Agios Announces Key 2025 Milestones for Innovative Rare Disease Portfolio

January 13, 2025

– FDA Accepted Agios' Supplemental New Drug Application for PYRUKYND ® (mitapivat) in Adult Patients with Non-Transfusion-Dependent and Transfusion-Dependent Alpha- or Beta-Thalassemia; PDUFA Goal Date is September 7, 2025 –

– Topline Results from Phase 3 RISE UP Study of Mitapivat in Sickle Cell Disease to be Announced in Late 2025, with Potential U.S. Commercial Launch in 2026 –

– Strong Financial Position Provides Opportunity to Maximize Potential PYRUKYND Commercial Launches, Advance Early- and Mid-Stage Clinical Programs and Expand Pipeline –

CAMBRIDGE, Mass., Jan. 13, 2025 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a leader in cellular metabolism and pyruvate kinase (PK) activation pioneering therapies for rare diseases, today announced its anticipated key 2025 milestones and value-driving catalysts through 2026. The company's management team will present this information at the 43 rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 7:30 a.m. PT / 10:30 a.m. ET.

"2024 was marked by exceptional progress at Agios. We delivered on all our key priorities, advanced our potential best- and first-in-class rare disease pipeline and further strengthened our financial position. Today, we are entering an era of growth and expansion for the company, building on a strong foundation and focus, and are well-positioned for a sustained trajectory of success," said Brian Goff, chief executive officer at Agios. "Our blueprint encompasses the potential for two additional commercial launches of PYRUKYND in thalassemia and sickle cell disease in 2025 and 2026, respectively, along with an early- and mid-stage pipeline that offers a strong foundation for innovation and growth, all supported by a highly experienced team with proven executional excellence and a strong balance sheet. Over the next 12 months, our priorities will be to maximize the potential of the PYRUKYND franchise, advance and diversify our key pipeline programs, and strategically focus our capital deployment to sustain our growth. We are excited about the future and the meaningful impact we can have in addressing the critical needs of rare disease patients."

2024 Highlights:

- *Thalassemia:* Presented positive results from the ENERGIZE and ENERGIZE-T Phase 3 trials evaluating mitapivat versus placebo in adults with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia, respectively. The ENERGIZE randomized clinical trial results were presented at the European Hematology Association 2024 Hybrid Congress in June 2024, and the ENERGIZE-T randomized clinical trial results were presented at the 66th American Society of Hematology Annual Meeting and Exposition in December 2024. Agios filed regulatory applications for mitapivat (PYRUKYND) for the treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia with the U.S., European Union, Kingdom of Saudi Arabia and United Arab Emirates health authorities.
- *Sickle Cell Disease:* Completed enrollment of the Phase 3 RISE UP study that is evaluating mitapivat in sickle cell disease patients who are 16 years of age or older. This Phase 3 study enrolled more than 200 patients worldwide.
- *Pediatric Pyruvate Kinase (PK) Deficiency:* Reported topline results from the Phase 3 ACTIVATE-KidsT trial of mitapivat in children with PK deficiency who are regularly transfused. Further, completed enrollment of the Phase 3 ACTIVATE-Kids study of mitapivat in children with PK deficiency who are not regularly transfused.
- *Lower-Risk Myelodysplastic Syndromes (LR-MDS):* Initiated patient enrollment in the Phase 2b study of tebapivat (AG-946) in LR-MDS. Additionally, the U.S. Food and Drug Administration (FDA) granted orphan drug designation to tebapivat for the treatment of MDS.
- *Early-Stage Pipeline*: Dosed the first healthy volunteer participants in the Phase 1 study of AG-181, a PAH stabilizer, in phenylketonuria.
- *Corporate Development*:
  - Announced a $905 million purchase agreement with Royalty Pharma for Agios' rights to its vorasidenib royalty. Under the agreement, Agios received a payment of $905 million following the approval of vorasidenib by the FDA. Royalty Pharma will receive the entirety of the 15% royalty on annual U.S. net sales of vorasidenib up to $1 billion, and a 12% royalty on annual U.S. net sales greater than $1 billion. Agios retains a 3% royalty on annual U.S. net sales greater than $1 billion. Agios also received a $200 million milestone payment from Servier following the FDA approval of vorasidenib. Altogether, Agios received a total of $1.1 billion in milestone payments as part of this purchase agreement.
  - Entered into a distribution agreement with NewBridge Pharmaceuticals to advance commercialization of PYRUKYND in the Gulf Cooperation Council (GCC) region. NewBridge, a leading specialty company headquartered in Dubai, will commercialize PYRUKYND in Bahrain, Kuwait, Oman, Qatar, Saudi Arabia and the United Arab Emirates.

