Agios Pharmaceuticals Announces Early Phase 1 Data Showing Clinical Activity of AG-120 as a Single Agent in Advanced Acute Myeloid Leukemia (AML)

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-Significant Clinical Responses and Reduction of 2HG Biomarker Provide Early Validation of Mutant IDH1 as a Therapeutic Target in AML -

-Data Support Initiation of Multiple Expansion Cohorts in the First Half of 2015-

CAMBRIDGE, Mass. and BARCELONA, Spain, Nov. 18, 2014 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO), a leader in the fields of cancer metabolism and rare genetic disorders of metabolism, today announced the first reported safety and clinical activity for AG-120 from the ongoing Phase 1 dose escalation study in patients with IDH1-mutant positive advanced hematologic malignancies, including acute myeloid leukemia (AML). Agios has exclusive U.S. development and commercial rights to AG-120, a first-in-class, oral, selective, potent inhibitor of the mutant IDH1 enzyme. Daniel Pollyea, M.D., clinical investigator at the University of Colorado School of Medicine, will present the data in a late-breaking oral presentation today at the 26th Annual EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics being held in Barcelona, Spain. The company will webcast an investor conference call from the symposium at 10:00 a.m. EST (4:00 p.m. CET) on Wednesday, November 19, 2014.

As of October 17, 2014, the ongoing Phase 1 trial for AG-120 had enrolled 17 patients with a documented IDH1 mutation whose cancer relapsed or failed to respond (refractory) to at least one prior treatment regimen. At the time of the data cut, 14 patients with relapsed and/or refractory AML were evaluable; three patients recently initiated therapy and were not evaluable.

The initial data showed investigator assessed objective responses in seven out of 14 evaluable patients, including four complete remissions, with responses observed across the four dose levels tested, and early evidence of durability. One additional patient remains stable on study. AG-120 was well tolerated, with the majority of adverse events reported as mild to moderate. The maximum tolerated dose has not yet been reached. One patient had a dose limiting toxicity of asymptomatic grade 3 QT prolongation at the highest dose tested to date, which improved to grade 1 after AG-120 dose reduction according to treatment protocol. This patient is in complete remission and remains on AG-120. AG-120 showed favorable drug exposure and pharmacokinetics at all doses tested and also substantially reduced plasma levels of the oncometabolite 2-hydroxyglutarate (2HG), which is produced by the mutant IDH1 protein, to the level observed in healthy volunteers. The mechanism of response is consistent with differentiation, as evidenced by the maturation of the leukemic cells into infection fighting white blood cells, or neutrophils. Based on these findings, the company plans to initiate multiple expansion cohorts in the first half of 2015.

"These data show very promising evidence of clinical activity for AG-120 in AML patients with an IDH1 mutation," said Chris Bowden, M.D., chief medical officer of Agios Pharmaceuticals. "Together with the data we reported from our ongoing Phase 1 study of AG-221 in advanced hematologic cancers, our lead investigational medicine and an IDH2-mutant inhibitor, we believe IDH inhibitors could potentially change the treatment paradigm for AML patients with these mutations. We look forward to moving rapidly into multiple expansion cohorts in the first half of 2015 to further characterize the potential of AG-120."

"We are highly encouraged to see the early favorable safety profile and clinical activity of AG-120, which includes four patients who achieved complete remission," said Dr. Pollyea. "For the first time in decades, we have the potential to offer certain AML patients an improved targeted treatment for this fatal disease that has historically had limited treatment options. I am hopeful that in the future we clinicians will be able to offer well tolerated and highly effective targeted therapies for our patients who have AML harboring an IDH mutation."

Patients in the ongoing Phase 1 trial have advanced AML whose cancer was refractory to available medical treatments or relapsed after treatment. The primary objectives of the Phase 1 trial are to determine the maximum tolerated dose (MTD) and the recommended dose for further study of AG-120. Secondary objectives include characterization of the safety profile, pharmacokinetics, pharmacodynamics and early anti-tumor activity. The trial uses an open-label, dose escalating design. Patients have been enrolled to date in four cohorts of AG-120 administered at 100 mg twice a day, 300 mg once a day, 500 mg once a day and 800 mg once a day. The median age of these patients is 73 (range 42-87).

