Agios Showcases RISE UP Phase 3 Results at EHA 2026 Plenary Session Reinforcing Strong Anti-Hemolytic Profile of Mitapivat in Sickle Cell Disease

June 13, 2026

- Mitapivat demonstrated statistically significant improvement in hemoglobin response compared with placebo, with rapid onset and durable effects
- New analyses showed patients in mitapivat arm had clinically meaningful reduction in transfusion burden compared with placebo
- Patients in mitapivat arm who achieved hemoglobin response had clinically meaningful benefits across measures of sickle cell pain crises, fatigue, and other patient-reported outcomes
- Mitapivat was well-tolerated, with a safety profile consistent with previous trials of mitapivat in sickle cell disease
- Company to host investor conference call and webcast today at 9:00 a.m. ET (3:00 p.m. CEST)

CAMBRIDGE, Mass., June 13, 2026 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a commercial-stage biopharmaceutical company focused on delivering innovative medicines for patients with rare diseases, today presented detailed results from the 52-week double-blind period of the global RISE UP Phase 3 trial of mitapivat, an oral pyruvate kinase (PK) activator, in patients aged 16 years or older with sickle cell disease. These efficacy and safety results, which include new transfusion burden and hemoglobin responder analyses reinforcing the strong anti-hemolytic profile of mitapivat, were presented during the distinguished Plenary Abstracts Session at the 31st European Hematology Association (EHA) Congress (EHA 2026) in Stockholm, Sweden.

In November 2025, topline results from RISE UP demonstrated a significant improvement in the trial's primary endpoint of hemoglobin response with mitapivat compared with placebo. The trial also met two key secondary endpoints, showing rapid and durable improvements in hemoglobin concentration and indirect bilirubin, a marker of hemolysis (red blood cell destruction). Although mitapivat showed a reduction in the annualized rate of sickle cell pain crises (SCPCs) compared with placebo, this primary endpoint did not reach statistical significance, and there was no overall difference between mitapivat and placebo for the key secondary endpoint measuring patient-reported fatigue. However, patients in the mitapivat arm who achieved a hemoglobin response experienced clinically meaningful reductions in the annualized rate of SCPCs and related hospitalizations, as well as improvements in fatigue.

New RISE UP analyses, not previously disclosed by the company, further highlight the potential for mitapivat to offer clinical benefits for patients with sickle cell disease, as evidenced by a clinically meaningful reduction in transfusion burden and, for hemoglobin responders in the mitapivat arm, improvements observed across additional measures of pain and physical function.

"Patients living with sickle cell disease are in critical need of new treatments that can effectively manage the debilitating impact of their condition," said Biree Andemariam, M.D., Professor of Medicine and American Red Cross Endowed Chair in Transfusion Medicine, University of Connecticut Health, and a RISE UP trial investigator. "The RISE UP Phase 3 data presented today showcase the strong anti-hemolytic profile of mitapivat, with rapid and durable improvements in both hemoglobin and indirect bilirubin as well as a meaningful reduction in transfusion burden. Importantly, this anti-hemolytic effect is translating to clear clinical benefits, including improvements for hemoglobin responders across measures of sickle cell pain crises, pain, sleep, and physical function compared with non-responders. Together, these data reinforce the potential for mitapivat to improve the relentless physical toll that comes with living with sickle cell disease."

New RISE UP Phase 3 Trial Results at EHA 2026

Reduction in Transfusion Burden

New analyses from RISE UP show that mitapivat was associated with a clinically meaningful reduction in transfusion burden compared with placebo. Patients in the mitapivat arm had a 41.1% relative reduction in the proportion of patients requiring blood transfusions compared with placebo (23.9% with mitapivat vs. 40.6% with placebo), as well as a 55.9% relative reduction in average red blood cell units transfused per patient compared with placebo (0.70 units with mitapivat vs. 1.59 with placebo). These benefits were observed regardless of whether patients were also taking hydroxyurea. A reduction in transfusion burden in sickle cell disease can reflect decreased dependence on supportive care.

Hemoglobin Responders Post-Hoc Analysis

As previously reported, 40.6% of patients in the mitapivat arm achieved the primary endpoint of hemoglobin response (≥1.0 g/dL increase from baseline in average hemoglobin from Week 24 through Week 52) compared with 2.9% in the placebo arm, a statistically significant improvement (2-sided $p<0.0001$). Among these hemoglobin responders, the mean change from baseline in average hemoglobin concentration from Week 24 through Week 52 was 1.6 g/dL.

