# New Data from Ivosidenib Phase 1 Dose-Escalation and Expansion Trial Demonstrate Durable Responses in Patients with IDH1m Relapsed or Refractory AML

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*- First Expansion Data and Updated Dose-Escalation Data Support NDA Submission for IDH1m R/R AML by Year End 2017 and Demonstrate Overall Efficacy and Safety Profile Consistent with Previously Reported Data -*

*- In 125 R/R AML Patients From the Primary Analysis Set, Combined CR+CRh Rate of 30.4% with a Median Duration of 8.2 Months -*

*- Company to Host Investor Event and Webcast Today at 8:00 p.m. ET -*

ATLANTA, Dec. 11, 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 new efficacy and safety data from the ongoing Phase 1 dose-escalation and expansion study evaluating oral ivosidenib (AG-120) in patients with relapsed or refractory acute myeloid leukemia (R/R AML) and an isocitrate dehydrogenase-1 (IDH1) mutation. Ivosidenib is an investigational, first-in-class, oral, targeted inhibitor of the mutant IDH1 enzyme. Data in an oral session at the 2017 American Society of Hematology (ASH) Annual Meeting and Exposition demonstrated a complete response (CR) and CR with partial hematologic recovery (CRh) rate of 30.4% and an overall response rate (ORR) of 41.6% in the primary analysis set of 125 patients with R/R AML who received ivosidenib at 500 mg once daily and received their first dose at least 6 months prior to the May 12, 2017 analysis cutoff date. The CR+CRh rate is the primary endpoint of the study.

“New ivosidenib data from the expansion phase of the Phase 1 study is compelling and demonstrates impressive single-agent efficacy with durable responses in these high-risk relapsed or refractory AML patients,” said Courtney DiNardo, M.D., lead investigator and assistant professor, department of leukemia at the University of Texas MD Anderson Cancer Center. “Important measures of clinical benefit for patients treated with ivosidenib were also observed and include increases in transfusion independence and a decrease in the frequency of comorbidities such as febrile neutropenia and infections in responding patients.”

A total of 258 patients with advanced hematologic malignances and an IDH1 mutation were treated on the Phase 1 study, which included 78 patients in the dose-escalation portion and 180 patients from four dose-expansion Arms. Enrollment to the study is closed. This is the first presentation of data from the dose-expansion portion of the study. Safety data reported include all treated patients, and includes those who received ivosidenib at total daily doses ranging from 200 mg to 1200 mg in dose-escalation and 500 mg daily in dose expansion. A maximum tolerated dose was not reached in the dose-escalation portion of the trial. The primary analysis set is comprised of 125 R/R AML patients (92 patients from Arm 1 of the expansion and 33 patients from the dose-escalation who met the eligibility criteria for Arm 1 and received ivosidenib at 500 mg once daily) who were enrolled at least 6 months prior to the primary analysis cutoff date of May 12, 2017. The median age of these patients is 67 (ranging from 18-87), and the median number of prior regimens is two (ranging from one to six).

“These data form the core of the efficacy analysis for our ivosidenib NDA submission, which is on track for the end of the year,” said Chris Bowden, M.D., chief medical officer of Agios. “We believe that these data validate the potential for ivosidenib to be a first-in-class therapy for patients with R/R AML and an IDH1 mutation.”

**Safety Data**
A safety analysis conducted for all 258 treated patients as of the data cut-off showed that ivosidenib continues to demonstrate a favorable safety profile. The most common adverse events (AEs) regardless of causality were diarrhea (33.3%), leukocytosis (30.2%), nausea (29.5%), fatigue (28.7%) and febrile neutropenia (25.2%).

Among the 125 R/R AML patients from the primary analysis set, adverse events of interest were the following:

- 8% reported Grade ≥3 leukocytosis, which was managed with hydroxyurea. No cases were fatal.
- 8% reported Grade 3 QT prolongation. Ivosidenib was reduced in one patient and held in five patients (for any grade of QT prolongation), and no cases were Grade 4 or fatal.
- 9.6% reported IDH-differentiation syndrome (IDH-DS), which was managed with corticosteroids and diuretics. None were Grade 4 or fatal.

**Efficacy Data**
Data from 125 R/R AML patients from the primary analysis set demonstrated a combined CR+CRh rate of 30.4% [95% CI 22.5, 39.3], which is the primary endpoint of the study. The CR rate was 21.6% (27 of 125 patients) [95% CI 14.7, 29.8] and the CRh rate was 8.8% (11 of 125 patients). CRh (complete remission with partial hematological recovery) is defined as <5% of blasts in the bone marrow, no evidence of disease and partial recovery of peripheral blood counts (platelets >50,000/microliter and ANC >500/microliter).

