Agios Presents Updated Phase 1 Data from Dose Expansion Cohort of Ivosidenib (AG-120) in Patients with IDH1 Mutant Positive Glioma

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- Durable Stable Disease and Reduction of Tumor Growth Rates Observed for Patients with Low Grade Glioma; Median Treatment Duration of 16 Months with 51% of Patients Still on Treatment –

- Ivosidenib Well-tolerated in Patients with Low Grade Glioma-

- Additional Preclinical Data Demonstrate that Ivosidenib and AG-881 Suppress 2-HG Levels in Brain Tumor Mouse Models -

SAN FRANCISCO, Nov. 17, 2017 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today presented updated data from the dose expansion cohort of the Phase 1 study evaluating single agent ivosidenib in patients with progressive low grade isocitrate dehydrogenase-1 mutant (IDH1m) glioma. The data were presented today in an oral presentation at the Society for Neuro-Oncology (SNO) Annual Meeting in San Francisco.

“Glioma is a difficult-to-treat disease with many patients diagnosed at a young age and exposed to surgery, radiation and chemotherapy and their associated side effects,” said Ingo Mellinghoff, M.D., Memorial Sloan Kettering Cancer Center, an investigator for the study. “The median treatment duration of 16 months and reduction in tumor growth rates compared to a pre-treatment interval is a signal of ivosidenib’s clinical activity in this population. I look forward to working with Agios and the neuro-oncology community to further refine imaging methodology and to assess the biological effects of IDH inhibitors in a perioperative study planned for the first half of 2018.”

Ivosidenib is being evaluated in an ongoing Phase 1 dose escalation and expansion trial in advanced IDH1 mutant positive solid tumors, including glioma. Enrollment was completed in January 2016 and data from the glioma dose escalation and expansion cohorts were presented in November 2016. An update on patients with non-enhancing glioma is reported below.

As of the May 12, 2017 data cut off, 35 patients (11 from escalation, 24 from expansion) with non-enhancing disease have been treated with single agent ivosidenib. Eighteen patients (51%) remain on treatment.

- Twenty-four patients had World Health Organization (WHO) classified Grade 2 tumors, eight had Grade 3 tumors, one had a Grade 4 tumor and two were unknown.
- Patients received daily doses of ivosidenib ranging from 300 mg to 900 mg. Twenty-eight patients received a daily dose of 500 mg, which was selected as the expansion dose.
- The median age of these patients is 38 (ranging from 21-71).
- The median treatment duration was 16 months (ranging from 1.4 – 27.1 months).
- The median number of prior therapies was 2 (ranging from one to five). The median duration of last systemic therapy was 9.6 months.
    - Sixty-three percent of patients had previously received temozolomide and 57% percent had previously received radiotherapy.

A safety analysis conducted for all 35 treated non-enhancing glioma patients as of the data cut-off demonstrated that ivosidenib was well-tolerated with a favorable safety profile in glioma patients.

- No dose limiting toxicities were observed.
- The majority of adverse events reported by investigators were mild to moderate, with the most common being headache, diarrhea, nausea and vomiting.
- There were 5 patients with serious adverse events (SAE) and all were deemed unrelated to study treatment.

Efficacy data from all 35 non-enhancing glioma patients as of the data cut-off showed:

- Two patients had a minor response by investigator assessment according to the Response Assessment in Neuro-Oncology for low grade glioma (RANO-LGG).
- Twenty-nine (83%) patients had stable disease.
- The median progression free survival (PFS) for all non-enhancing patients was 13 months, the median PFS for Grade 2 patients (n=24) has not been reached.
- For patients in the expansion arm (n=24), the average six-month tumor growth was 24% prior to treatment and 11% following treatment with ivosidenib.

In addition, preclinical data for ivosidenib and AG-881, a brain-penetrant pan-IDH inhibitor, in an orthotopic mouse xenograft model of human mIDH1-R132H glioma are also being presented as posters.

- Preliminary data suggest that both molecules suppress the oncometabolite D-2-hydroxyglutarate (2-HG) in an orthotopic

brain tumor model.
- At the doses explored, treatment with ivosidenib resulted in 85% maximal 2-HG inhibition and treatment with AG-881 resulted in >98% inhibition of 2-HG levels.
- Neither molecule impeded the therapeutic effect of concomitant or sequenced radiation therapy.

"We are encouraged by both the ivosidenib clinical data demonstrating prolonged stable disease in patients with progressive, low grade glioma and the preclinical data with ivosidenib and AG-881 demonstrating reductions in the oncometabolite 2-HG," said Chris Bowden, M.D., chief medical officer of Agios. "We look forward to quantitatively assessing 2-HG and other biomarker effects with both molecules in our planned perioperative study."

Next Steps in Glioma

On November 1st, 2017, Agios announced plans to initiate a perioperative 'window' study in the first half of 2018 with ivosidenib and AG-881 in approximately 45 low grade glioma patients with progressive disease to further investigate their effects on brain tumor tissue. Patients will be randomized to either ivosidenib or AG-881 and treated for four weeks prior to previously scheduled surgery. An additional five patients will serve as a control arm. The study is designed with the following objectives:

- To determine the amount of drug penetration in the brain
- To confirm the magnitude of IDH target engagement as measured by 2HG levels in brain tumor tissue
- To assess the impact of IDH inhibition on differentiation and epigenetic profiles in tumor tissue and
- To assess the safety of both molecules.

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 and neurologic deficits. 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 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 an approved oncology precision medicine 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.

About Agios/Celgene Collaboration
IDHIFA® (enasidenib) and AG-881 are part of Agios' global strategic collaboration with Celgene Corporation focused on cancer metabolism. Under the terms of the 2010 collaboration agreement, Celgene has worldwide development and commercialization rights for IDHIFA® (enasidenib). Agios continues to conduct certain clinical development activities within the IDHIFA® (enasidenib) development program and is eligible to receive reimbursement for those development activities and up to $95 million in remaining payments assuming achievement of certain milestones, and royalties on any net sales. Celgene and Agios are currently co-commercializing IDHIFA® (enasidenib) in the U.S. Celgene will reimburse Agios for costs incurred for its co-commercialization efforts. For AG-881, the companies have a joint worldwide development and 50/50 profit share collaboration, and Agios is eligible to receive regulatory milestone payments of up to $70 million. The program focused on MTAP (methylthioadenosine phosphorylase)-deleted cancers is part of a 2016 global co-development and co-commercialization agreement with Celgene focused on metabolic immuno-oncology. Celgene has the option to participate in a worldwide 50/50 cost and profit share with Agios, under which Agios is eligible for up to $169 million in clinical and regulatory milestone payments for the program.

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 ivosidenib and AG-881; Agios' plans for the further clinical development of ivosidenib and AG-881; 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, 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' 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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