Agios Announces Phase 3 ENERGIZE-T Study of Mitapivat Met Primary Endpoint and All Key Secondary Endpoints in Adults with Transfusion-Dependent Alpha- or Beta-Thalassemia

June 3, 2024

– Study Achieved the Primary Endpoint; Mitapivat Demonstrated a Statistically Significant Transfusion Reduction Response Compared to Placebo –

– Statistical Significance Achieved for All Key Secondary Endpoints Evaluating Additional Measures of Reduction of Transfusion Burden Compared to Placebo –

– ENERGIZE-T is the First Phase 3 Study to Demonstrate Efficacy of an Oral, Disease-Modifying Treatment for Transfusion-Dependent Alpha- and Beta-Thalassemia –

– As Part of Global Submission Strategy, U.S. Marketing Application for Mitapivat in Thalassemia Based on ENERGIZE and ENERGIZE-T Studies to be Submitted by End of 2024 –

– Agios to Host Investor Webcast Event Today at 8:00 a.m. ET –

CAMBRIDGE, Mass., June 03, 2024 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a leader in cellular metabolism and pyruvate kinase (PK) activation pioneering therapies for rare diseases, today announced that the global Phase 3 ENERGIZE-T study of mitapivat in adults with transfusion-dependent (TD) alpha- or beta-thalassemia achieved its primary endpoint of transfusion reduction response. Statistical significance was also achieved for all key secondary endpoints evaluating additional measures of reduction of transfusion burden compared to placebo.

“Building on the compelling data generated in the Phase 3 ENERGIZE study of mitapivat in adults with non-transfusion-dependent alpha- or beta-thalassemia announced earlier this year, today’s results underscore the potential of mitapivat, with its unique mechanism of action improving red blood cell health, to be a meaningful oral treatment option for all thalassemia patients, regardless of transfusion needs,” said Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. “We are grateful to all patients who participated in this trial, as well as our collaborators, study investigators, and advisors in the patient and clinical communities for their partnership. We look forward to submitting a marketing application in the U.S. encompassing data from ENERGIZE and ENERGIZE-T by the end of this year.”

“Taken together with the positive data from the ENERGIZE study, the data from the ENERGIZE-T study have the potential to be transformative for thalassemia patient care. Treatment options for patients with transfusion-dependent thalassemia are limited, and transfusions carry significant risks for patients, such as iron overload and immune reactions. There is a tremendous need for alternative ways to manage this chronic disease,” said Maria Domenica Cappellini, M.D., Professor, Internal Medicine, University of Milan, Italy. “Based on these data demonstrating that treatment with mitapivat significantly reduces transfusion burden across alpha- and beta-thalassemia patients, along with its convenient oral formulation, mitapivat has the potential to become a novel advancement in care for thalassemia patients.”

With the positive data generated in the Phase 3 ENERGIZE-T and ENERGIZE studies of mitapivat in patients with alpha- or beta- thalassemia regardless of transfusion needs, the company intends to submit a marketing application for PYRUKYND® (mitapivat) in the U.S. by the end of 2024 based on all available data from both studies. The company also plans to submit marketing applications in Europe and the Gulf Cooperation Council (GCC) countries.

Topline results for the Phase 3 ENERGIZE-T study were as follows:

- A total of 258 patients were enrolled in the study, with 171 randomized to mitapivat 100 mg twice-daily (BID) and 87 randomized to matched placebo. 155 patients (90.6%) in the mitapivat arm and 83 patients (95.4%) in the placebo arm completed the 48-week double-blind period of the study.
- The study met its primary endpoint of transfusion reduction response (TRR, defined as a ≥50% reduction in transfused red blood cell (RBC) units with a reduction of ≥2 units of transfused RBCs in any consecutive 12-week period through Week 48 compared with baseline).
    - Treatment with mitapivat demonstrated a statistically significant reduction in transfusion burden compared to placebo, as measured by the TRR endpoint. In the mitapivat arm, 30.4% of patients achieved a transfusion reduction response, compared to 12.6% of patients in the placebo arm (2-sided p=0.0003).
- Treatment with mitapivat also demonstrated a statistically significant reduction in additional measures of transfusion reduction response compared to placebo as assessed by the three key secondary endpoints:
    - ≥50% reduction in transfused RBC units in any consecutive 24-week period through week 48 compared with baseline.
    - ≥33% reduction in transfused RBC units from week 13 through week 48 compared with baseline.
    - ≥50% reduction in transfused RBC units from week 13 through week 48 compared with baseline.
- In addition, a higher proportion of patients in the mitapivat arm (9.9%) compared to the placebo arm (1.1%) achieved the

secondary endpoint of transfusion independence (transfusion-free for ≥8 consecutive weeks through week 48).

- Overall, during the 48-week double-blind period, incidence of adverse events (AEs) was similar across mitapivat and placebo arms. In the mitapivat arm, 5.8% of the patients experienced an AE leading to discontinuation, compared to 1.2% of patients in the placebo arm.
- Based on the safety and efficacy data observed in ENERGIZE-T, the company will proceed with the previously stated plans of U.S. regulatory submission by end of this year.

Agios plans to present a more detailed analysis of the Phase 3 ENERGIZE-T data at an upcoming medical meeting. Data from the Phase 3 ENERGIZE study of mitapivat in non-transfusion-dependent thalassemia will be presented at the European Hematology Association 2024 Hybrid Congress in a plenary session on June 15, 2024, and in a poster session on June 14, 2024.

Conference Call Information

Agios will host a webcast investor event today at 8:00 a.m. ET to review the ENERGIZE-T Phase 3 data and next steps for the mitapivat development program in thalassemia. The event 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; Agios’ plans for future regulatory submissions; 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 Agios' cash and cash equivalents; 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.

Contacts:
Investor Contact
Chris Taylor, VP Investor Relations and Corporate Communications
Agios Pharmaceuticals
IR@agios.com

Media Contact
Dan Budwick
1AB
dan@1abmedia.com

Source: Agios Pharmaceuticals, Inc.