Agios Presents Mitapivat Data Highlighting Long-term Safety Profile and Durable Improvement in Hemoglobin and Markers of Hemolysis in Non-transfusion-dependent α- and β-Thalassemia at 63rd ASH Annual Meeting and Exposition

December 13, 2021

– Global Phase 3 ENERGIZE and ENERGIZE-T Studies of Mitapivat in Transfusion-dependent and Non-transfusion-dependent α- and β-Thalassemia Initiated –

– Agios to Host Investor Webcast on Dec. 14, 2021, at 7:30 a.m. ET –

CAMBRIDGE, Mass., Dec. 13, 2021 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism to treat genetically defined diseases, today reported data for the first time from the ongoing long-term extension period of the Phase 2 open-label study of mitapivat, a first-in-class, investigational, oral, small molecule allosteric activator of wild-type and a variety of mutated pyruvate kinase (PK) enzymes, in adults with non-transfusion dependent α- or β-thalassemia. Data from the study were featured in an oral presentation at the American Society of Hematology (ASH) Annual Meeting and Exposition, hosted virtually and in person from Dec. 11-14, 2021, in Atlanta.

Consistent with previously reported data, durable improvements in hemoglobin concentration and markers of hemolysis and ineffective erythropoiesis, were observed for up to 72 weeks of treatment in both α- and β-thalassemia patients. Mitapivat was well tolerated, and the safety profile was consistent with previous studies.

“The data presented today continue to demonstrate that chronic treatment with mitapivat is well tolerated and has the potential to meaningfully improve hallmarks of thalassemia, including hemolysis and ineffective erythropoiesis. I am particularly excited by the data generated in α-thalassemia, as there are no currently approved therapies for this subtype,” said Kevin Kuo, M.D., hematologist at University Health Network, University of Toronto, and an investigator in the study. “Mitapivat has the potential to be an important treatment option for people with this lifelong disease characterized by severe complications, and I look forward to its continued advancement in pivotal clinical trials.”

Long-term Efficacy and Safety of the Oral Pyruvate Kinase Activator Mitapivat in Adults with Non-transfusion-dependent Alpha- or Beta-Thalassemia (Abstract #576)
The open-label Phase 2 study evaluated the efficacy, safety, pharmacokinetics and pharmacodynamics of mitapivat treatment in adults with either non-transfusion-dependent α- or β-thalassemia who have a baseline hemoglobin concentration of ≤10 g/dL. The trial enrolled 20 patients. All patients were treated with an initial dose of 50 mg mitapivat twice daily followed by a dose-level increase to 100 mg twice daily at the Week 6 visit based on safety evaluations and hemoglobin concentrations. Following the completion of the 24-week core period, patients had the opportunity to enroll in an optional 10-year extension period to evaluate long-term efficacy and safety of mitapivat in this population. As of the data cut-off date of March 27, 2021, 17 of the 20 patients remain in the extension phase with a median treatment duration of 70.9 weeks (range 54.7-105.6).

As of the data cut-off, efficacy results were as follows:

- Mean hemoglobin increase from baseline to Week 60 (α-thalassemia, n = 4; β-thalassemia, n = 9) was 1.5 g/dL.
- Mean hemoglobin increase from baseline to Week 72 (β-thalassemia, n = 8) was 1.7 g/dL.
- Improvements in markers of hemolysis and ineffective erythropoiesis achieved during the core period were sustained among both α- and β-thalassemia patients, up to Week 72.

Adverse events (AEs) for patients who continued in the study (n=17) were comparable in the core and extension periods. No new safety signals were identified in the extension period.

“Following encouraging results from our Phase 2 trial of mitapivat – the first clinical study of a PK activator in thalassemia and the first drug trial in α-thalassemia – we are now focused on advancing the development of mitapivat for patients as quickly and efficiently as possible,” said Sarah Gheuens, M.D., Ph.D., chief medical officer at Agios. “Our two global, placebo-controlled pivotal trials of mitapivat – ENERGIZE and ENERGIZE-T – have been initiated, and we look forward to enrolling the first patients soon.”