Anticipated 2025 Milestones:

- *Thalassemia:* Receive FDA regulatory decision for PYRUKYND for the treatment of adult patients with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia. The review classification for the company's supplemental New Drug Application is Standard and the Prescription Drug User Fee Act (PDUFA) goal date is September 7, 2025.
- *Sickle Cell Disease*: Announce topline results from the Phase 3 RISE UP study of mitapivat in sickle cell disease in late 2025, with a potential U.S. commercial launch in 2026. Additionally, begin patient enrollment for the Phase 2 study of tebapivat in sickle cell disease in mid-2025.
- *Pediatric Pyruvate Kinase (PK) Deficiency:* Announce topline results from the Phase 3 ACTIVATE-Kids study of mitapivat in children with PK deficiency who are not regularly transfused in early 2025.
- *Lower-Risk Myelodysplastic Syndromes (LR-MDS):* Complete patient enrollment in the Phase 2b study of tebapivat for LR-MDS in late 2025.
- *Early-Stage Pipeline:* File an Investigational New Drug Application for AG-236, a siRNA targeting TMPRSS6 intended for the treatment of polycythemia vera, in mid-2025.

Presentation at 43rd Annual J.P. Morgan Healthcare Conference

Agios' management team will present at the 43 rd Annual J.P. Morgan Healthcare Conference on Wednesday, January 15, 2025, at 7:30 a.m. PT / 10:30 a.m. ET. The live webcast will be accessible on the Investors section of the company's website (www.agios.com) under the "Events & Presentations" tab. A replay of the webcast will be archived on the company's website for at least two weeks following the presentation.

About PYRUKYND® (mitapivat)

U.S. INDICATION

PYRUKYND is a pyruvate kinase activator indicated for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

U.S. 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.

Hepatocellular Injury in Another Condition: In patients with another condition treated with PYRUKYND at a higher dose than that recommended for patients with PK deficiency, liver injury has been observed. These events were characterized by a time to onset within the first 6 months of treatment with peak elevations of alanine aminotransferase of >5× upper limit of normal (ULN) with or without jaundice. All patients discontinued treatment with PYRUKYND, and these events improved upon treatment discontinuation.

Obtain liver tests prior to the initiation of PYRUKYND and monthly thereafter for the first 6 months and as clinically indicated. Interrupt PYRUKYND if clinically significant increases in liver tests are observed or alanine aminotransferase is >5x ULN. Discontinue PYRUKYND if hepatic injury due to PYRUKYND is suspected.

Adverse Reactions: 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 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), tebapivat (AG-946), AG-236 and AG-181, Agios' PAH

stabilizer; Agios' plans, strategies and expectations for its preclinical, clinical and commercial advancement of its drug development, including PYRUKYND®, tebapivat, AG-181 and AG-236; the submission of PYRUKYND® to regulators for approval in alpha-and-beta thalassemia; Agios' strategic vision and goals, including its key milestones for 2025; and the potential benefits of Agios' strategic plans and focus. The words "anticipate", "expect", "goal", "hope", "milestone", "opportunity", "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 AG-236, 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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