U.S. FDA Approves Agios' AQVESME™ (mitapivat) for the Treatment of Anemia in Adults with Alpha- or Beta-Thalassemia

December 24, 2025

- AQVESME is the only FDA-approved medicine for anemia in both non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia
- Marketed under AQVESME brand name in the U.S. for thalassemia indication; PYRUKYND® (mitapivat) remains the U.S. brand name for PK deficiency indication
- AQVESME expected to be available in late January 2026, following AQVESME REMS program implementation
- Company will host investor conference call and webcast tomorrow, December 24 at 8:00 a.m. ET

CAMBRIDGE, Mass., Dec. 23, 2025 (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 approved AQVESME™ (mitapivat), an oral pyruvate kinase (PK) activator, for the treatment of anemia in adults with alpha- or beta-thalassemia. With this approved indication, AQVESME becomes the only FDA-approved medicine for anemia in both non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia.

"Thalassemia is a debilitating disease that demands lifelong management and vigilant monitoring for many life-threatening complications, such as blood clots, heart disease, and liver disease. Despite its severity, treatments have historically been limited, leaving some patients without any options," said Hanny Al-Samkari, M.D., Peggy S. Blitz Endowed Chair in Hematology/Oncology at Mass General Brigham Cancer Institute, Associate Professor at Harvard Medical School, and an investigator for the mitapivat thalassemia Phase 3 clinical program. "The ENERGIZE and ENERGIZE-T Phase 3 trial results demonstrate that AQVESME can help address anemia, fatigue, and the need for regular transfusions – key challenges of the disease. Today's FDA approval represents an important step forward for individuals with thalassemia."

The FDA approval of AQVESME in thalassemia is based on results from the global, randomized, double-blind, placebo-controlled ENERGIZE and ENERGIZE-T Phase 3 trials in adults with non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia, respectively. A total of 452 patients who are representative of the real-world thalassemia population were enrolled in the trials. The ENERGIZE and ENERGIZE-T Phase 3 trials met all primary and key secondary efficacy endpoints, demonstrating that AQVESME improves hemolytic anemia and a key quality-of-life measure compared to placebo, including significant reductions in transfusion burden and significant improvements in hemoglobin and fatigue.

"Today is a landmark moment for the thalassemia community, bringing forward an innovative, disease-modifying oral medicine to address the urgent needs of people living with this devastating rare blood disorder," said Brian Goff, Chief Executive Officer, Agios. "With this approval, AQVESME becomes the only medicine indicated for the treatment of anemia in both non-transfusion-dependent and transfusion-dependent alpha- or beta-thalassemia. We are deeply grateful to the patients, caregivers, healthcare providers, and advocacy partners who participated in and supported our clinical trials and helped ensure that our efforts reflected their priorities. Our focus now is on ensuring a successful launch and delivering meaningful impact for the community."

"This year marks 100 years since thalassemia was first described in medical literature, and the progress we've made as a community is truly extraordinary," said Ralph Colasanti, National President, Cooley's Anemia Foundation. "Innovative medicines like AQVESME help make this progress possible, offering new hope to patients like me by helping to address the complex needs and challenges of this disease. This approval provides an important new treatment option for the thousands of adults living with thalassemia in the U.S., including those with non-transfusion-dependent thalassemia who previously had no approved alternatives."

In the ENERGIZE and ENERGIZE-T Phase 3 trials, five patients receiving AQVESME experienced adverse reactions suggestive of hepatocellular injury (HCI), with two of these patients requiring hospitalization. These adverse reactions occurred within the first six months of exposure, and liver tests improved upon discontinuation of AQVESME. To mitigate the risk of HCI, AQVESME is available only through the AQVESME REMS, a Risk Evaluation and Mitigation Strategy (REMS) program approved by the FDA. The AQVESME REMS program requires liver tests prior to the first AQVESME dose, every four weeks thereafter for 24 weeks, and then as clinically indicated. It also includes education and certification requirements for patients, prescribing physicians, and pharmacists, which are common components of REMS programs.

Due to the AQVESME REMS program, mitapivat will be marketed under the brand name AQVESME in the U.S. for the thalassemia indication. Mitapivat will continue to be marketed as PYRUKYND® (mitapivat) in the U.S. for the PK deficiency indication, which does not require a REMS program. Outside the U.S., mitapivat will continue to be marketed as PYRUKYND for its PK deficiency and thalassemia indications in regions where it is approved, and will retain this name upon approval in regions currently under regulatory review.

Agios expects AQVESME to be available in the U.S. in late January 2026, following implementation of the AQVESME REMS program. For more information, visit AQVESME.com.

Conference Call Information
Agios will host a virtual investor event tomorrow, December 24, 2025, at 8:00 a.m. ET, to discuss the FDA approval of AQVESME in thalassemia. 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 available on the company's website approximately two hours after the event.

About Thalassemia
Thalassemia is a rare, inherited blood disease that affects the production of hemoglobin, the protein in red blood cells responsible for carrying oxygen

throughout the body. The disease is categorized into two main types: alpha-thalassemia and beta-thalassemia, depending on which globin chain of the hemoglobin is affected. By disrupting hemoglobin production, thalassemia reduces the number of circulating red blood cells and shortens their lifespan, which leads to anemia, fatigue, and serious complications.

Some individuals with thalassemia require regular transfusions (classified as transfusion-dependent thalassemia), while others only need them intermittently (classified as non-transfusion-dependent thalassemia). All patients with thalassemia experience a significant disease burden, including comorbidities, reduced quality of life, and shortened life expectancy.

In the U.S., approximately 6,000 adult patients are diagnosed with thalassemia.

About ENERGIZE and ENERGIZE-T
ENERGIZE (NCT04770753) and ENERGIZE-T (NCT04770779) are global, double-blind, placebo-controlled Phase 3 trials evaluating the efficacy and safety of mitapivat in adults with alpha- or beta-thalassemia.

The ENERGIZE trial randomized 194 non-transfusion-dependent alpha- or beta-thalassemia patients 2:1 to receive either mitapivat 100 mg twice daily or placebo. The primary endpoint was hemoglobin response, defined as an increase of ≥1.0 g/dL in average hemoglobin concentration from Week 12 through Week 24 compared with baseline. Key secondary endpoints included changes from baseline in average fatigue scores and in average hemoglobin concentration from Week 12 to Week 24. The trial also assessed safety and tolerability.

The ENERGIZE-T trial randomized 258 transfusion-dependent alpha- or beta-thalassemia patients 2:1 to receive either mitapivat 100 mg twice daily or placebo. The primary endpoint was transfusion reduction response, defined as a ≥50% reduction in transfused red blood cell (RBC) units with a reduction of ≥2 units of RBCs transfused in any consecutive 12-week period through Week 48 compared with baseline. Several transfusion reduction measures were included as key secondary endpoints, and achievement of transfusion independence was a secondary endpoint. The trial also assessed safety and tolerability.

For each trial, patients who completed the double-blind phase had the option to transition into a corresponding open-label extension phase, during which all patients receive mitapivat.

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 (≥5%) 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 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 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.

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 Agios' products, including AQVESME™, and its 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: 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' results of clinical trials and preclinical studies, including subsequent analysis of existing data and new data received from ongoing and future studies; 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' 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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