



## **New Agios Clinical Data from Ongoing Phase 1 Trial of AG-221 Continue to Show Complete and Durable Remissions in Patients with Difficult to Treat Hematologic Malignancies**

June 14, 2014

*Data Support Initiation of Multiple Expansion Cohorts in Second Half of 2014*

*AgiOS Pharmaceuticals to Host Investor Webcast on June 16, 2014 at 8:30 a.m. EDT*

CAMBRIDGE, Mass. & MILAN--(BUSINESS WIRE)--Jun. 14, 2014-- Agios Pharmaceuticals, Inc. (NASDAQ: AGIO), a leader in the fields of cancer metabolism and inborn errors of metabolism (IEMs), today announced new clinical data from the ongoing Phase 1 study of AG-221, which includes 35 patients with IDH2 mutant positive hematologic malignancies. These data confirm and build upon previously presented data on AG-221's clinical activity, safety profile and unique mechanism of action. The data were presented today in a late-breaker oral presentation at the 19<sup>th</sup> Congress of the European Hematology Association (EHA) in Milan, Italy by Stéphane de Botton, M.D., the principal investigator at the Institut de Cancérologie Gustave Roussy, Villejuif, France.

The new data show objective responses in 14 out of 25 evaluable patients on AG-221 and an additional five patients with stable disease. In six patients who achieved a complete remission (CR), evidence of durability was observed, ranging from one to four months in duration. All responses are ongoing. AG-221 continues to show favorable drug exposure and pharmacokinetics at all doses tested with substantial reductions in plasma levels of the oncometabolite 2-hydroxyglutarate (2HG). Safety data show that AG-221 is well tolerated, with the majority of adverse events reported as mild to moderate. There were no discontinuations of AG-221 due to adverse events, and the maximum tolerated dose has not been reached. These promising safety and efficacy data support the company's plan to initiate four expansion cohorts in the second half of 2014. Agios also expects to submit additional data from the ongoing Phase 1 trial for potential presentation at the 2014 American Society of Hematology Annual Meeting.

"These data demonstrate that treatment with AG-221 leads to a profound differentiation effect and is associated with durable complete remissions in patients who are extremely ill and have limited treatment options," said Dr. de Botton. "We believe these data support comprehensive investigation of AG-221 in IDH2-mutant positive cancers and look forward to participating in Agios' planned expansion cohorts and future clinical trials."

"AML is a devastating disease with a dismal prognosis, and AG-221 is the first targeted agent showing clinical activity in patients with IDH2-mutant disease," said David Schenkein, M.D., chief executive officer of Agios. "We are encouraged for patients that AG-221 has shown durable clinical activity, and no patients have relapsed after having a response. We are also encouraged by the clinical activity and safety profile that continue to emerge as doses escalate and patient numbers increase. The durability of responses observed to date and unique mechanism of action hold promise that AG-221 may change the paradigm for the treatment of these cancers."

AG-221 is an orally available, selective, potent inhibitor of the mutated IDH2 protein. In the ongoing Phase 1 study, patients have been enrolled in six study cohorts to receive AG-221 administered at 30 mg twice a day, 50 mg twice a day, 75 mg twice a day, 100 mg once a day, 100 mg twice a day and 150 mg once a day. As of May 23, 2014, the study had enrolled 35 patients with IDH2 mutant positive advanced hematological malignancies, including relapsed or refractory AML, myelodysplastic syndrome (MDS) and one patient with chronic myelomonocytic leukemia (CMML). The median age of these patients is 68 (range 48-81).

### **Safety Data**

A safety analysis was conducted as of April 25, 2014 and showed that the majority of adverse events (AEs) reported by investigators were Grade 1 and 2 and most common include nausea, pyrexia, and thrombocytopenia. As of May 23, 2014, possible drug-related severe AEs were reported in four patients, which included confusion, respiratory failure (in the setting of disease-related infection), leukocytosis, anorexia, nausea, and diarrhea. There were seven patient deaths, all unrelated to study drug. Dose escalation continues, as the maximum tolerated dose has not been achieved.

### **Efficacy Data**

Of the 25 evaluable patients, 14 patients achieved objective responses, including six complete remissions, two complete remissions with incomplete platelet recovery (CRp), one complete remission with incomplete hematologic recovery (CRI) and five partial responses. Five patients have stable disease and remain on AG-221. These data include clinical activity beyond AML: four patients diagnosed with MDS achieved objective responses, including one CR and one CRp. There have been no patient relapses once objective response was achieved. Of the 14 responding patients, 12 remain on AG-221, with duration of responses ranging from 15 days to four months and ongoing as of May 23, 2014. One patient with a CR was removed from the study to undergo a bone marrow transplant, and one patient with a CRp died from a surgical complication unrelated to AG-221.

