Agios Announces FDA Orphan Drug Designation Granted to Mitapivat for Treatment of Sickle Cell Disease

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CAMBRIDGE, Mass., Nov. 12, 2020 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation to the company's first-in-class pyruvate kinase R (PKR) activator mitapivat for the treatment of patients with sickle cell disease. Mitapivat is an investigational, oral, small molecule allosteric activator of wild-type and a variety of mutated PKR enzymes.

"Receiving orphan drug designation for mitapivat in sickle cell disease is an important recognition of the tremendous unmet need among this patient community, which has historically been underserved," said Chris Bowden, M.D., chief medical officer at Agios. "As the pioneers in PKR activation, we believe this mechanism has the potential to transform the course of sickle cell disease and are researching mitapivat's ability to improve red blood cell energy, health and longevity. We look forward to continued partnership with the sickle cell disease community and expect to initiate our Phase 3 study next year."

The FDA's Office of Orphan Drug Products grants orphan status to support the development of medicines for rare disorders that affect fewer than 200,000 people in the U.S. Orphan drug designation provides certain benefits, including market exclusivity upon regulatory approval if received, exemption of FDA application fees and tax credits for qualified clinical trials.

Mitapivat was previously granted orphan drug designation by the FDA and the European Medicines Agency for the treatment of pyruvate kinase (PK) deficiency, a rare, debilitating, hemolytic anemia, and by the FDA for the treatment of thalassemia.

Mitapivat Clinical Development
Mitapivat is being evaluated as a potential treatment for sickle cell disease under a Cooperative Research and Development Agreement (CRADA) with the U.S. National Institutes of Health. Mitapivat has been shown to decrease 2,3-diphosphoglycerate (2,3-DPG) and increase adenosine triphosphate (ATP), and through this mechanism, it may reduce hemoglobin S polymerization and red blood cell sickling. Preliminary clinical data establishing proof-of-concept for mitapivat in sickle cell disease were disclosed in June 2020, and updated data from this trial will be presented at the American Society of Hematology (ASH) Annual Meeting, which is being held virtually December 5–8, 2020. Agios expects to initiate a Phase 3, global, pivotal study of mitapivat in sickle cell disease in 2021.

In addition, Agios has two ongoing global, pivotal trials in adults with PK deficiency that are fully enrolled.

- ACTIVATE: A placebo-controlled trial with a 1:1 randomization evaluating mitapivat in patients who do not receive regular transfusions. The primary endpoint of the trial is hemoglobin response, defined as a sustained hemoglobin increase of ≥1.5 g/dL from baseline. Agios anticipates reporting ACTIVATE topline data by the end of 2020.
- ACTIVATE-T: A single arm trial evaluating mitapivat in patients who receive regular transfusions. The primary endpoint of the trial is the proportion of patients who achieve a reduction in transfusion burden compared to individual historical transfusion burden standardized to 24 weeks. Agios anticipates reporting topline ACTIVATE-T data in Q1 2021.

Agios is also conducting a Phase 2 study evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of treatment with mitapivat in adults with non-transfusion-dependent β- or α-thalassemia. The trial is fully enrolled, and the primary endpoint is hemoglobin response, defined as a ≥1.0 g/dL increase in Hb concentration from baseline. Agios expects to initiate a Phase 3 pivotal program evaluating mitapivat in thalassemia, including both α-and β-thalassemia, as well as transfusion dependent and non-transfusion dependent patient populations, in 2021.

Mitapivat is not approved for use by any regulatory authority.

About Agios
Agios is focused on discovering and developing novel investigational medicines to treat malignant hematology, solid tumors and rare genetic diseases through scientific leadership in the field of cellular metabolism. In addition to an active research and discovery pipeline across these three therapeutic areas, Agios has two approved oncology precision medicines and multiple first-in-class investigational therapies in clinical and/or 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 the potential benefits of mitapivat; Agios' plans regarding future data presentations; and the benefit of Agios' strategic plans and focus. The words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook," "goal", "potential" 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, a positive opinion on Agios' application for orphan drug designation for mitapivat is not a guarantee of approval. 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: risks and uncertainties related to 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 current or future approved products, and launching, marketing and selling current or future approved products; the results of Agios' 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 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 and conduct its current and future 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 maintain key collaborations; and general economic, market and global health 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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