A post-hoc analysis showed patients in the mitapivat arm who achieved a hemoglobin response also experienced clinically meaningful reductions in pain crises and related hospitalizations, including a 26% reduction in the annualized rate of SCPCs (2.20 for responders vs. 2.98 for non-responders) and 34% fewer related hospitalizations (1.16 for responders vs. 1.76 for non-responders). These patients also had improvements in healthcare utilization, with a 53% reduction in the annualized rate of emergency room visits for SCPCs (1.11 for responders vs. 2.33 for non-responders) and a 37% decrease in the annualized rate of hospitalization days for SCPCs (7.83 for responders vs. 12.34 for non-responders).

Hemoglobin responders in the mitapivat arm also reported greater improvements in patient-reported fatigue scores than non-responders (-5.19 for responders vs. -2.55 for non-responders), as measured by change from baseline in average Patient-Reported Outcomes Measurement Information System (PROMIS) Fatigue 13a Short Form scores from Week 24 through Week 52. The magnitude of this improvement in hemoglobin responders exceeded the predefined 4.1-point threshold required to be considered clinically meaningful.

In the mitapivat arm, improvements across several additional patient-reported outcomes, including measures of pain, sleep, and physical function, were observed for hemoglobin responders compared with non-responders:

- **PROMIS Pain Intensity 1a:** The mean change from baseline was -1.63 points for hemoglobin responders and -0.59 for non-responders, with a least squares mean (LSM) difference of -1.04 (95% confidence interval [CI]: -1.66 to -0.42), favoring hemoglobin responders. The LSM difference is used throughout to represent the model-adjusted difference between hemoglobin responders and non-responders.
- **Adult Sickle Cell Quality of Life Measurement Information System (ASCQ-Me) Pain Impact:** The mean change from baseline was 4.09 points for hemoglobin responders and 0.85 for non-responders, with an LSM difference of 3.24 (95% CI: 1.18 to 5.30), favoring hemoglobin responders.
- **PROMIS Physical Functioning 8a:** The mean change from baseline was 5.30 points for hemoglobin responders and 1.79 for non-responders, with an LSM difference of 3.51 (95% CI: 0.62 to 6.39), favoring hemoglobin responders.
- **ASCQ-Me Sleep Impact:** The mean change from baseline was 2.39 points for hemoglobin responders and -0.48 for non-responders, with an LSM difference of 2.87 (95% CI: 0.22 to 5.53), favoring hemoglobin responders.
- **EuroQol-5 Dimension Visual Analog Scale (EQ-5D VAS):** The mean change from baseline was 3.27 points for hemoglobin responders and -6.77 for non-responders, with an LSM difference of 10.04 (95% CI: 2.41 to 17.66), favoring hemoglobin responders.

“Having the opportunity to present these comprehensive results during the EHA 2026 Plenary Session highlights the strength of the RISE UP Phase 3 data – the first pivotal trial to validate pyruvate kinase activation as a new treatment approach in sickle cell disease,” said Sarah Gheuens, M.D., Ph.D., Chief Medical Officer and Head of R&D, Agios. “Building on over a decade of clinical experience with mitapivat across several hemolytic anemias, these results reinforce both its consistent benefits and its well-established safety profile, which is supported by over 1,300 patient-years of data. Taken together, mitapivat represents a differentiated anti-hemolytic approach that can provide meaningful clinical benefits for patients with sickle cell disease – an underserved population in desperate need of innovative therapies.”

Safety Profile
Mitapivat was well-tolerated, with a safety profile consistent with previous trials of mitapivat in sickle cell disease. The percentage of patients with any reported treatment-emergent adverse events was similar between the mitapivat and placebo arms (97.1% vs. 98.6%, respectively). No treatment-related deaths occurred during the trial.

EHA 2026 Investor Event
Agios will host a conference call and live webcast during EHA 2026 today, June 13, 2026, at 9:00 a.m. ET (3:00 p.m. CEST). 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 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. In May 2026, Agios announced the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) for the accelerated approval of mitapivat in sickle cell disease.

About the RISE UP Phase 3 Trial
The global RISE UP Phase 3 trial (NCT05031780) is evaluating the efficacy and safety of mitapivat in patients with sickle cell disease aged 16 years or older, representative of the global population. The trial included 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).

To comprehensively evaluate objective measures of hemolysis alongside other clinically relevant outcomes in sickle cell disease, the double-blind period of RISE UP included two primary endpoints – hemoglobin response 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) opted to transition into a 216-week open-label

extension (OLE) period, during which all participants receive mitapivat.

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 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.

Contacts:
Investor Contact
Morgan Sanford, Vice President, Investor Relations
Agios Pharmaceuticals
morgan.sanford@agios.com

Media Contact
Eamonn Nolan, Senior Director, Corporate Communications
Agios Pharmaceuticals
eamonn.nolan@agios.com