Agios Advances Mitapivat Toward Potential U.S. Accelerated Approval in Sickle Cell Disease Following Pre-sNDA Meeting with FDA

March 31, 2026

- Company has already submitted proposed confirmatory trial for FDA review, as required under accelerated approval pathway
- Company plans to submit mitapivat sNDA in sickle cell disease in the coming months, and is actively working with FDA to achieve alignment on confirmatory trial required for submission

CAMBRIDGE, Mass., March 31, 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 it will pursue U.S. accelerated approval for mitapivat, an oral pyruvate kinase (PK) activator, in sickle cell disease, following completion of its pre-supplemental New Drug Application (sNDA) meeting with the U.S. Food and Drug Administration (FDA).

The purpose of the pre-sNDA meeting was to present the data from the mitapivat RISE UP clinical program in sickle cell disease, including both the Phase 2 and Phase 3 trials. Based on the discussion, the FDA recommended submission of a proposal for a confirmatory clinical trial to support U.S. accelerated approval of mitapivat. The FDA's accelerated approval pathway expedites the availability of medicines that can fill a medical need for a serious condition, with the requirement of a confirmatory clinical trial to convert to a traditional approval.

"Our engagements with the FDA continue to underscore both the unmet need in sickle cell disease and the importance of expeditiously advancing new treatment options for patients living with this complex, debilitating, and deadly disease," said Sarah Gheuens, M.D., Ph.D., Chief Medical Officer and Head of R&D, Agios. "The clinically meaningful benefits observed in the RISE UP clinical program, combined with our ongoing, constructive, and collaborative dialogue with the FDA, reinforce our confidence in mitapivat's potential in sickle cell disease. We are focused on advancing mitapivat as rapidly as possible with the rigor required for potential U.S. accelerated approval."

Agios has already submitted its proposal for the required confirmatory clinical trial to the FDA for review. This proposal incorporates a primary endpoint that is different from those in the RISE UP clinical program and is informed by both analyses of RISE UP data and discussions with the FDA. Based on current planning assumptions, the proposed confirmatory clinical trial is not expected to change the company's previously issued operating expense guidance, which remains approximately flat compared to 2025.

The company plans to submit a mitapivat sNDA for sickle cell disease in the coming months, and is actively working with the FDA to achieve alignment on the confirmatory clinical trial required for submission.

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 vaso-occlusive crises.

About the RISE UP Phase 3 Trial Topline Results
The global RISE UP Phase 3 trial (NCT05031780) is evaluating the efficacy and safety of mitapivat in sickle cell disease patients aged 16 years or older, representative of the global population. The trial consisted of a 52-week, double-blind, randomized, placebo-controlled phase, in which 207 participants were randomized 2:1 to receive oral mitapivat (100 mg) twice daily (n=138) or matched-placebo (n=69). Upon completion, participants could transition into an open-label extension phase where all receive mitapivat.

To comprehensively evaluate objective measures of hemolysis alongside other clinically relevant outcomes in sickle cell disease, the double-blind phase of RISE UP included two primary endpoints – hemoglobin response and annualized rate of sickle cell pain crises – as well as five key secondary endpoints measuring hemoglobin concentration, indirect bilirubin (a biomarker of hemolysis), patient-reported fatigue, hospitalizations for sickle cell pain crises, and percent reticulocyte levels (a biomarker of erythropoiesis).

Mitapivat demonstrated a statistically significant improvement compared to placebo in the study's primary endpoint of hemoglobin response, defined as a ≥1.0 g/dL increase from baseline in average hemoglobin concentration from Week 24 through Week 52. Although mitapivat showed a reduction in the annualized rate of sickle cell pain crises compared with placebo, this primary endpoint did not reach statistical significance.

Patients receiving mitapivat who achieved the hemoglobin response primary endpoint had clinically meaningful improvements in hemoglobin concentration. These patients also experienced other clinically meaningful benefits, including reductions in pain crises and related hospital visits, along with improvements in fatigue.

The safety profile was favorable and consistent with prior mitapivat trials in sickle cell disease. The 52-week double-blind phase was completed by

87.0% (n=120/138) of patients in the mitapivat arm and 81.2% (n=56/69) of patients in the placebo arm. All but two of these patients (174/176) opted to enter the ongoing open-label extension phase of the trial.

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 mitapivat; Agios' expectations for its submission of a sNDA and the review of such sNDA by the FDA; Agios' commercial expectations for mitapivat; 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, 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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Source: Agios Pharmaceuticals, Inc.