



## Updated Data from Phase 1 Trial of Oral IDHIFA® (enasidenib) Demonstrate Complete Responses and Duration of Response in Patients with Relapsed or Refractory AML and an IDH2 Mutation

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*40.3% Overall Response Rate (ORR) with Median Duration of Response of 5.8 Months and 19.3% Complete Response (CR) Rate with Median Duration of Response of 8.8 Months in Patients With a CR*

*Overall Safety Profile was Consistent with Previously Reported Data*

*Simultaneous Online Publications of Clinical and Translational Data Presented in Journal Blood*

CHICAGO--(BUSINESS WIRE)--Jun. 6, 2017-- Celgene Corporation (NASDAQ:CELG) and Agios Pharmaceuticals, Inc. (NASDAQ:AGIO) today announced new efficacy and safety data from the ongoing Phase 1 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 is an investigational first-in-class, oral, targeted inhibitor of the mutant IDH2 enzyme, which demonstrated an overall response rate of 40.3 percent, including a complete response rate of 19.3 percent in the study. The data were presented in an oral session at the American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published online in the journal [Blood](#).\*

"The updated results, including duration of response, from the Phase 1 study reinforce the potential for enasidenib as a first-in-class therapy for patients with relapsed or refractory AML and an IDH2 mutation," said Michael Pehl, President, Hematology/Oncology at Celgene. "Patients have very few treatment options for relapsed or refractory AML, so we are eager to advance this potential targeted therapy as quickly as possible."

As of April 15, 2016, a total of 239 patients with advanced hematologic malignancies and an IDH2 mutation were enrolled into the Phase 1 study, of which 176 patients had R/R AML. 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 once daily in the Phase 1 expansion arms. A maximum tolerated dose was not reached. The median age of the patients enrolled in the study is 70 (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. Twenty-four percent of patients had treatment-related serious adverse events (SAEs), notably IDH differentiation syndrome (8%), leukocytosis (4%), tumor lysis syndrome (3%) and hyperbilirubinemia (2%). The most common treatment-emergent AEs were nausea (46%) hyperbilirubinemia (45%), diarrhea (40%) and fatigue (40%).

Data from 176 R/R AML patients with an IDH2 mutation demonstrated a 40.3 percent (71 of 176 patients) overall response rate, which was the primary endpoint of the study. Further, the complete response rate was 19.3 percent (34 of 176 patients). Median duration of response was 5.8 months [95% CI 3.9, 7.4] for all patients who responded and 8.8 months [95% CI 6.4, NR] for patients who achieved a CR. Median time to first response was 1.9 months (0.5-9.4) and median time to CR was 3.8 months (0.5-11.2). Median overall survival (OS) for R/R AML patients as observed in the study was 9.3 months [95% CI 8.2, 10.9]. 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.

"In addition to the complete response in this study, we also observed changes in responses and hematologic parameters over time," said Eytan Stein, M.D., lead investigator and attending physician in the leukemia service at Memorial Sloan Kettering Cancer Center. "This suggests that differentiation of myeloblasts – made possible by inhibition of mutated IDH2 – may drive the clinical efficacy of enasidenib."

"Targeting IDH mutations is thought to allow for the differentiation of malignant cells and introduces a new paradigm in the treatment of AML," said Chris Bowden, M.D., chief medical officer of Agios. "These data show that IDH inhibition plays an important role in segments of AML and will continue to inform our research into this novel class of potential therapies."

### Additional Data Available – IDH Differentiation Syndrome & Translational Analyses

A separate analysis of IDH-inhibitor-associated differentiation syndrome (IDH-DS) associated with enasidenib was also presented as a poster discussion during the ASCO meeting and detailed the findings of an independent Differentiation Syndrome Review Committee (DSRC). The committee reviewed investigator reported IDH-DS cases and determined that 13 of the 27 potential cases were consistent with IDH-DS (11.9% of 109 patients). These data demonstrate that the signs and symptoms of IDH-DS are recognizable. IDH-DS represents a novel clinical finding in patients with mutated IDH2 AML treated with enasidenib, and is likely due to its purported mechanism of action, differentiation of leukemic cells.

In addition to the clinical data publication, additional analyses describing the mechanism of action of enasidenib were also published online in *Blood*. An analysis of patient samples confirmed that the preclinical efficacy and mechanism of action of mutated IDH2 inhibition by enasidenib is through differentiation of AML cells. The authors conclude that the data provide insights into enasidenib resistance to inform future mechanism-based combination treatment studies.

### 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 Aug. 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 Celgene**

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit [www.celgene.com](http://www.celgene.com). Follow Celgene on Social Media: [@Celgene](#), [Pinterest](#), [LinkedIn](#), [Facebook](#) and [YouTube](#).

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

IDHIFA® (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. Agios continues to conduct clinical development activities within the IDHIFA 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 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, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. Neither Celgene nor Agios undertake any obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond each company's control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in the Annual Report on Form 10-K and other reports of each company filed with the Securities and Exchange Commission.*

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