The mechanism of response is consistent with preclinical studies, including 2HG inhibition leading to cellular differentiation, normalization of cell counts in the bone marrow and blood and ultimately complete remissions. This differentiation effect is a distinct mechanism of action as compared to traditional chemotherapy, which is the current standard of care for AML patients.

### **AG-221 Clinical Development Plans**

The clinical activity and favorable safety profile observed to date support Agios' strategy for progressing to multiple expansion cohorts in the second half of 2014. The company plans to initiate four expansion cohorts of approximately 25 patients each, including relapsed/refractory AML patients 60 years of age and older, relapsed/refractory AML patients under age 60, untreated AML patients who decline standard of care chemotherapy, and patients with other IDH2 mutant positive hematologic malignancies (e.g. lymphoma, MDS, multiple myeloma, etc.).

AG-221 is a part of Agios' global strategic collaboration with Celgene Corporation, a leading biotechnology company. On June 13, Celgene exercised its exclusive option to license AG-221. Under the terms of the agreement, Celgene gained worldwide development and commercialization rights for

AG-221. Agios continues to conduct early clinical development and regulatory activities within the AG-221 development program in collaboration with Celgene. The companies are also collaborating on the development of AG-120, an oral, selective, potent inhibitor of the mutated IDH1 protein, which is being studied in two Phase 1 trials in patients whose hematologic malignancies and solid tumors carry an IDH1 mutation. Agios retains U.S. development and commercial rights for AG-120, and Celgene has an exclusive option to the ex-U.S. rights.

#### **Investor Event and Webcast**

Agios will host a conference call and webcast on Monday, June 16, 2014 at 8:30 a.m. EDT to review the clinical data presented at EHA from the ongoing Phase 1 study of AG-221. To participate in the conference call, please dial 1-877-377-7098 (domestic) or 1-631-291-4547 (international) and refer to conference ID 49387254. A replay of the call will be available approximately two hours after the conclusion of the call and will be accessible until June 23, 2014. To access the replay, please dial 1-855-859-2056 (domestic) or 1-404-537-3406 (international) and provide the access code 49387254. The webcast can be accessed live or in archived form under "Events & Presentations" in the Investors and Media section of the company's website at [www.agios.com](http://www.agios.com).

#### **About the Study**

The ongoing Phase 1 multicenter, open-label, dose-escalation clinical trial of AG-221 is designed to assess the safety and tolerability of AG-221 as a single agent administered orally once or twice daily in a 28-day cycle. The study is only enrolling patients who have an IDH2-mutant hematologic malignancy, including AML and MDS. Key objectives in the study include determining maximum tolerated dose, pharmacokinetics, pharmacodynamics (including inhibition of 2HG) and preliminary clinical activity of AG-221. Please refer to [www.clinicaltrials.gov](http://www.clinicaltrials.gov) for additional clinical trial details.

#### **About IDH Mutations and Cancer**

IDH1 and IDH2 are two metabolic enzymes that are mutated in a wide range of hematologic and solid tumor malignancies. The prevalence of IDH mutations is expected to evolve as genomic analysis of tumors increase. Agios' research revealed the potential of IDH1 and IDH2 mutations as novel therapeutic targets in cancer, which may lead to clinical benefit for the subset of cancer patients whose tumors carry them. Patients carry either an IDH1 or IDH2 mutation, but not both.

Agios is developing two oral, first-in-class IDH mutant inhibitors: AG-221 is an IDH2 mutant inhibitor and AG-120 is an IDH1 mutant inhibitor. AG-221 is currently being evaluated in a Phase 1 dose-escalation study in patients with advanced hematologic malignancies. AG-120 is currently being evaluated in two Phase 1 trials, one in hematologic malignancies and another in solid tumors. Both compounds were discovered and developed in the laboratory of Agios.

#### **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 is 66. Less than 10 percent of U.S. patients are eligible for bone marrow transplant, and the vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory AML. AML prevalence is estimated to be approximately 115,000 to 160,000 patients worldwide, with approximately 20 percent of patients carrying an IDH mutation. The five-year survival rate for AML is approximately 20 to 25 percent.

#### **About Agios Pharmaceuticals, Inc.**

Agios Pharmaceuticals is focused on discovering and developing novel drugs to treat cancer and inborn errors of metabolism, or IEMs, which are rare genetic metabolic 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 lead product candidates in cancer metabolism and IEMs 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 our website at [www.agios.com](http://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 Agios' expectations and beliefs about: the potential of IDH1/IDH2 as therapeutic targets; the potential benefits of Agios' product candidates AG-221 and AG-120; its plans and timelines for the clinical development of AG-221 and AG-120; and the benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "could," "would" 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: 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 agreement 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' Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, and other filings that Agios may make with the Securities and Exchange Commission in the future. 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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