- Overall response rate (ORR) was 41.6% (52 of 125 patients).
- Median duration of response was 9.3 months [95% CI 5.6, 18.3] for patients who achieved a CR, 8.2 months [95% CI 5.5, 12.0] for patients who achieved a CR/CRh and 6.5 months [95% CI 4.6, 9.3] for all patients who responded.
- Median time to first response was 1.9 months (0.8-4.7) for all patients who responded, median time to CR was 2.8 months (0.9-8.3) for patients who achieved a CR, and median time to CR/CRh was 2.7 months (0.9-5.6) for patients who achieved a CR/CRh.

- At the time of the data cut-off, median overall survival (OS) as observed in the study has not yet been reached for patients who achieved a CR/CRh. OS was 9.3 months [95% CI 3.7, 10.8] for non-CR/CRh responders, 3.9 months [95% CI 2.8, 5.8] for non-responders, and 8.8 months [95% CI 6.7, 10.2] overall.
- Of the patients who were transfusion dependent at baseline and achieved a CR, 100% became independent of platelet transfusions and 84.6% became independent of red blood cell (RBC) transfusions during any 56-day post baseline period.
- Of the patients who were transfusion dependent at baseline and achieved a CRh, 71.4% became independent of platelet transfusions and 75.0% became independent of RBC transfusions during any 56-day post baseline period. Transfusion independence was also seen among non-CR/CRh responders and non-responders. Non-CR/CRh responders include patients with CR with incomplete hematologic recovery (CRi), CR with incomplete platelet recovery (CRp) and morphologic leukemia-free state (MLFS) who are not CRh.

**Response in Untreated AML and MDS**
An efficacy analysis was also presented for 34 untreated AML patients not eligible for standard of care therapies in expansion Arm 2 and from dose escalation whose starting dose was 500 mg daily and 12 myelodysplastic syndrome (MDS) patients in expansion Arm 3 and from dose escalation whose starting dose was 500 mg daily.

- Data from 34 untreated AML patients demonstrated a 55.9% ORR and a CR rate of 20.6%. The median duration of response was 9.2 months [95% CI 1.9, NE], and median duration of CR has not yet been reached.
- Data from 12 MDS patients demonstrated a 91.7% ORR and a CR rate of 41.7%.

**Clinical Development in AML**
Ivosidenib continues to be studied in the following ongoing clinical trials in AML:

- Phase 3 AGILE study evaluating the safety and efficacy of ivosidenib + azacitidine vs. placebo + azacitidine in adults with previously untreated IDH1m AML who are considered appropriate candidates for non-intensive therapy
- Phase 1b study of either ivosidenib or enasidenib in combination with standard induction and consolidation chemotherapy in newly diagnosed AML
- Phase 1/2 study of either ivosidenib or enasidenib in combination with azacitidine in newly diagnosed AML

Agios is on track to file a New Drug Application (NDA) for ivosidenib with the U.S. Food and Drug Administration by the end of 2017.

**About the Phase 1 Trial for Ivosidenib in Advanced Hematologic Malignancies**
Ivosidenib (AG-120) is being evaluated in an ongoing Phase 1 trial that includes a dose-escalation phase and four expansion arms, including:

- Arm 1: IDH1 mutant positive AML patients who relapsed after bone marrow transplantation, are in second or later relapse, refractory to initial induction or reinduction treatment, or who relapse within one year of initial treatment, excluding patients with favorable-risk status
- Arm 2: untreated IDH1 mutant positive AML patients who are not candidates for standard-of-care chemotherapy
- Arm 3: patients with other non-AML IDH1 mutant, relapsed or refractory advanced hematologic malignancies
- Arm 4: patients with relapsed IDH1 mutant positive AML not eligible for arm 1 who have failed or are unable to receive standard of care

**About Acute Myelogenous Leukemia (AML)**
AML, a cancer of blood and bone marrow characterized by rapid disease progression, is the most common acute leukemia affecting adults. Undifferentiated blast cells proliferate in the bone marrow rather than mature into normal blood cells. AML incidence significantly increases with age, and according to the American Cancer Society, the median age of onset is 66. The vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory AML. The five-year survival rate for AML is approximately 20 to 25 percent. IDH1 mutations are present in about 6 to 10 percent of AML cases.

**Investor Event and Webcast Information**
Agios will host an investor event on Monday, December 11, 2017 beginning at 8:00 p.m. ET in Atlanta to review data presented at ASH. The event will be webcast live and can be accessed under "Events & Presentations" in the Investors section of the company's website at www.agios.com.

**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.

**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; Agios' plans for the further clinical development of ivosidenib; 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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