Agios Presents Updated Data from the Phase 1 Dose-escalation Study of Vorasidenib in Patients with IDH-mutant Non-enhancing Glioma

May 29, 2020

– Vorasidenib Demonstrated Prolonged Disease Control and Encouraging Preliminary Activity with Median Progression-free Survival of 31.4 Months –

– Vorasidenib Demonstrated a Favorable Safety Profile at Doses Below 100mg Consistent with Previously Reported Data –

– Registration-enabling Phase 3 INDIGO Trial of Vorasidenib Enrolling Patients with IDH-mutant Grade 2 Residual or Recurrent Non-enhancing Glioma –

CAMBRIDGE, Mass., May 29, 2020 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today reported updated data from the ongoing Phase 1 study evaluating single agent vorasidenib in isocitrate dehydrogenase (IDH)-mutant advanced solid tumors, including glioma. Data from the non-enhancing glioma population were featured in an oral presentation at the 2020 American Society of Clinical Oncology (ASCO) annual meeting, which is being held virtually. Vorasidenib, an investigational, oral, selective, brain-penetrant inhibitor of mutant IDH1 and IDH2 enzymes, is currently being evaluated in the registration-enabling Phase 3 INDIGO study as a potential treatment for patients with residual or recurrent Grade 2 non-enhancing glioma.

“For patients with IDH-mutant non-enhancing glioma who currently have limited treatment options beyond chemotherapy and radiation, targeted oral options such as vorasidenib are urgently needed,” said Ingo Mellinghoff, M.D., Memorial Sloan Kettering Cancer Center, an investigator for the Phase 1 dose-escalation study. “The updated results of this study in non-enhancing glioma patients provide further evidence of the potential benefit of vorasidenib for these patients, with a favorable safety profile and encouraging preliminary activity, including prolonged disease control, objective tumor responses, and clinically meaningful progression-free survival rates.”

“These promising efficacy and safety data in patients with IDH-mutant non-enhancing glioma provide further support for our registration-enabling Phase 3 INDIGO study,” said Chris Bowden, M.D., chief medical officer at Agios. “With vorasidenib – the first and only brain-penetrant IDH inhibitor in Phase 3 trials for low-grade glioma – we have an opportunity to target a highly prevalent driver mutation early in the disease evolution, providing a therapeutic alternative to ‘watch and wait’ that can potentially delay the need for chemotherapy and radiation.”

Vorasidenib Phase 1 Dose-Escalation Study

Vorasidenib is being evaluated as a single agent in an ongoing Phase 1 dose-escalation trial in IDH1/2 mutant advanced solid tumors (n=93), including glioma (n=52). Enrollment was completed in June 2017. As of the March 3, 2020 data cut-off, study design, enrollment and baseline characteristics of the 22 non-enhancing glioma patients are reported below:

- Seventy-seven percent of patients (n=17) had World Health Organization (WHO) classified Grade 2 tumors and 23% (n=5) had Grade 3 tumors.
- Ninety-one percent of patients (n=20) had an IDH1 mutation and 5% (n=1) 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 47 years (ranging from 16 to 73).
- Sixty-four percent of patients (n=14) had received prior systemic therapy. Patients had received a median of two prior systemic therapies (ranging from 1 to 4).
    - Fifty-nine percent of patients (n=13) had previously received temozolomide and 36% (n=8) of patients received prior radiation therapy.
- Patients received daily doses of vorasidenib ranging from 10 mg to 200 mg.
- Thirty-six percent of patients (n=8) remain on treatment.

Safety Data

The safety analysis conducted on the 22 patients with non-enhancing glioma as of the data cut-off demonstrated that vorasidenib has a favorable safety profile at dose levels below 100 mg once daily. Safety data for this population are consistent with the results reported for all patients enrolled in this trial at the 2018 ASCO Annual Meeting.

