Agios Announces Data from Dose-Escalation Phase 1 Study of AG-120 in Patients with IDH1 Mutant Positive Advanced Solid Tumors

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- Safety Profile Confirmed; Signs of Clinical and Biological Activity Observed; Recommended Phase 2 Dose Selected -

- Phase 1 Expansion Cohorts for Patients with IDH1 Mutant Positive Glioma, Cholangiocarcinoma, Chondrosarcoma and Other Advanced Solid Tumors Are Open and Enrolling -

- Randomized Phase 2 Study of AG-120 in Cholangiocarcinoma Planned for 2016 -

- Company to Host Investor Event and Webcast Today -

CAMBRIDGE, Mass., Nov. 8, 2015 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO), a leader in the fields of cancer metabolism and rare genetic metabolic disorders, today announced the first data from the dose-escalation portion of the ongoing Phase 1 study evaluating single agent AG-120, a first-in-class, oral, selective, potent inhibitor of mutant isocitrate dehydrogenase-1 (IDH1), in advanced solid tumors. The data are being presented today at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics in Boston. AG-120 is being developed in collaboration with Celgene.

"Glioma, cholangiocarcinoma and chondrosarcomas are all extremely difficult-to-treat diseases with limited therapeutic options," said Howard Burris, M.D., Sarah Cannon Research Institute, an investigator for the study. "Today's Phase 1 dose-escalation data are encouraging, as they confirm a well-tolerated safety profile and show signals of clinical activity that support further evaluation in patients with IDH1 mutant positive solid tumors."

"We are excited to present the first data from AG-120 in solid tumors as we explore the novel mechanism of action of our IDH inhibitors in these indications," said Chris Bowden, M.D., chief medical officer at Agios. "These early data suggest that inhibiting mutant IDH1 can alter the biology of these diseases, and we are committed to moving AG-120 forward into the next phase of clinical development."

This ongoing Phase 1 trial is assessing the safety and tolerability of AG-120 in advanced solid tumors, including glioma, intrahepatic cholangiocarcinoma (IHCC) and chondrosarcomas that harbor an IDH1 mutation in a dose-escalation phase followed by an expansion phase. As of September 3, 2015 (data cut-off), 62 patients have been treated with single agent AG-120, and 25 patients remain on treatment. Data reported at the meeting are from patients who received AG-120 administered from 200 mg to 1200 mg total daily doses in the dose-escalation arm. The median age of these patients is 56 (ranging from 23-88). Over half of the patients enrolled had high-grade tumors and received a median of three prior lines of therapy (ranging from one to six).

Safety Data

The safety analysis conducted for all 62 treated patients as of September 3, 2015 demonstrated that AG-120 was well-tolerated with a favorable safety profile in advanced solid tumors including glioma, IHCC and chondrosarcoma. Specifically the analysis showed:

- No dose limiting toxicities have been observed.
- The majority of adverse events reported by investigators were mild to moderate, with the most common being nausea, diarrhea, vomiting, anemia and QT prolongation.
- The majority of serious adverse events (SAE) were disease-related.
- A maximum tolerated dose (MTD) has not been reached.

Efficacy Data

Agios also analyzed efficacy data from 55 response-evaluable patients as of September 3, 2015, which showed:

- Treatment with AG-120 showed substantial reduction of the oncometabolite 2-hydroxglutarate (2HG) in plasma and tumor tissue.
- Imaging (magnetic resonance spectroscopy) results suggest that AG-120 can lower 2HG in the brain.
- Chondrosarcoma: Seven of the 11 patients with IDH1 mutant positive chondrosarcoma had stable disease. Five of these patients maintained stable disease for six months or more. The six-month clinical benefit response rate was 5/9 or 56 percent.
- IHCC: One out of 20 patients with IDH1 mutant positive IHCC had a partial response (PR) and 11 patients had stable disease. Six of these patients, including one with a PR and five with stable disease, maintained their response for six months or more. The six-month clinical benefit response rate was 6/14 or 43 percent.
- Glioma: Ten out of 20 patients with IDH1 mutant positive glioma had stable disease. Four of these patients maintained stable disease for six months or more. The six-month clinical benefit response rate was 4/16 or 25 percent.
- Other: One of the four patients with other IDH1 mutant positive solid tumors had stable disease.

Next Steps for AG-120 in Solid Tumors

- Currently enrolling four expansion cohorts of 25 patients each, who receive the recommended dose of 500 mg of AG-120 once daily, with:
    - Low grade glioma with ≥ six months of prior scans to assess volumetric changes
    - Second-line cholangiocarcinoma
    - High grade (metastatic) chondrosarcoma
    - Other solid tumors with an IDH1 mutation
- Initiate a randomized Phase 2 study of AG-120 in cholangiocarcinoma in 2016.

Investor Event and Webcast Information

Agios will host an investor event with Dr. Howard Burris today at 1:00 p.m. ET in Boston to review data presented at the conference. 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. A replay of the webcast will be archived on the Agios website for approximately 30 days following the presentation.

About Chondrosarcoma

Chondrosarcoma is a heterogeneous group of cancers that arise from cartilage in the bone and joint. It is the most common type of bone cancer with 700-1,000 people diagnosed per year in the U.S. IDH1/2 mutations occur in 40-50 percent of central chondrosarcomas. The prognosis is based on disease burden – for localized disease, there is curative potential with surgery, but metastatic disease has a low five-year survival rate. Radiation is not effective, and chemotherapy is of limited benefit and primarily used to convert non-resectable cancer to resectable. Treatment for metastatic disease is mainly palliative.

About Intrahepatic Cholangiocarcinoma (IHCC)

IHCC occurs within the liver, and the prognosis is worse than for other biliary tract tumors. The incidence of IHCC is increasing due to cirrhosis, alcoholic liver disease and hepatitis C. IHCC has a poor five-year survival rate, with 15-30 percent for local disease and 2 percent for metastatic disease. IDH1/2 mutations are present in approximately 25 percent of IHCCs. Surgery is the only chance for curing localized disease. Surgery, radiation and chemotherapy are palliative for metastatic disease.

About Glioma

Glioma presents in varying degrees of tumor aggressiveness, ranging from slower growing (low grade glioma) to rapidly progressing (high grade glioma). Common symptoms include memory disturbance, sensory impairment neurologic deficits and seizures. The long-term prognosis is poor with a five-year survival rate of 33 percent. Median survival is 12-15 months for glioblastoma and 2-5 years for anaplastic glioma. IDH1 mutations are highly prevalent.

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. Normally, IDH enzymes help to break down nutrients and generate energy for cells. When mutated, IDH increases production of an oncometabolite 2-hydroxyglutarate (2HG) that alters the cells' epigenetic programming, thereby promoting cancer. 2HG has been found to be elevated in several tumor types. Agios believes that inhibition of the mutated IDH proteins may lead to clinical benefit for the subset of cancer patients whose tumors carry them.

About Agios

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and rare genetic disorders of metabolism 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 investigational medicines in cancer metabolism and rare genetic disorders of metabolism in clinical and/or preclinical development. All Agios programs focus on genetically identified patient populations, leveraging the company's knowledge of metabolism, biology and genomics. For more information, please visit Agios' 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 Agios' product candidates targeting IDH mutations, including AG-120; its plans for the clinical development of AG-120; its plans regarding future data presentations; and the benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "hope," "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, 2015, 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.

CONTACT: Renee Leck, Senior Manager,
Investor Relations and Public Relations
Renee.Leck@agios.com
617-649-8299

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