, abdominal swelling, dark urine and reduced life expectancy. Current management strategies for β-thalassemia can include red blood cell transfusions splenectomy and stem cell transplant, which are associated with short- and long-term risks. There are currently no approved therapies for

α-thalassemia.

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 and 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 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) and AG-946; 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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