Agios Announces Clinical Proof-of-Concept in Phase 2a Trial of AG-946 for the Treatment of Anemia in Lower-Risk Myelodysplastic Syndromes

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– 40 Percent of Low Transfusion Burden Cohort Achieved Transfusion Independence; One Study Patient Achieved Hemoglobin Response Endpoint –

– Safety Profile Consistent with Data Reported in Healthy Volunteers Study –

– Company Expects to Initiate Phase 2b Study in Mid-2024 –

CAMBRIDGE, Mass., Nov. 20, 2023 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq: AGIO), a leader in the field of cellular metabolism pioneering therapies for rare diseases, today announced that clinical proof-of-concept has been achieved in the Phase 2a portion of a study of investigational pyruvate kinase (PK) activator AG-946 as a potential treatment for anemia in adults with lower-risk myelodysplastic syndromes (LR-MDS). Four of the 10 patients with low transfusion burden (LTB) achieved the transfusion independence endpoint, and one of the 22 patients treated in the study achieved the hemoglobin response endpoint in the 16-week treatment (core) period. The safety profile observed was consistent with data reported in the healthy volunteer study. Based on the favorable efficacy data and positive benefit-risk profile in the Phase 2a core period, Agios intends to advance its clinical program evaluating AG-946 in LR-MDS by initiating the placebo-controlled Phase 2b portion of the study in mid-2024.

“We are pleased with the results of the Phase 2a study, which underscore the potential of AG-946 to be a first-in-class, oral, safe and effective option for the treatment of anemia in adults with LR-MDS by improving red blood cell health through its unique mechanism of action. Regular blood transfusions are burdensome for patients. A meaningful reduction in transfusions allows patients to potentially decrease visits to the clinic and experience improved quality of life. We are grateful to all of the patients who participated in this trial, our collaborators, study investigators and advisors in the patient and clinical communities for their partnership in achieving this milestone, and we look forward to advancing the clinical program to Phase 2b,” said Sarah Gheuens, M.D., Ph.D., chief medical officer and head of R&D at Agios. “Agios is proud to be the leader in PK activation with two distinct PK activators – AG-946 and mitapivat – that have the potential to be meaningful treatment options for a wide range of blood disorders and positively impact many patients’ lives.”

A total of 22 patients enrolled in the Phase 2a portion of the study, including 12 classified as non-transfused (NTD) and 10 classified as LTB. Of the 22 patients enrolled in Phase 2a, 19 patients elected to continue to the extension period. Agios intends to complete a full evaluation of the Phase 2a data and assess the impact on the Phase 2b portion of the protocol, and present results of the Phase 2a portion of the study at a medical meeting in 2024.

Phase 2a Design
The open-label, proof-of-concept, Phase 2a portion of the study was designed to evaluate the safety and efficacy of AG-946 in adults with anemia due to lower-risk MDS. Patients with a documented diagnosis of MDS were eligible for the study if they met the Revised International Prognostic Scoring System (IPSS-R) classification of lower-risk disease (risk score: ≤3.5) and <5% blasts, as determined by the participant’s bone marrow biopsy/aspirate during the screening period, and if their hemoglobin concentration measured <11.0 g/dL during the 4-week screening period. Participants were classified as non-transfused (NTD) if they had received <3 red blood cell (RBC) units in the 16-week period before administration of the first dose of study drug and no transfusions in the 8-week period before administration of the first dose of study drug, or low transfusion burden (LTB) if they had received 3 to 7 RBC units in the 16-week period before administration of the first dose of study drug and <4 RBC units in the 8-week period before administration of the first dose of study drug. Participants with a high transfusion burden were not eligible for the Phase 2a portion of the study.

Participants received 5mg of oral AG-946 once daily for up to 16 weeks in the core period. At the discretion of the investigator, participants who completed the core period of the study are eligible to receive the same dose in an extension period for up to 156 weeks.

The two primary endpoints of the study were transfusion independence (for participants classified as LTB), defined as transfusion-free for ≥8 consecutive weeks during the core period, and hemoglobin response, defined as a ≥1.5 g/dL increase from baseline in the average hemoglobin concentration from Week 8 through Week 16.

Next month, Agios and its collaborators are presenting preclinical data supporting its MDS clinical development program – as well as additional data across the company’s additional therapeutic areas of focus, including PK deficiency, thalassemia and sickle cell disease – at the American Society of Hematology (ASH) Annual Meeting, which is being held December 9-12, 2023, in San Diego.

About Agios
Agios is the pioneering leader in PK activation and is dedicated to developing and delivering transformative therapies for patients living with rare diseases. In the U.S., Agios markets a first-in-class pyruvate kinase (PK) activator for adults with PK deficiency, the first disease-modifying therapy for this rare, lifelong, debilitating hemolytic anemia. Building on the company's deep scientific expertise in classical hematology and leadership in the field of cellular metabolism and rare hematologic diseases, Agios is advancing a robust clinical pipeline of investigational medicines with programs in alpha- and beta-thalassemia, sickle cell disease, pediatric PK deficiency and MDS-associated anemia. In addition to its clinical pipeline, Agios is advancing a preclinical TMPRSS6 siRNA as a potential treatment for polycythemia vera, and a preclinical PAH stabilizer as a potential treatment for phenylketonuria (PKU). For more information, please visit the company’s website at www.agios.com.

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 AG-946; Agios’ plans for the future clinical development of AG-946 in LR-MDS; and the potential benefit of its strategic plans and focus. The words “anticipate,” “expect,” “intend,” “potential,” “milestone,” “goal,” “will,” “on track,”

“upcoming,” 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. Moreover, there can be no guarantee that any medicines ultimately commercialized by Agios will receive commercial acceptance. 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 the COVID-19 pandemic 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; Agios' ability to obtain, maintain and enforce patent and other intellectual property protection for any product candidates it is developing; Agios’ ability to maintain key collaborations; uncertainty regarding any milestone or royalty payments related to the sale of its oncology business or its in-licensing of TMPRSS6 siRNA, and the uncertainty of the timing of any such payments; uncertainty of the results and effectiveness of the use of proceeds from the transaction with Servier; competitive factors; 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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