- The majority of adverse events (AEs) reported by investigators were mild to moderate, with the most common (>40%) across all grades being increased alanine aminotransferase (ALT) (64%), increased aspartate aminotransferase (AST) (59%), nausea (46%) and headache (41%).
- Grade 3 or higher AEs were observed in 27% of patients (n=6) with the most common being increased ALT (9%) and AST (9%).
- AEs of Grade 2 or higher elevated transaminases occurred in seven non-enhancing glioma patients at the higher dose levels (≥100 mg) and resolved to Grade ≤1 with dose modification or discontinuation.
    - No AEs of Grade 2 or higher elevated transaminases were observed in patients at the lower dose levels (<100 mg).

- Of the 14 (64%) patients who discontinued treatment, 9% (n=2) discontinued due to an AE.

Efficacy Data

Efficacy data from the 22 non-enhancing glioma patients as of the data cut-off showed:

- The investigator-reported objective response rate (ORR) was 18% with one patient exhibiting a partial response and three patients exhibiting minor responses using the Response Assessment in Neuro-Oncology for low-grade glioma (RANO-LGG) criteria.
- Seventy-three percent of patients (n=16) achieved stable disease according to the investigator as assessed by RANO-LGG.
- With 59% of events reported, median progression free survival (PFS) was 31.4 months (95% CI 11.2, 40.8).
- Twenty-four month PFS rate was 55.4%.
- The median treatment duration was 25.8 months (ranging from 1.0 to 47.9) with 68% (n=15) remaining on treatment for ≥1 year.

Ongoing Phase 3 INDIGO Trials in Progress Poster
A trials in progress poster was presented at the 2020 ASCO Annual Meeting to highlight the ongoing global, randomized, placebo-controlled Phase 3 INDIGO study of vorasidenib in approximately 366 patients with residual or recurrent, non-enhancing, Grade 2 low-grade glioma with an IDH1 or IDH2 mutation and who have undergone surgery as their only treatment. The goal of the study is to evaluate the efficacy of vorasidenib compared with placebo based on radiographic PFS and determine whether vorasidenib could provide a therapeutic alternative to “watch and wait” to help control low-grade glioma and potentially delay the need for chemotherapy and/or radiation. The study is currently enrolling. More information can be found on the INDIGO study website.

Vorasidenib is not approved in any country for the treatment of patients with low-grade glioma.

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). Tumor enhancement is an imaging characteristic assessed by magnetic resonance imaging (MRI), and enhancing tumors are more likely to be high-grade.

Common symptoms of glioma include seizures, memory disturbance, sensory impairment and neurologic deficits. The long-term prognosis is poor, and regardless of treatment, the majority of patients with low-grade gliomas will have recurrent disease that will progress over time. Approximately 11,000 low-grade glioma patients are diagnosed annually in the U.S. and EU and approximately 80 percent have an IDH mutation.

About Agios
Agios is focused on discovering and developing novel investigational medicines to treat malignant hematology, solid tumors and rare genetic diseases through scientific leadership in the field of cellular metabolism. In addition to an active research and discovery pipeline across these three therapeutic areas, Agios has two approved oncology precision medicines and multiple first-in-class investigational therapies in clinical and/or preclinical development. For more information, please visit the company's website at www.agios.com.

Disclosures
Dr. Mellinghoff has provided compensated advisory services for Agios. Additionally, an institutional leader at Memorial Sloan Kettering (MSK) not involved in the research that is the subject of this release serves on the Scientific Advisory Board of Agios.

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 vorasidenib; Agios’ plans for the further clinical development of vorasidenib; 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 or its collaborators 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, without limitation: risks and uncertainties related to the impact of the COVID-19 pandemic to Agios’ business, operations, strategy, goals and anticipated milestones, including its ongoing and planned research activities, ability to conduct ongoing and planned clinical trials, clinical supply of current or future drug candidates, commercial supply of current or future approved products, and launching, marketing and selling current or future approved products; 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, the EMA or 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; 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, except as required by law.

Contacts

Investors:
Holly Manning, 617-844-6630

Director, Investor Relations
Holly.Manning@agios.com

Media:
Jessica Rennekamp, 857-209-3286
Associate Director, Corporate Communications
Jessica.Rennekamp@agios.com

Source: Agios Pharmaceuticals, Inc.