Data from Phase 1 Studies of Ivosidenib or Enasidenib in Combination with Full Doses of Standard of Care Chemotherapy Demonstrate Tolerability and Preliminary Clinical Activity in Newly Diagnosed AML Patients With an IDH Mutation

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- Ivosidenib and Enasidenib Evaluated in Combination with Standard Induction (7+3) Chemotherapy or Azacitadine in Newly Diagnosed Patients From Two Phase 1 Studies -

- Phase 3 Trial of Ivosidenib or Enasidenib Combined with Standard Induction Therapy Planned for 2018 and Phase 3 AGILE Study of Ivosidenib in Combination with Azacitidine Ongoing, Both in Newly Diagnosed AML Patients with an IDH Mutation -

- 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 data from two studies evaluating ivosidenib (AG-120) and an investigational use of IDHIFA® (enasidenib) in patients with newly diagnosed acute myeloid leukemia (AML) and an isocitrate dehydrogenase (IDH)1 or IDH2 mutation. The data were presented as part of the scientific program at the 59thAmerican Society of Hematology Annual Meeting in Atlanta.

“The totality of the data presented at ASH demonstrate the potential benefit of IDHm inhibitors in the frontline setting for patients with AML,” said Eytan Stein, M.D., study investigator and attending physician in the leukemia service at Memorial Sloan Kettering Cancer Center. “The Phase 1 frontline combination trials showed that ivosidenib and enasidenib are well tolerated when combined with standard induction chemotherapy or azacitadine and both trials demonstrated early encouraging signs of efficacy. I look forward to evaluating both ivosidenib and enasidenib in late-stage, placebo-controlled clinical trials to understand the full impact of these medicines on newly diagnosed AML patients.”

Combination with Standard Induction Chemotherapy
The first presentation, given by Dr. Stein, evaluated ivosidenib or enasidenib in combination with standard induction chemotherapy in patients with newly diagnosed AML and an IDH1 or IDH2 mutation. During induction, patients received either 500 mg of ivosidenib and 7 + 3 standard chemotherapy (daunorubicin 60 mg/m2/day or idarubicin 12 mg/m2/day x 3 days with cytarabine 200 mg/m2/day x 7 days) (n=32) or 100 mg of enasidenib and 7 + 3 standard chemotherapy (n=56). Of these patients, 69% in the ivosidenib arm and 57% in the enasidenib arm had de novo AML, while the remaining patients had secondary AML (sAML). For patients with sAML, 40% in the ivosidenib arm and 63% in the enasidenib arm had received prior hypomethylating agent therapy. After induction, patients could receive up to four cycles of consolidation chemotherapy while continuing ivosidenib or enasidenib. Patients who achieved a complete response (CR) or a complete response with incomplete neutrophil or platelet recovery (CRi/CRp) after consolidation could continue to take single agent ivosidenib or enasidenib daily for up to two years from day one of induction.

Ivosidenib Results
In the ivosidenib arm, the most common Grade 3 or higher non-hematologic adverse events during the induction period were febrile neutropenia (60%), blood bilirubin increased (9%), hypertension (9%), colitis (9%), increased alanine aminotransferase (9%) and increased aspartate aminotransferase (9%). The 30 and 60-day mortality rates were both 6%, and there were no dose-limiting toxicities. The median time to absolute neutrophil count (ANC) recovery (>500/µL) was 28.5 days (95% CI 27,34). Median time to platelet recovery (>50,000/µL) was 28 days (95% CI 26,34).

The CR+CRi/CRp rate for de novo patients was 91% (19/21) and 44% (4/9) for sAML patients. The overall best response of CR+ CRi/CRp rate for all patients was 77% (23/30).

Enasidenib Results
In the enasidenib arm, the most common Grade 3 or higher non-hematologic adverse events during the induction period were febrile neutropenia (63%), blood bilirubin increased (9%), hypertension (9%) and bacteremia (9%). The 30 and 60-day mortality rates were 5% and 7%, respectively. There was one dose-limiting toxicity in the enasidenib combination arm consisting of persistent Grade 4 thrombocytopenia lasting beyond 42 days from the start of induction. The median time to ANC recovery (>500/µL) was 34 days (95% CI 29,35). Median time to platelet recovery (>50,000/µL) was 33 days (95% CI 29,50).

The CR+CRi/CRp rate for de novo patients was 67% (18/27) and 57% (13/23) for sAML patients. The overall best response of CR+CRi/CRp rate for all patients was 62% (31/50).

“The early results from these studies of ivosidenib and enasidenib in combination with traditional frontline AML treatment are highly encouraging and support the strategy to advance IDHm inhibitors into the newly diagnosed setting,” said Chris Bowden, M.D., chief medical officer of Agios. “We are focused on evaluating the IDHm inhibitors in late-stage studies that span the entire frontline setting with our ongoing Phase 3 AGILE study of ivosidenib in combination with azacitidine versus azacitidine and a planned Phase 3 study of ivosidenib and enasidenib in combination with 7+3 intensive chemotherapy.”

