Agios Presents Positive Results from Phase 3 ENERGIZE Study of Mitapivat in Non-Transfusion-Dependent Thalassemia in Plenary Session at the European Hematology Association 2024 Hybrid Congress

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– ENERGIZE is the First Study to Demonstrate Efficacy of an Oral Treatment for Non-Transfusion-Dependent Alpha- and Beta-Thalassemia –

– Additional ENERGIZE Poster Presentation Highlights Improvements in Fatigue and Exercise Capacity in Patients Treated with Mitapivat Compared to Placebo –

– Agios to Webcast Virtual Investor Event on June 16, 2024 at 10 a.m. Eastern Time or 4 p.m. Central European Summer Time –

CAMBRIDGE, Mass., June 15, 2024 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a leader in cellular metabolism and pyruvate kinase (PK) activation pioneering therapies for rare diseases, today presented detailed results from the global Phase 3 ENERGIZE study of mitapivat in adults with non-transfusion-dependent (NTD) alpha- or beta-thalassemia in a plenary session (abstract #S104) at the European Hematology Association 2024 (EHA2024) Hybrid Congress, which is being held June 13-16, 2024, in Madrid, Spain. In a related poster presentation (abstract #P1529), the company presented additional data from the ENERGIZE study highlighting clinically meaningful improvements in health-related quality of life measures and patient-reported outcomes among patients in the mitapivat arm compared to those in the placebo arm.

The ENERGIZE study achieved its primary endpoint, with mitapivat demonstrating a statistically significant increase in hemoglobin response rate compared to placebo. Statistical significance was also achieved for both key secondary endpoints associated with change from baseline in FACIT-Fatigue Score and hemoglobin concentration. These improvements were observed across all pre-specified subgroups.

“The data from the ENERGIZE study are compelling, with mitapivat-treated patients achieving meaningful improvements in non-transfusion-dependent thalassemia’s hallmark symptom of anemia as well as in key measures of how patients feel and function,” said Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. “Together with the recently announced positive results from the ENERGIZE-T study of mitapivat in adults with transfusion-dependent thalassemia, the detailed ENERGIZE results underscore mitapivat’s potential to become an important treatment option for all subtypes of thalassemia – alpha- and beta-thalassemia, transfusion-dependent and non-transfusion-dependent – with the convenience of a pill. We look forward to working with regulators as we anticipate filing for approval in the U.S. by the end of this year.”

“I am pleased to present the results of the ENERGIZE study to my esteemed colleagues and believe they will share my enthusiasm for the positive impact mitapivat may have for patients with non-transfusion-dependent alpha- or beta-thalassemia,” said Ali Taher, M.D., Ph.D., Professor of Medicine, Hematology & Oncology and Director – Naef K. Basile Cancer Institute, American University of Beirut Medical Center in Beirut, Lebanon; an investigator in the ENERGIZE study. “Globally, there are currently no approved oral treatments for non-transfusion-dependent thalassemia, which is characterized by anemia, ineffective erythropoiesis, hemolysis and iron overload and can cause severe complications, reduced quality of life and shortened lifespan. Based on the data collected in the ENERGIZE study, mitapivat has the potential to become a foundational treatment for non-transfusion-dependent thalassemia.”

“The ENERGIZE data presented at this congress show that non-transfusion-dependent alpha- or beta-thalassemia patients treated with mitapivat experienced clinically meaningful improvements in fatigue and walking capacity, as well as improvements in patient-reported outcomes across a range of disease symptoms,” said Kevin Kuo, M.D., MSc, FRCPC; Division of Hematology, University of Toronto in Ontario, Canada; an investigator in the ENERGIZE study. “There is a tremendous need for oral therapies that can improve how people with thalassemia feel and function and reduce the impact of the disease on their lives. Patients with alpha- or beta-thalassemia, regardless of transfusion status, frequently report negative effects on daily activities and physical functioning. On a number of domains of health-related quality of life, adults with non-transfusion-dependent thalassemia experience even greater symptom burden than their transfusion-dependent counterparts. I am excited about the potential of mitapivat to support quality of life improvements for these individuals.”

Agios also recently announced positive results from the Phase 3 ENERGIZE-T study of mitapivat in adults with transfusion-dependent alpha- or beta-thalassemia. The company intends to file for regulatory approval of mitapivat as a treatment for thalassemia by the end of 2024, incorporating all available data from both studies.

