European Commission Adopts Positive Decision for Orphan Medicinal Product Designation of Agios' Mitapivat in Sickle Cell Disease

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CAMBRIDGE, Mass., Dec. 18, 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 European Commission has adopted a positive decision for the designation of mitapivat, an oral, small molecule PK activator, as an orphan medicinal product (OMP) for the treatment of sickle cell disease. Earlier, in November 2020, the U.S. Food and Drug Administration (FDA) also granted orphan drug designation to mitapivat for sickle cell disease.

"Alongside the FDA's orphan drug designation in the U.S., the European Commission's orphan medicinal product designation for mitapivat underscores the urgent need for novel therapies for sickle cell disease and highlights its potential to provide clinically meaningful benefits to patients navigating this debilitating condition," said Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. "With the trial fully enrolled, we look forward to sharing the results of our Phase 3 RISE UP study evaluating the efficacy and safety of mitapivat in sickle cell disease with the community in late 2025."

The European Commission offers OMP designation to innovative therapies that address life-threatening or chronically debilitating conditions affecting fewer than five in 10,000 individuals in the European Union, and that have the potential to provide a significant benefit over existing treatments. This designation provides extensive benefits to encourage the development of these medicines, including reduced fees and a 10-year period of market exclusivity.

About Phase 2/3 RISE UP Study
The RISE UP Phase 2 and 3 studies are evaluating the efficacy and safety of mitapivat in sickle cell disease patients who are 16 years of age or older, have had between two and 10 sickle cell pain crises in the past 12 months, and have hemoglobin within the range of 5.5 to 10.5 g/dL during screening. The Phase 2 and Phase 3 studies are conducted under a single operationally seamless Phase 2/3 protocol. The two studies enrolled different participants and achieved operational efficiency through leveraging the same sites, vendors and other resources.

The Phase 2 study included a 12-week randomized, placebo-controlled period in which participants were randomized in a 1:1:1 ratio to receive 50 mg mitapivat twice daily, 100 mg mitapivat twice daily or matched placebo. The primary endpoints were hemoglobin response, defined as ≥1.0 g/dL increase in average hemoglobin concentration from Week 10 through Week 12 compared to baseline, and safety. In December 2023, Agios presented positive results from the Phase 2 study at the 65th American Society of Hematology (ASH) Annual Meeting and Exposition.

The Phase 3 study includes a 52-week randomized, placebo-controlled period in which participants will be randomized in a 2:1 ratio to receive 100 mg of mitapivat twice daily or matched placebo. The primary endpoints are hemoglobin response, defined as a ≥1.0 g/dL increase in average hemoglobin concentration from Week 24 through Week 52 compared with baseline, and annualized rate of sickle cell pain crises. In October 2024, Agios announced that enrollment in the Phase 3 study had been completed, with more than 200 patients enrolled worldwide.

Participants who complete the double-blind period of the Phase 2 or Phase 3 studies will have the option to move into a 216-week open-label extension period to receive mitapivat.

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, myelodysplastic syndrome (MDS)-associated anemia and phenylketonuria (PKU). In addition to its clinical pipeline, Agios is advancing a preclinical TMPRSS6 siRNA as a potential treatment for polycythemia vera. 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, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®; Agios' strategic vision and goals, including its key milestones; 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. For example, there can be no guarantee that any product candidate Agios 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. 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; 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 key collaborations; uncertainty regarding any royalty payments related to the sale of its oncology business or any milestone or royalty payments related to 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; 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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