U.S. FDA Grants Priority Review to Agios' sNDA for Mitapivat in Sickle Cell Disease

July 7, 2026

- FDA's PDUFA goal date is November 1, 2026
- If approved, mitapivat is positioned to become the first oral PK activator for patients with sickle cell disease

CAMBRIDGE, Mass., July 07, 2026 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a commercial-stage biopharmaceutical company focused on delivering innovative medicines for patients with rare diseases, today announced that the U.S. Food and Drug Administration (FDA) has accepted its supplemental New Drug Application (sNDA) for mitapivat, an oral pyruvate kinase (PK) activator, in sickle cell disease with a Priority Review. The Prescription Drug User Fee Act (PDUFA) goal date for this sNDA, submitted under the FDA's accelerated approval pathway, is November 1, 2026.

The FDA's Priority Review designation is granted to applications for medicines that may offer significant improvements in safety or efficacy for serious conditions, shortening the target review timeline from the standard 10 months to six months.

"The Priority Review designation for the mitapivat sNDA marks an important milestone for the sickle cell community – a large, underserved population that has long needed new treatment options to help manage the significant burden of disease," said Sarah Gheuens, M.D., Ph.D., Chief Medical Officer and Head of R&D, Agios. "Mitapivat is well positioned to address this treatment gap, supported by results from the RISE UP clinical program and a foundational dataset spanning more than a decade of research that includes over 1,300 patient-years of clinical experience across multiple hemolytic anemias. We look forward to working collaboratively with the FDA throughout this review, with the goal of delivering the first oral PK activator in sickle cell disease."

The mitapivat sNDA is based on data from the global, randomized, double-blind, placebo-controlled RISE UP Phase 2 and Phase 3 trials in patients aged 16 years or older with sickle cell disease. Mitapivat is currently approved in the U.S. for adult patients in two hemolytic anemias: PK deficiency (2022) and thalassemia (2025).

About U.S. Accelerated Approval
The U.S. Food and Drug Administration's (FDA) accelerated approval pathway expedites the availability of medicines that can fill a medical need for a serious condition. U.S. accelerated approval is subject to the same rigorous FDA review standards as medicines reviewed through the traditional approval pathway. A confirmatory clinical trial to further demonstrate the medicine's clinical benefit is required to convert the accelerated approval to a traditional approval, and this trial must be underway when the FDA makes its approval decision.

About the REIGNITE Phase 3 Confirmatory Trial
REIGNITE is the confirmatory clinical trial required to be conducted under the U.S. accelerated approval pathway.

The global REIGNITE Phase 3 trial (NCT07656415) is designed to demonstrate the clinical benefit of mitapivat on reducing transfusion burden in patients with sickle cell disease aged 12 years or older. REIGNITE includes a 52-week, double-blind, randomized, placebo-controlled period, in which approximately 159 participants are randomized 2:1 to receive oral mitapivat (100 mg) twice daily or matched placebo. Upon completing this period, participants have the option to transition into an open-label extension period where all receive mitapivat. The primary endpoint of REIGNITE is the proportion of patients achieving transfusion-free status from Week 4 through Week 52, and the first key secondary endpoint is the number of red blood cell units transfused from Week 4 through Week 52. To further assess the anti-hemolytic benefits of mitapivat, the trial also includes key secondary endpoints measuring the average change from baseline in hemoglobin, indirect bilirubin, and lactate dehydrogenase.

About Sickle Cell Disease
Sickle cell disease is a rare, inherited blood disorder caused by the production of abnormal hemoglobin that disrupts the ability of red blood cells to carry oxygen throughout the body. As a result, red blood cells become rigid and sickle-shaped, causing deformation of red blood cell membranes and the premature death of the cells. These effects lead to chronic hemolytic anemia, vaso-occlusion, and a cascade of severe and life-threatening complications, including long-term damage to the lungs, kidneys, and cardiovascular system. Due to its physical toll, sickle cell disease imposes a profound burden on patients and their families, marked by increased healthcare needs and early mortality.

About Mitapivat in Sickle Cell Disease
Mitapivat, an oral pyruvate kinase (PK) activator, is designed to enhance the process by which red blood cells produce energy. This approach has the potential to improve red blood cell health by increasing ATP levels to support increased energy demands and lowering levels of a molecule called 2,3-diphosphoglycerate (2,3-DPG). In sickle cell disease, increased stress on red blood cells results in elevated levels of 2,3-DPG, which raises the likelihood that red blood cells develop the abnormal "sickle" shape that triggers hemolysis.

About the RISE UP Phase 3 Trial
The global RISE UP Phase 3 trial (NCT05031780) was designed to evaluate the efficacy and safety of mitapivat in patients with sickle cell disease aged 16 years or older, representative of the global population. The trial design encompassed a 52-week, double-blind, randomized, placebo-controlled period, in which 207 participants were randomized 2:1 to receive oral mitapivat (100 mg) twice daily (n=138) or matched-placebo (n=69), followed by an open-label extension (OLE) period, during which all participants receive mitapivat.

To evaluate the effect of mitapivat on clinically relevant outcomes in sickle cell disease, the RISE UP Phase 3 trial design included two primary endpoints – hemoglobin response (≥1.0 g/dL increase from baseline in average hemoglobin from Week 24 through Week 52) and annualized rate of sickle cell pain crises – as well as five key secondary endpoints:

- Average change from baseline in hemoglobin concentration from Week 24 through Week 52

- Average change from baseline in indirect bilirubin from Week 24 through Week 52
- Average change from baseline in Patient Reported Outcome Measurement Information System Fatigue 13a (PROMIS Fatigue) Short Form scores from Week 24 through Week 52
- Annualized frequency of hospitalizations for sickle cell pain crises
- Average change from baseline in percent reticulocyte levels from Week 24 through Week 52

Of the 176 participants who completed the double-blind period of the trial, nearly all (n=174/176) entered the OLE period.

