



## New Data from Phase 1/2 Trial of Oral IDHIFA® (enasidenib) Demonstrate Durable Complete Responses in Patients with IDH2 Mutant Relapsed or Refractory AML

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*Inclusion of Phase 2 Expansion Data Demonstrates Overall Efficacy and Safety Profile Consistent with Previously Reported Data*

*In 214 R/R AML Patients Treated with Enasidenib at 100 mg Daily Dose in Phase 1/2 Trial, 20.1% Complete Response (CR) Rate with Median Duration of Response of 8.8 Months in Patients with a CR*

MADRID, Spain, June 24, 2017 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ:AGIO) today announced new efficacy and safety data from the ongoing Phase 1/2 dose-escalation and expansion study evaluating investigational oral IDHIFA® (enasidenib) in patients with relapsed or refractory acute myeloid leukemia (R/R AML) and an isocitrate dehydrogenase-2 (IDH2) mutation. IDHIFA®, being developed in collaboration with Celgene Corporation, is an investigational first-in-class, oral, targeted inhibitor of the mutant IDH2 enzyme. Data in an oral session at the 22nd Congress of the European Hematology Association (EHA) demonstrated an overall response rate (ORR) of 37 percent, including a complete response (CR) rate of 20.1 percent in 214 patients with R/R AML who received enasidenib at 100 mg daily, which was the recommended starting dose in the expansion phases of the trial.

"With data from an additional 105 patients and the first look at data from the Phase 2 expansion in R/R AML patients treated at the recommended Phase 2 starting dose of 100 mg once daily, these updated results underscore the consistency and durability of response for enasidenib as a potential first-in-class therapy for patients with relapsed or refractory AML and an IDH2 mutation," said Chris Bowden, M.D., chief medical officer of Agios. "We are working with our partner Celgene to quickly bring this oral, targeted therapy to patients with limited treatment options."

As of October 14, 2016, a total of 345 patients with advanced hematologic malignancies and an IDH2 mutation were enrolled into the Phase 1/2 study, which includes three parts: a Phase 1 dose escalation, a part 1 (Phase 1) expansion and a Phase 2 expansion. In the study, 281 patients had R/R AML and 214 of the R/R AML patients were treated at 100 mg daily. This is the first presentation of data from the Phase 2 expansion. Data reported include patients receiving enasidenib at total daily doses ranging from 50 mg to 650 mg in the dose-escalation arm and 100 mg daily in the Phase 1 and Phase 2 expansion arms. A maximum tolerated dose was not reached. The median age of the R/R AML patients enrolled in the study is 68 (ranging from 19-100). Patients with R/R AML received a median of two prior lines of therapy (ranging from one to 14).

The overall safety profile observed for enasidenib was consistent with previously reported data. The most common treatment-emergent AEs were nausea (48%), diarrhea (41%), fatigue (41%), decreased appetite (34%) and blood bilirubin increased (33%). For all patients in the study, 26.1 percent had treatment-related serious adverse events (SAEs), notably IDH differentiation syndrome (7%), leukocytosis (4%), tumor lysis syndrome (3%) and hyperbilirubinemia (2%).

Data from 214 of the R/R AML patients with an IDH2 mutation who were treated at the recommended Phase 2 starting dose of 100 mg daily demonstrated a 37 percent (79 of 214 patients) overall response rate, which was the primary endpoint of the study. Further, the complete response rate was 20.1 percent (43 of 214 patients). Median duration of response was 5.6 months [95% CI 4.6, 7.4] for all patients who responded and 8.8 months [95% CI 5.6, NR] for patients who achieved a CR. Median time to first response was 1.9 months (0.5-11.1) and median time to CR was 3.7 months (0.7-11.2). At the time of the data cut-off, median overall survival (OS) as observed in the study was 8.3 months [95% CI 7.5,9.4]. Additional results including qualitative improvement in response over time, improvement in hematological parameters over time, OS for patients achieving a CR and transfusion independence were also reported.

