Agios Establishes Proof-of-Concept for Mitapivat in Non-transfusion-dependent Thalassemia Based on Preliminary Phase 2 Results

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– Treatment with Mitapivat Induced Hemoglobin Increase of ≥1.0 g/dL in 7 of 8 Evaluable Patients –

– Safety Profile Consistent with Previously Published Phase 2 Data for Mitapivat in Patients with Pyruvate Kinase Deficiency –

– Additional Data for the Phase 2 Study of Mitapivat in Thalassemia to be Presented at a Medical Meeting in the First Half of 2020 –

– Company to Host ASH Investor Event and Webcast Monday, December 9 at 8:00 p.m. ET –

CAMBRIDGE, Mass., Dec. 08, 2019 (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 clinical proof-of-concept has been established based on a preliminary analysis of the Phase 2 trial of mitapivat (AG-348) in patients with non-transfusion-dependent thalassemia. Mitapivat is an investigational, first-in-class, oral, small molecule allosteric activator of wild-type and a variety of mutated pyruvate kinase-R (PKR) enzymes.

The Phase 2 study has enrolled 12 of the intended 17 patients (nine with β-thalassemia and three with α-thalassemia). As of the November 14, 2019 data cutoff date, eight patients, all with β-thalassemia, were evaluable for the primary endpoint of a hemoglobin increase of ≥1.0 g/dL from baseline in at least one assessment during Weeks 4-12. All eight patients were treated with 50 mg of mitapivat twice daily for the first six weeks and escalated to 100 mg twice daily, and all patients remain on treatment (range 12.4-34.3 weeks). Seven of eight efficacy evaluable patients achieved a hemoglobin increase of ≥1.0 g/dL, and for responders the mean hemoglobin increase from baseline was 1.76 g/dL (range, 0.9–3.3 g/dL) during Weeks 4-12. The majority of adverse events were Grade 1 or 2 and consistent with previously published Phase 2 data for mitapivat in patients with pyruvate kinase (PK) deficiency. Updated results from the Phase 2 thalassemia study will be presented at a medical meeting in the first half of 2020.

“These data demonstrate proof of concept that activation of wild-type PKR has the potential to convey clinical benefit in thalassemia and provides compelling evidence to broaden mitapivat clinical development in this disease,” said Chris Bowden, M.D., chief medical officer at Agios. “The safety and tolerability profile observed in this trial and in adults with pyruvate kinase deficiency supports the continued investigation of mitapivat treatment across severe, lifelong hemolytic anemias such as pyruvate kinase deficiency, thalassemia and sickle cell disease.”

Mitapivat Phase 2 Trial in Thalassemia
The ongoing Phase 2 study is evaluating the efficacy, safety, pharmacokinetics and pharmacodynamics of treatment with mitapivat in adults with non-transfusion-dependent β- and α-thalassemia (NTDT). This study includes a 24-week core period followed by a 2-year extension period for eligible participants. The primary endpoint is hemoglobin response. Approximately 17 participants with NTDT who have a baseline hemoglobin concentration of ≤10 g/dL will be enrolled. The initial dose of mitapivat is 50 mg twice daily with one potential dose-level increase to 100 mg twice daily, at the week six visit based on the participant's safety and hemoglobin (Hb) concentrations. With a total of 17 patients enrolled, the study would have 80% power to reject a ≤30% response rate at a one-sided 0.05 type 1 error rate.

Mitapivat Clinical Development
Agios has two ongoing global, pivotal trials in adults with PK deficiency that are on track to complete enrollment by year-end 2019. Learn more at activatetrials.com.

- ACTIVATE: A placebo-controlled trial with a 1:1 randomization, expected to enroll approximately 80 patients who do not receive regular transfusions. The primary endpoint of the trial is the proportion of patients who achieve a sustained hemoglobin increase of ≥1.5 g/dL.
- ACTIVATE-T: A single arm trial of up to 40 regularly transfused patients with a primary endpoint of reduction in transfusion burden over six months compared to individual historical transfusion burden over prior 12 months.

In addition to the thalassemia Phase 2 study, mitapivat is being studied in sickle cell disease under a Cooperative Research and Development Agreement (CRADA) with the U.S. National Institutes of Health.

Mitapivat is not approved for use by any regulatory authority.

Investor Event and Webcast Information
Agios will host an investor event on Monday, December 9, 2019 at 8:00 p.m. ET in Orlando, Fla. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors 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 Agios
Agios is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic diseases through scientific leadership in the field of cellular metabolism. In addition to an active research and discovery pipeline across both therapeutic areas, Agios has two approved oncology precision medicines and multiple first-in-class investigational therapies in clinical and/or preclinical development. All Agios programs focus on genetically identified patient populations, leveraging our knowledge of metabolism, biology and genomics. 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 for the further clinical development of mitapivat and Agios' strategic plans and prospects. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "would," "could," "potential," "possible," "hope" 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; that positive safety and efficacy findings observed in early stage clinical trials will be replicated in later stage trials; 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: 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 and 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 maintain key 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. 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.

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