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 mitapivat 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 >5x upper limit of normal (ULN) with or without jaundice. All patients discontinued treatment with mitapivat, 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 AQVESME™ (mitapivat)
U.S. INDICATION
AQVESME is indicated for the treatment of anemia in adults with alpha- or beta-thalassemia.

U.S. IMPORTANT SAFETY INFORMATION
BOXED WARNING: HEPATOCELLULAR INJURY

AQVESME can cause serious hepatocellular injury. Measure liver laboratory tests (ALT, AST, alkaline phosphatase and total bilirubin with fractionation) at baseline and every 4 weeks for 24 weeks and then as clinically indicated. Avoid use of AQVESME in patients with cirrhosis. Discontinue AQVESME if hepatic injury is suspected.
Because of the risk of hepatocellular injury, AQVESME is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the AQVESME REMS.

WARNINGS AND PRECAUTIONS

Hepatocellular Injury
AQVESME can cause hepatocellular injury. Avoid use of AQVESME in patients with cirrhosis. In patients with thalassemia treated with AQVESME, liver injury with and without jaundice has been observed within the first 6 months of exposure. Obtain liver tests (including ALT, AST, alkaline phosphatase, total bilirubin with fractionation) prior to the initiation of AQVESME, then every 4 weeks for the first 24 weeks, and as clinically indicated thereafter. Interrupt AQVESME if clinically significant increases in liver tests are observed or alanine aminotransferase is >5 times the upper limit of normal (ULN). Complete a comprehensive evaluation to rule out other causes of liver injury when drug-induced liver injury is suspected. Discontinue AQVESME if hepatocellular injury due to AQVESME is suspected.

Symptoms and signs of early liver injury may mimic those of thalassemia. Advise patients to report new or worsening symptoms of loss of appetite, nausea, right-upper-quadrant abdominal pain, vomiting, scleral icterus, jaundice, or dark urine while on AQVESME treatment.

During the double-blind period, 2 of 301 patients (0.66%) with thalassemia treated with AQVESME experienced adverse reactions suggestive of hepatocellular injury. Three additional patients experienced adverse reactions suggestive of hepatocellular injury during the open-label extension periods after switching from placebo to AQVESME. Of these 5 patients, 2 had serious liver injury requiring hospitalization, including 1 patient who developed jaundice (peak bilirubin 32 mg/dL). Another patient developed jaundice (peak bilirubin 4 mg/dL) without requiring hospitalization. These reactions were characterized by a time to onset within the first 6 months of treatment with peak elevations of alanine aminotransferase of >5×ULN with or without jaundice. All patients discontinued treatment with AQVESME, and these reactions improved upon treatment discontinuation.

AQVESME REMS
AQVESME is available only through a restricted program under a REMS called the AQVESME REMS because of the risk of hepatocellular injury.

Adverse Reactions
The most common adverse reactions among patients taking AQVESME were headache and insomnia.

Drug Interactions

- Strong CYP3A Inhibitors and Inducers: Avoid concomitant use.
- Moderate CYP3A Inhibitors: Avoid concomitant use.
- Moderate CYP3A Inducers: Consider alternatives that are not moderate inducers. If there are no alternatives, see full Prescribing Information for recommended dosage for drug interactions with moderate CYP3A inducers.
- Sensitive CYP3A Substrates, including hormonal contraceptives: Avoid concomitant use with substrates that have narrow therapeutic index.
- CYP2B6, CYP2C, and UGT1A1 Substrates: Monitor patients for efficacy of the substrates with narrow therapeutic index.
- P-gp Substrates: Monitor patients for adverse reactions of the substrates with narrow therapeutic index.

Hepatic Impairment
Avoid use of AQVESME in patients with cirrhosis (Child-Pugh Class A, B, or C).

Please see full Prescribing Information for AQVESME, including Boxed Warning.

About Agios: Fueled by Connections to Transform Rare Diseases™
At Agios, our vision is to redefine the future of rare disease treatment. Fueled by connections, we build trusted partnerships with communities – collaborating to develop and deliver innovative medicines that have the potential to transform lives. With a foundation in hematology, we combine biological expertise with real-world insights to advance a growing pipeline of rare disease medicines that reflect the priorities of the people we serve. Agios is a commercial-stage biopharmaceutical company headquartered in Cambridge, Massachusetts. To learn more, visit www.agios.com and follow us on LinkedIn and X.

Available Information about Agios
To achieve broad dissemination, Agios may disclose information to the public through a variety of disclosure channels including press releases, SEC filings, and public conference calls and webcasts. Some of the information distributed through these disclosure channels may be considered material information. Investors and others should note that Agios plans to use its website (www.agios.com) as a distribution channel to announce and give notice of Agios' upcoming events and presentations (including, but not limited to, presentations at medical or healthcare conferences). Such information, which may be deemed material, will be available on the Investors section of the company's website under the "Events & Presentations" tab. In addition, you may sign up to automatically receive email alerts about Agios' upcoming events and presentations ("Calendar Alerts") by visiting the "Email Alerts" option under the "IR Resources" tab of the Investors section of the company's website and submitting your email address.

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' expectations for the review of its sNDA for mitapivat by the FDA; 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 AG-236 or cevidoplenib, 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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