Agios Presents Data from Phase 1 Dose-Escalation Study of AG-881 in Patients with IDH Mutant Positive Advanced Glioma and Other Solid Tumors

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- Favorable Safety Profile at Dose Levels Below 100 mg; 10 mg and 50 mg Doses Under Evaluation in Recently Initiated Glioma Perioperative Study -

- Evidence of Prolonged Disease Control Observed in Non-Enhancing Glioma Population with a Median Treatment Duration of 12 Months -

CHICAGO, June 01, 2018 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ:AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today presented the first data from the ongoing Phase 1 study evaluating single agent AG-881 in advanced glioma and other solid tumors. The data were featured in an oral presentation at the American Society of Clinical Oncology (ASCO) Annual Meeting. AG-881 is an investigational, oral, selective, potent inhibitor of mutant isocitrate dehydrogenase-1 (IDH1) and IDH2 enzymes, which was designed for enhanced brain penetrance for development in IDH-mutant glioma.

“IDH mutant glioma is a distinct disease where patients are typically diagnosed in their thirties and forties and endure a deteriorating quality of life from the side effects associated with multiple rounds of surgery, radiation and chemotherapy and ultimately die of their disease,” said Ingo Mellinghoff, M.D., Memorial Sloan Kettering Cancer Center, an investigator for the study. “The AG-881 Phase 1 dose-escalation data are encouraging, as they demonstrate a favorable safety profile at lower dose levels and show signals of clinical activity that support further evaluation of the role of inhibiting mutant IDH in low-grade glioma.”

“With no curative or approved targeted therapies for low-grade glioma and a poor long-term prognosis, we are committed to exploring the novel mechanism of action of our IDH inhibitors in this indication,” said Chris Bowden, M.D., chief medical officer at Agios. “Data from our ivosidenib and AG-881 Phase 1 trials and the ongoing perioperative study, combined with feedback from regulators and the neurology community, will inform our pivotal development plan.”

The ongoing Phase 1 dose-escalation trial is assessing the safety and tolerability of AG-881 in IDH1/2 mutant advanced solid tumors, including glioma. As of the March 29, 2018 data cut-off, 93 patients (52 with glioma and 41 with other solid tumors) have been treated with single agent AG-881. Enrollment is complete and 17 glioma patients and 1 non-glioma solid tumor patient remain on treatment. Study design, status and baseline characteristics for the 52 glioma patients are reported below.

- Forty-eight percent of patients (n=25) had World Health Organization (WHO) classified Grade 2 tumors, 42% (n=22) had Grade 3 tumors, 8% (n=4) had Grade 4 tumors and 2% (n=1) was unknown.
- Ninety-two percent of patients (n=48) had an IDH1 mutation and 6% (n=3) had an IDH2 mutation. One patient did not have a biopsy but was confirmed as IDH mutant positive due to 2-HG elevation by magnetic resonance spectroscopy (MRS).
- The median age of these patients is 42.5 years (ranging from 16-73 years).
- Patients received a median of two prior systemic therapies (ranging from one to six).
  -- Seventy-three percent of patients (n=38) had previously received temozolomide and 58% percent (n=30) had previously received radiotherapy.
- Patients received daily doses of AG-881 ranging from 10 mg to 300 mg.
- The median treatment duration was seven months (ranging from 0-27 months) for all glioma patients, 12 months (ranging from 1-27 months) for non-enhancing glioma and 3 months (ranging from 0- 27 months) for patients with enhancing disease.

Safety Data

The safety analysis conducted for all 93 treated patients as of the data cut-off demonstrated that AG-881 has a favorable safety profile at dose levels below 100 mg.

- The majority of adverse events (AEs) reported by investigators were mild to moderate, with the most common (>33%) being fatigue, nausea, increases in alanine aminotransferase (ALT) and increases in aspartate aminotransferase (AST).
- Grade 3 or higher AEs were observed in 33% of all patients (n=31).
- Dose limiting toxicities (DLTs) of Grade 2 or higher elevated transaminases occurred in five glioma patients at the higher dose levels (≥100 mg) and resolved to Grade ≤1 with dose modification or discontinuation. There were no treatment-related on-treatment deaths.
- A maximum tolerated dose (MTD) was not reached by Bayesian model; the doses chosen for further clinical development were based on safety, pharmacokinetics and pharmacodynamics data.

Efficacy Data

Efficacy data from the 52 glioma patients (23 with non-enhancing and 29 with enhancing disease) as of the data cut-off showed:

- One patient with non-enhancing disease and a 1p19q co-deletion had a sustained minor response according to the

investigator by Response Assessment in Neuro-Oncology for low grade glioma (RANO-LGG) and remains on treatment.
- Seventy-five percent of patients (n=39) had a best response of stable disease, including 20 patients with non-enhancing disease.
- Thirty-five percent of patients (n=18, including 13 patients with non-enhancing disease) remained on treatment for ≥1 year.

Efficacy data from the 41 patients with non-glioma solid tumors as of the data cut-off showed:

- One patient with cholangiocarcinoma had a partial response, 37% of patients (n=15) had stable disease and 44% (n=18) had progressive disease.
- The median treatment duration was 2 months (ranging from 0-18 months).

Ongoing Perioperative Study in Glioma
A perioperative 'window' trial with ivosidenib and AG-881 (10 mg and 50 mg) in up to 45 IDH1m non-enhancing low-grade glioma patients is ongoing. The goal of the trial is to confirm CNS penetrance and tumor 2-HG suppression of ivosidenib and AG-881 as part of the strategy to finalize pivotal development plans by year-end 2018.

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. Approximately 11,000 low-grade glioma patients are diagnosed annually in the U.S. and EU and approximately 80 percent have an IDH1 mutation.

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
AG-881 is part of Agios' global strategic collaboration with Celgene Corporation focused on cancer metabolism. 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.

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 TIBSOVO® (ivosidenib) and AG-881; Agios' plans for the further clinical development of TIBSOVO® 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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