Mitapivat is not approved for use by any regulatory authority.

ENERGIZE Trial Design
ENERGIZE is a Phase 3, double-blind, randomized, placebo-controlled multicenter study evaluating the efficacy and safety of mitapivat as a potential treatment for adults with non-transfusion-dependent α- or β-thalassemia, defined as ≤5 red blood cell units during the 24-week period before randomization and no red blood cell transfusions ≤8 weeks before providing informed consent or during the screening period.

The primary endpoint of the trial is percentage of patients with hemoglobin response, defined as a ≥1.0 g/dL increase in average hemoglobin concentration from Week 12 through Week 24 compared with baseline. Secondary endpoints include markers of hemolysis and ineffective erythropoiesis, as well as patient-reported outcome (PRO) measures.

ENERGIZE-T Trial Design
ENERGIZE-T is a Phase 3, double-blind, randomized, placebo-controlled multicenter study evaluating the efficacy and safety of mitapivat as a potential treatment for adults with transfusion-dependent α- or β-thalassemia, defined as 6 to 20 red blood cell units transfused and ≤6-week transfusion-free period during the 24-week period before randomization.

The primary endpoint of the trial is percentage of patients with transfusion reduction response, defined as a ≥50% reduction in transfused red blood

cell units with a reduction of ≥2 units of transfused red blood cells in any consecutive 12-week period through Week 48 compared with baseline. Secondary endpoints include additional transfusion reduction measures and percentage of participants with transfusion-independence.

Conference Call Information
Agios will host a virtual investor event at 7:30 a.m. ET on Dec. 14, 2021, to review the key clinical oral and poster presentations from this year's ASH meeting. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors and Media section of the company's website at www.agios.com. The archived webcast will be available on the company's website beginning approximately two hours after the event.

About Thalassemia
Thalassemia is a rare, inherited blood disorder caused by mutations in either alpha (α)- or beta (β)-globin genes, resulting in excessive destruction of red blood cells. Globin precipitates in thalassemia cause oxidative damage, leading to hemolytic anemia, ineffective erythropoiesis and iron overload.

Thalassemia is associated with serious complications, including fatigue, jaundice, facial bone deformities, delayed growth and development, abdominal swelling, dark urine and reduced life expectancy. Current management strategies for β-thalassemia can include red blood cell transfusions, splenectomy and stem cell transplant, which are associated with short- and long-term risks. There are no currently approved therapies for α-thalassemia.

About Agios
Agios is focused on discovering and developing novel investigational medicines to treat genetically defined diseases through scientific leadership in the field of cellular metabolism. The company's most advanced drug candidate is a first-in-class pyruvate kinase (PK) activator, mitapivat, that is currently being evaluated for the treatment of three distinct hemolytic anemias. In addition to its active late-stage clinical pipeline, Agios has multiple novel, investigational therapies in clinical and preclinical development. 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 Agios' plans, strategies and expectations for the preclinical, clinical and commercial advancement of its drug development programs, including mitapivat; the potential benefits of Agios' products and product candidates, including 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. 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 failure of Agios to receive milestone or royalty payments related to the sale of its oncology business, the uncertainty of the timing of any receipt of any such payments, and the uncertainty of the results and effectiveness of the use of proceeds from the transaction; the impact of the COVID-19 pandemic 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 future approved products, and launching, marketing and selling 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 and 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 collaborations; 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, or SEC, including the risks and uncertainties set forth under the heading Risk Factors in our filings with the SEC. While the list of factors presented here is considered representative, this list should not be considered to be a complete statement of all potential risks and uncertainties. Any forward-looking statements contained in this communication are made only as of the date hereof, and we undertake no obligation to update forward-looking statements to reflect developments or information obtained after the date hereof and disclaim any obligation to do so other than as may be required by law.

Contacts

Investors:
Holly Manning, 617-844-6630
Senior Director, Investor Relations
Holly.Manning@agios.com

Media:
Jessica Rennekamp, 857-209-3286
Director, Corporate Communications
Jessica.Rennekamp@agios.com

Source: Agios Pharmaceuticals, Inc.