Early Safety Data

A data analysis conducted as of October 17, 2014 showed the majority of adverse events (AEs) reported by investigators were grade 1 and 2 and most commonly included nausea, fatigue and dyspnea. Serious AEs were reported in eight patients and were primarily related to disease progression. There were six patient deaths, all unrelated to study drug – five deaths occurred after discontinuation of AG-120 due to progressive disease and one patient died due to disease-related intracranial hemorrhage while on treatment. One patient had a dose limiting toxicity of asymptomatic grade 3 QT prolongation at the highest dose tested to date, which improved to grade 1 with dose reduction subject to treatment protocol. This patient is in complete remission and remains on AG-120. Dose escalation continues in a once-daily regimen. The maximum tolerated dose has not been achieved.

Early Efficacy Data as of October 17, 2014

- Of the 14 evaluable patients, seven patients achieved investigator assessed objective responses, including four complete remissions, two marrow complete remissions and one partial remission. Responses were observed at all dose levels tested. In the four patients who achieved a complete remission, early evidence of durability was observed ranging from 15 days to five months. All responding patients remain on AG-120.
- One patient with stable disease remains on AG-120.
- There have been no patient relapses as of the data cut-off after objective response was achieved.
- Treatment with AG-120 showed substantial lowering of 2HG to levels observed in healthy volunteers.

Investor Event and Webcast

Agios plans to host a conference call and webcast on Wednesday, November 19 at 4:00 p.m. CET (10:00 a.m. EST) to review the Phase 1 clinical data for AG-120 being presented at the symposium. To participate in the conference call, please dial 1-877-377-7098 (domestic) or 1-631-291-4547 (international) and refer to conference ID 31391928. A replay of the call will be available approximately two hours after the conclusion of the call. The webcast can be accessed live or in archived form under "Events & Presentations" in the Investors & Media section of the company's website at www.agios.com.

AG-120 Clinical Development Plans

The company plans to advance into the next phase of development with the initiation of multiple expansion cohorts within this Phase 1 trial at a fixed dose in the first half of 2015. AG-120 is also currently being studied in a Phase 1 trial in patients with advanced solid tumors whose cancers carry an IDH1 mutation. Agios expects to present data from the Phase 1 advanced solid tumor trial at a medical conference in 2015.

AG-120 is a part of Agios' global strategic collaboration with Celgene Corporation, an integrated global biopharmaceutical company. Agios has exclusive U.S. development and commercial rights for AG-120, and Celgene has an exclusive option to the ex-U.S. rights. Celgene has also licensed worldwide development and commercialization rights for AG-221. Agios continues to conduct early clinical development activities within the AG-221 development program.

About IDH Mutations and Cancer

IDH1 and IDH2 are two metabolic enzymes that are mutated in a wide range of hematologic and solid tumor malignancies, including AML. Normally, IDH enzymes help to break down nutrients and generate energy for cells. When mutated, IDH creates a molecule that alters the cells' genetic programming, and instead of maturing, the cells remain primitive and proliferate quickly. Agios believes that inhibition of these mutated proteins may lead to clinical benefit for the subset of cancer patients whose tumors carry them. AG-120 and AG-221 were developed by Agios as a selective, potent inhibitor of the mutated IDH1 and IDH2 protein, respectively.

About Acute Myelogenous Leukemia (AML)

AML, a cancer of blood and bone marrow characterized by rapid disease progression, is the most common acute leukemia affecting adults. Undifferentiated blast cells proliferate in the bone marrow rather than mature into normal blood cells. AML incidence significantly increases with age, and according to the American Cancer Society the median age is 66. Less than 10 percent of U.S. patients are eligible for bone marrow transplant, and the vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory AML. The five-year survival rate for AML is approximately 20 to 25 percent. IDH1 mutations are present in about 6-10 percent of AML cases. IDH mutations are also found in solid tumor cancers, including glioma, chondrosarcoma and intrahepatic cholangiocarcinoma.

About Agios Pharmaceuticals, Inc.

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and inborn errors of metabolism, or IEMs, which are rare genetic metabolic 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 multiple first-in-class lead product candidates in cancer metabolism and IEMs 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 our 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' expectations and beliefs about: the potential of IDH1/IDH2 as therapeutic targets; the potential benefits of Agios' product candidates AG-221 and AG-120, including the potential for AG-120 to effectively treat AML patients with an IDH1 mutation; its plans and timelines for the clinical development and data presentation of AG-221 and AG-120; and the benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "could," "would" 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: 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, such as its agreement with Celgene; and general economic and market conditions. These and other risks are described in greater detail under the caption "Risk Factors" included in Agios' Quarterly Report on Form 10-Q for the quarter ended September 30, 2014, and other filings that Agios may make with the Securities and Exchange Commission in the future. 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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