Agios Announces Phase 1 Data from Dose Expansion Cohorts of AG-120 in Patients with IDH1 Mutant Positive Glioma and Chondrosarcoma

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- Durable Stable Disease Observed for Patients with Non-enhancing Low Grade Glioma and Chondrosarcoma Patients; 42% of Glioma Patients Still on Treatment -

- AG-120 Well-tolerated in Pre-Treated Populations -

- Potential for Centralized Volumetric Assessments to Shape Future Development in Glioma -

CAMBRIDGE, Mass., Nov. 18, 2016 (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 expansion cohorts of the Phase 1 study evaluating single agent AG-120 in isocitrate dehydrogenase-1 (IDH1) mutant positive glioma and chondrosarcoma. The glioma data were presented today at the Society for Neuro-Oncology (SNO) Annual Meeting in Scottsdale, AZ and the chondrosarcoma data were presented last week at the annual meeting of the Connective Tissue Oncology Society (CTOS) in Lisbon, Portugal.

“Glioma and chondrosarcomas are extremely difficult-to-treat diseases where patients are in need of new therapies,” said Chris Bowden, M.D., chief medical officer at Agios. “These Phase 1 dose expansion data are encouraging, as they continue to demonstrate a well-tolerated safety profile for AG-120 at a fixed daily dose of 500 mg. The prolonged stable disease in both patient populations is encouraging in light of AG-120’s unique differentiation mechanism of action. In addition, our initial experience utilizing centralized volumetric assessments in patients with glioma has been informative, and along with our ongoing AG-881 Phase 1 trial, will help determine the next steps in clinical development.”

“In glioma, AG-120 has the potential to help a large number of patients with IDH1 mutations,” said Ingo Mellinghoff, M.D., Memorial Sloan Kettering Cancer Center, an investigator for the study. “The SNO presentation is the first look at data for AG-120 in a defined cohort of glioma patients where we evaluated the potential for volumetric analyses to improve our understanding of the response patterns beyond the conventional bi-dimensional methods. This methodology could be instrumental in developing more effective, targeted therapies for patients with this disease.”

The 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. The dose-escalation phase was followed by four expansion cohorts in the following patient groups.

1. Low grade glioma with ≥ 6 months prior scans
2. High grade (metastatic) chondrosarcoma
3. 2nd-line cholangiocarcinoma
4. Solid tumors not eligible for cohorts 1-3

Enrollment is now complete for the dose escalation and expansion cohorts.

Glioma Expansion Data Presented at SNO Annual Meeting

As of the August 1, 2016 data cut off, 66 patients have been treated with single agent AG-120, and 28 patients (42%) remain on treatment.

- Data reported are from 20 patients who received AG-120 administered from 200 mg to 1200 mg total daily doses in the dose-escalation phase.
- Forty-six patients who received 500 mg daily doses of AG-120 administered in two expansion cohorts, including 24 patients enrolled in a cohort with non-enhancing glioma and 22 glioma patients with enhancing disease enrolled in a basket cohort.
- The median age of these patients is 41 (ranging from 21-71).
- The median number of prior therapies was two (ranging from one to six) and included temozolomide (71%). Seventy-four percent of patients received radiotherapy.

A safety analysis conducted for all 66 treated patients as of the data cut-off demonstrated that AG-120 was well-tolerated with a favorable safety profile in glioma patients.

- No dose limiting toxicities have been observed.
- The majority of adverse events reported by investigators were mild to moderate, with the most common being headache, nausea, diarrhea and vomiting.
- There were 11 patients with serious adverse events (SAE) and none of them were drug-related.

Efficacy data from 65 response-evaluable patients as of the data cut-off showed:

- Two patients had a minor response according to the Response Assessment in Neuro-Oncology for low grade glioma (RANO-LGG).

- Forty-one (63%) patients had stable disease, including 27 with non-enhancing disease; the median treatment duration for non-enhancing glioma was 8.1 months (ranging from 1.4 – 17.8 months).
- Volumetric analysis conducted centrally demonstrated stabilization or a decrease in tumor growth rate compared to the pretreatment rate in 64% (n=14 of 22) of glioma patients with non-enhancing disease receiving AG-120 and requires further development as a response evaluation tool.

Chondrosarcoma Expansion Data Presented at CTOS Annual Meeting

Agios also analyzed data from 21 chondrosarcoma patients as of September 23, 2016 in the dose escalation (n=12) and expansion cohorts (n=9) and 7 remain on treatment.

- Doses received were 100 mg twice daily, and 300, 400, 500, 600, 800, 900 and 1200 mg once a day. Expansion cohort patients received 500 mg once a day. Median treatment duration was 2.6 months (ranging from 0.0–24.4 months).
- Prior therapy included surgery (57%), radiotherapy (33%) and chemotherapy (24%). The median number of prior systemic therapies was one (ranging from one to five).
- No dose-limiting toxicities were reported; the majority of adverse events reported by investigators were mild to moderate, with the most common being diarrhea, nausea, decreased appetite, QT prolongation and fatigue.
- Most SAEs were considered unrelated to treatment with one case of hypophosphatemia (low phosphorous blood level) considered to be possibly related to treatment.
- Of 20 response-evaluable patients, 11 (55%) experienced stable disease as their best response; the 3-month progression-free survival rate was 58%.
- Baseline plasma levels of the oncometabolite D-2-hydroxyglutarate (2-HG) were elevated above the healthy volunteer range. Treatment with AG-120 resulted in significant reduction of plasma 2-HG compared to baseline. Up to 99.7% tissue 2-HG reduction was documented in paired biopsies obtained from 3 patients treated with AG-120. Together these data indicate the on-target pharmacodynamic effects of AG-120.

About Glioma
Glioma presents in varying degrees of tumor aggressiveness, ranging from slower growing (low grade glioma) to rapidly progressing (high grade glioma-Glioblastoma Multiforme). Common symptoms include seizures, 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, accounting for approximately 68-74 percent of low grade glioma and secondary glioblastoma.

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 approximately 46-63 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. Treatment for metastatic disease is mainly palliative.

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 of IDH1/IDH2 as therapeutic targets; the potential benefits of Agios' product candidates targeting IDH1/IDH2, including AG-120 and AG-881; its plans regarding future data presentations; and the potential benefit of its strategic plans and focus. 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, 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 agreements 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, 2016, 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, except as required by law.

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