Results for the Phase 3 ENERGIZE study were as follows:

- A total of 194 patients were enrolled in the study, with 130 randomized to mitapivat 100 mg twice-daily (BID) and 64 randomized to matched placebo. 122 (93.8%) in the mitapivat arm and 62 (96.9%) in the placebo arm completed the 24-week double-blind period of the study.
- Baseline demographics and characteristics were balanced between mitapivat and placebo arms, and representative of a population of non-transfusion dependent thalassemia patients.
- The study met the primary endpoint of hemoglobin response. Hemoglobin response was defined as an increase of ≥1 g/dL in average hemoglobin concentrations from week 12 through week 24 compared with baseline.
    - 42.3% (n=55/130) of patients in the mitapivat arm achieved a hemoglobin response, compared to 1.6% (n=1/64) of patients in the placebo arm (2-sided p<0.0001).
    - Among patients who achieved hemoglobin response in the mitapivat arm, the mean change from baseline in

average hemoglobin concentration from week 12 to 24 was 1.56 g/dL.
    - Hemoglobin response rates were higher among those treated with mitapivat compared to placebo across all prespecified subgroups, including:
        - Thalassemia genotype: 23.8% (n=10/42) of alpha-thalassemia patients in the mitapivat arm achieved a hemoglobin response, compared to no alpha-thalassemia patients in the placebo arm. 51.1% (n=45/88) of beta-thalassemia patients in the mitapivat arm achieved a hemoglobin response, compared to 2.3% (n=1/44) of beta-thalassemia patients in the placebo arm.
        - Baseline hemoglobin concentration: 47.4% (n=45/95) of patients whose baseline hemoglobin concentration was ≤9.0 g/dL in the mitapivat arm achieved a hemoglobin response, compared to 2.1% (n=1/47) of patients in the placebo arm. 28.6% (n=10/35) of patients whose baseline hemoglobin concentration was between 9.1 and 10.0 g/dL achieved a hemoglobin response, compared to no patients in the placebo arm.
- Treatment with mitapivat also demonstrated statistically significant improvements compared to placebo for both key secondary endpoints:
    - The average change from baseline (95% confidence interval) in FACIT-Fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue) subscale score from week 12 to week 24 was 4.85 (3.41, 6.30) in the mitapivat arm compared to 1.46 (–0.43, 3.34) in the placebo arm (p=0.0026).
    - The average change from baseline (95% confidence interval) in average hemoglobin concentration from week 12 to week 24 was 0.86 (0.73, 0.99) g/dL in the mitapivat arm compared to –0.11 (–0.28, 0.07) g/dL in the placebo arm (p<0.0001).
- Improvements were observed in patients treated with mitapivat across measures of health-related quality-of-life, including the six-minute walk test and the Patient Global Impression of Change (PGIC) fatigue, walking capacity, and thalassemia symptoms subscales.
    - Six-minute walk test: The average change (95% confidence interval) from baseline to week 24 was 30.48 (19.31, 41.64) meters in the mitapivat arm compared to 7.11 (–7.39, 21.62) in the placebo arm.
    - PGIC: A higher proportion of patients in the mitapivat arm reported improvements in fatigue as per PGIC versus those in the placebo arm at weeks 12, 16, 20, and 24. A higher proportion of patients in the mitapivat arm reported improvements in thalassemia symptoms and walking capacity as per PGIC at week 24 versus those in the placebo arm.
- Overall, during the 24-week double-blind period, incidence of adverse events was similar across mitapivat and placebo arms, with 82.9% (n=107) of patients in the mitapivat arm and 79.4% (n=50) of patients in the placebo arm experiencing treatment-emergent adverse events (TEAEs).
    - The most frequently reported TEAEs were headache, initial insomnia, nausea and upper respiratory tract infection.
    - 3.9% (n=5) of patients in the mitapivat arm experienced Grade ≥3 treatment-related TEAEs. There were no serious TEAEs.
    - 3.1% (n=4) of patients in the mitapivat arm experienced TEAEs leading to discontinuation; there were no TEAEs leading to discontinuation in the placebo arm.

Conference Call Information
Agios will host a virtual investor breakout session tomorrow, June 16, 2024, at 10:00 a.m. ET (4 p.m. CEST) to review the key clinical oral and poster presentations from the EHA2024 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 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 the pioneering leader in PK activation and is dedicated to developing and delivering transformative therapies for patients living with 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 deep scientific expertise in classical hematology and leadership in the field of cellular metabolism and rare hematologic diseases, 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 is advancing a preclinical TMPRSS6 siRNA as a potential treatment for polycythemia vera, and a preclinical PAH stabilizer as a potential treatment for phenylketonuria (PKU). 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 mitapivat; Agios' plans for the future clinical development of mitapivat in alpha-and-beta thalassemia; and Agios' strategic plans and prospects. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would," "could," "potential," "possible," "hope" 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 pandemics or other public health emergencies 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; 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 key collaborations; uncertainty regarding any milestone or royalty payments related to the sale of Agios' oncology business or its in-licensing of TMPRSS6 siRNA, and the uncertainty of the timing of any such payments; uncertainty of the results and effectiveness of the use of proceeds from the transaction with Servier; competitive factors; 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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