Combination with Azacitidine
The second presentation, given by Courtney DiNardo, M.D., evaluated an investigational use of enasidenib or ivosidenib in combination with azacitidine in patients with newly diagnosed AML unable to receive intensive chemotherapy. In the study, patients received 100mg (n=3) or 200mg (n=3) of enasidenib daily plus azacitidine or 500 mg of ivosidenib (n=11) plus azacitidine. At the data cutoff, 11 patients remained on the study (3 enasidenib, 8 ivosidenib).

Enasidenib Results

For patients receiving the enasidenib combination, the most common Grade 3-4 hematologic adverse event was neutropenia (33%, 2/6). The most common Grade 3-4 non-hematologic adverse events were pneumonia (33%, 2/6) and hyperbilirubinemia (33%, 2/6). IDH differentiation syndrome was reported in one patient.

Four of six patients had a response, including two CRs, one partial response (PR) and one morphologic leukemia-free state (MLFS).

Ivosidenib Results
For patients receiving the ivosidenib combination, the most common Grade 3-4 hematologic adverse events were anemia (18%, 2/11) and febrile neutropenia (18%, 2/11) with neutropenia and thrombocytopenia each with one event (9% each). The most common Grade 3-4 non-hematologic adverse event was pneumonia (18%, 2/11). IDH differentiation syndrome was reported in one patient.

Eight of 11 patients had a response, including four CRs, one CRi, one PR and two MLFS.

Neither IDHIFA nor ivosidenib are approved for the treatment of patients with newly diagnosed AML or approved in combination with azacitidine.

About IDHIFA

IDHIFA (enasidenib) is indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia with an isocitrate dehydrogenase-2 mutation as detected by an FDA-approved test.

Important Safety Information

WARNING: DIFFERENTIATION SYNDROME

Patients treated with IDHIFA have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, acute respiratory distress, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, lymphadenopathy, bone pain, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS
Differentiation Syndrome: See Boxed WARNING. In the clinical trial, 14% of patients treated with IDHIFA experienced differentiation syndrome, which may be life-threatening or fatal if not treated. Differentiation syndrome has been observed with and without concomitant hyperleukocytosis, as early as 10 days and at up to 5 months after IDHIFA initiation. Symptoms in patients treated with IDHIFA included acute respiratory distress represented by dyspnea and/or hypoxia and need for supplemental oxygen; pulmonary infiltrates and pleural effusion; renal impairment; fever; lymphadenopathy; bone pain; peripheral edema with rapid weight gain; and pericardial effusion. Hepatic, renal, and multi-organ dysfunction have also been observed. If differentiation syndrome is suspected, initiate systemic corticosteroids and hemodynamic monitoring until improvement. Taper corticosteroids only after resolution of symptoms. Differentiation syndrome symptoms may recur with premature discontinuation of corticosteroids. If severe pulmonary symptoms requiring intubation or ventilator support and/or renal dysfunction persist for more than 48 hours after initiation of corticosteroids, interrupt IDHIFA until signs and symptoms are no longer severe. Hospitalization for close observation and monitoring of patients with pulmonary and/or renal manifestation is recommended.

Embryo-Fetal Toxicity: Based on animal embryo-fetal toxicity studies, IDHIFA can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential and males with female partners of reproductive potential to use effective contraception during treatment with IDHIFA and for at least 1 month after the last dose. Pregnant women, patients becoming pregnant while receiving IDHIFA, or male patients with pregnant female partners should be apprised of the potential risk to the fetus.

ADVERSE REACTIONS

- The most common adverse reactions (≥20%) included total bilirubin increased (81%), calcium decreased (74%), nausea (50%), diarrhea (43%), potassium decreased (41%), vomiting (34%), decreased appetite (34%), and phosphorus decreased (27%)
- The most frequently reported ≥Grade 3 adverse reactions (≥5%) included total bilirubin increased (15%), potassium decreased (15%), phosphorus decreased (8%), calcium decreased (8%), diarrhea (8%), differentiation syndrome (7%), non-infectious leukocytosis (6%), tumor lysis syndrome (6%), and nausea (5%)
- Serious adverse reactions were reported in 77.1% of patients. The most frequent serious adverse reactions (≥2%) were leukocytosis (10%), diarrhea (6%), nausea (5%), vomiting (3%), decreased appetite (3%), tumor lysis syndrome (5%), and differentiation syndrome (8%). Differentiation syndrome events characterized as serious included pyrexia, renal failure acute, hypoxia, respiratory failure, and multi-organ failure

LACTATION
Many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants, advise women not to breastfeed during treatment with IDHIFA and for at least 1 month after the last dose.

Please see full Prescribing Information, including Boxed WARNING.

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.

About Agios/Celgene Collaboration
IDHIFA® (enasidenib) is 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.

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 IDHIFA® (enasidenib); Agios' plans for the further clinical development of ivosidenib and IDHIFA®; 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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