"Enasidenib's unique profile as a targeted differentiation agent distinguishes it in a field that has seen few new medicines in decades," said Eytan Stein, M.D., lead investigator and attending physician in the leukemia service at Memorial Sloan Kettering Cancer Center. "Even in the absence of CR, some patients became transfusion independent with enasidenib treatment, suggesting a proportion of patients on study are deriving clinical benefit from an oral, single agent therapy in the relapsed/refractory setting."

### Clinical Development

Enasidenib continues to be studied in the following ongoing clinical trials:

- Phase III IDHENTIFY study evaluating the efficacy and safety of enasidenib versus conventional care regimens in older patients with R/R AML with an IDH2 mutation (NCT02577406)
- Phase 1b study of either enasidenib or ivosidenib in combination with standard induction and consolidation chemotherapy in newly diagnosed AML (NCT02632708)
- Phase 1/2 study of either enasidenib or ivosidenib in combination with azacitidine in newly diagnosed AML (NCT02677922)

The New Drug Application (NDA) for IDHIFA® is currently under Priority Review with the U.S. Food and Drug Administration for the treatment of patients with relapsed or refractory AML with an IDH2 mutation. The NDA has been given a Prescription Drug User Fee Act (PDUFA) action date of August 30, 2017.

Ivosidenib (AG-120, wholly owned by Agios) is an investigational, oral, targeted inhibitor of the mutant IDH1 enzyme.

### About AG221-C-001

Study AG221-C-001 includes three parts: a Phase 1 dose escalation, a part 1 (Phase 1) expansion and a Phase 2 expansion.

The Phase 1 dose escalation study was designed to determine the maximum tolerated dose and recommended Phase 2 dose, and to evaluate

efficacy and safety of enasidenib (AG-221/CC-90007) in subjects with advanced hematologic malignancies with an IDH2 mutation. The Part 1 expansion further evaluated the safety, tolerability, and efficacy of enasidenib in subjects with R/R AML, untreated AML, myelodysplastic syndrome or other advanced hematologic malignancies with an IDH2 mutation. Based on the clinical activity observed in R/R AML subjects, the Phase 2 expansion was designed to assess efficacy of enasidenib at recommended 100 mg daily dose and to further evaluate safety in subjects with R/R AML and with IDH2 mutation. The study was not designed or statistically powered to reach a conclusion on OS. A phase 3 randomized controlled trial with OS as a primary endpoint has been initiated.

#### **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. IDH2 mutations are present in about 8 to 19 percent of AML cases.

#### **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 multiple first-in-class investigational medicines 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](http://www.agios.com).

#### **About Agios/Celgene Collaboration**

IDHIFA<sup>®</sup> (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<sup>®</sup>. Agios continues to conduct clinical development activities within the IDHIFA<sup>®</sup> 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 net sales. Celgene and Agios intend to co-commercialize IDHIFA<sup>®</sup> 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 of the IDH2 mutation as a therapeutic target; the potential benefits of IDHIFA<sup>®</sup> (enasidenib); and the potential benefit of Agios' strategic plans and focus. 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, 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: 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; the ability to obtain and maintain requisite regulatory approvals and to enroll patients in planned clinical trials; unplanned cash requirements and expenditures; competitive factors; the 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, except as required by law.

#### **Agios Contacts**

##### **Investors:**

Kendra Adams, 617-844-6407  
Senior Director, Investor & Public Relations  
[Kendra.Adams@agios.com](mailto:Kendra.Adams@agios.com)

Renee Leck, 617-649-8299  
Senior Manager, Investor & Public Relations  
[Renee.Leck@agios.com](mailto:Renee.Leck@agios.com)

##### **Media:**

Holly Manning, 617-844-6630  
Associate Director, Corporate Communications  
[Holly.Manning@agios.com](mailto:Holly.Manning@agios.com)

