Agios Announces New Clinical Data from Dose-Escalation Portion of Phase 1 Trial of Single Agent AG-120 Showing Durable Molecular Responses in Patients with Advanced Hematologic Malignancies

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- Overall Response Rate of 38% and Complete Remission Rate of 18% with Patients on Study up to 24.2 Months -

- For Relapsed/Refractory Acute Myeloid Leukemia Patients, Overall Response Rate of 33% and Complete Remission Rate of 16% with 6.5 Month Median Duration of Response -

- First Demonstration that Treatment with Single Agent AG-120 Can Result in Clearance of Mutant IDH1 -

SAN DIEGO, Dec. 05, 2016 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (Nasdaq:AGIO) presented new clinical data from the ongoing Phase 1 study evaluating single agent AG-120 in advanced hematologic malignancies at the 2016 American Society of Hematology Annual Meeting and Exposition (ASH). AG-120 is a first-in-class, oral, selective, potent inhibitor of mutant isocitrate dehydrogenase-1 (IDH1).

As of August 1, 2016, data from the completed dose-escalation portion of the Phase 1 trial from 78 patients with advanced IDH1 mutant positive hematologic malignancies treated with AG-120, including 63 patients with relapsed and/or refractory (R/R) acute myeloid leukemia (AML), continue to show a favorable safety profile and durable clinical activity. Data from the ongoing expansion phases were not reported. For all dose escalation patients, an overall response rate of 38% (30 of 78) and a complete remission rate of 18% (14 of 78) were observed. For the 63 R/R AML patients, the overall response rate and complete remission rates were 33% (21 of 63) and 16% (10 of 63) respectively. Patients were on study treatment for up to 24.2 months with a median duration of response of 10.2 months for all responders and 6.5 months for the R/R AML responding patients.

In order to study the depth of response to single agent AG-120, molecular detection of the mutant IDH1 burden in blood and bone marrow samples (collected at pre-treatment and at least one on-treatment time point) were analyzed using next generation sequencing (NGS, FoundationOne® Heme assay) in 67 patients from the dose-escalation portion of the study. Molecular clearance was defined as reduction of the IDH1 mutation below the limit of detection of the assay (1% for IDH). Molecular data show that treatment with AG-120 resulted in clearance of the IDH1 mutation in 36% of patients (5 of 14) in complete remission compared to 4% of patients (2 of 53) that did not achieve complete remission (p-value=0.003). This is the first demonstration that treatment with single agent AG-120 can result in mIDH1 clearance.

“AG-120 continues to demonstrate an impressive single-agent efficacy and safety profile in this cohort of high-risk relapsed or refractory AML patients, with some responses maintained for approximately two years,” said Courtney DiNardo, M.D., lead investigator and assistant professor, department of leukemia at the University of Texas MD Anderson Cancer Center. “In addition, new molecular data for AG-120 suggests some patients experience clearance of the IDH1 mutant gene in their blood or bone marrow as assessed by next generation sequencing, demonstrating the depth of response that can occur with AG-120 therapy.”

“We are encouraged by the durable clinical activity of AG-120 and are working to bring this medicine to waiting patients with IDH1 mutant positive AML whose disease has progressed after standard treatments,” said Chris Bowden, M.D., chief medical officer of Agios. “We plan to explore a similar expedited regulatory strategy for AG-120 that is being utilized for enasidenib (AG-221), which could result in an NDA submission in 2017.”

Updated Phase 1 Dose-Escalation Data for AG-120 in Advanced Hematologic Malignancies

Clinical and molecular data reported are from 78 patients treated with AG-120 in the dose escalation phase of the ongoing Phase 1; data from the ongoing expansions were not reported. Doses were administered from 200 mg to 1,200 mg total daily doses. As of August 1, 2016, seven patients (9%) remain on treatment. The median age of these patients is 68 (ranging from 36-89). Patients received a median of two prior chemotherapy regimens (ranging from zero to five). A safety and efficacy analysis was conducted for all 78 treated dose-escalation patients. In addition, longitudinal mutant IDH1 (mIDH1) variant allele frequency (VAF) data were available for 67 patients.

Safety Data

A safety analysis conducted for all 78 treated patients as of the data cut-off shows that AG-120 continues to demonstrate a favorable safety profile.

- The majority of adverse events reported by investigators were mild to moderate, with the most common regardless of causality being fatigue, nausea, diarrhea, pyrexia and peripheral edema.
- Fifty-three patients experienced at least one serious adverse event (SAE), the majority being disease related.
- The maximum tolerated dose was not reached. The recommended Phase 2 dose was 500 mg once daily, which is being studied in the ongoing expansion phase of the trial.
- Nine patients discontinued from the study due to death, including one reported as possibly related to AG-120.
- All cause mortality at 30 and 60 days were 12% and 21%, respectively.

Efficacy Data

Thirty out of 78 treated patients achieved investigator-assessed objective responses for an overall response rate of 38%.

- Of the 30 patients who achieved an objective response, there were 14 (18%) complete remissions (CR), eight CRs with incomplete neutrophil recovery or platelet recovery (CRi/CRp), six marrow CR (mCR)/morphologic leukemia-free state (MLFS) and two partial remissions (PR).

- Of the 63 patients with R/R AML, 21 (33%) achieved an objective response, including 10 (16%) CRs, eight CRi/CRp, two MLFS and one PR.
- Responses were durable, with a median response duration of 10.2 months (3.7- not estimable (NE)) overall and 6.5 months (3.7-NE) in the subset of patients with R/R AML.
- Median duration of treatment is 3.2 months (ranging from 0.1 to 24.2 months).

IDH1 Mutational Clearance

Longitudinal mIDH1 VAF data were reported for 67 patients. Patients with IDH1 mutational clearance (IDH1-MC) were defined as having:

- mIDH1 detected at screening (any sample type), and
- no reported mIDH1 mutation in at least one on-study time point (FoundationOne® Heme sensitivity of 1%).

Importantly, IDH1-MC was observed in 36% of CRs (5 of 14) and 4% of non-CRs (2 of 53). IDH1-MC was enriched in patients achieving CR (p-value = .003). The median time to mutational clearance was 2.7 months (ranging from 1.1 to 3.8 months). This is the first demonstration that treatment with single agent AG-120 can result in mIDH1 clearance. Agios is continuing to study the potential relationship between IDH1-MC and clinical benefit for patients with AML.

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

- Arm 1: 125 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: 25 untreated IDH1 mutant positive AML patients who are not candidates for standard-of-care chemotherapy
- Arm 3: 25 patients with other non-AML IDH1 mutant, relapsed or refractory advanced hematologic malignancies
- Arm 4: 25 patients with relapsed IDH1 mutant positive AML not eligible for arm 1 who have failed or are unable to receive standard of care

About Variant Allele Frequency (VAF)
Sequencing studies have demonstrated that most tumors exhibit extensive intra-tumor genetic heterogeneity characterized by individual cells that have different somatic mutations. For single-nucleotide mutations, or variants, the VAF is defined as the fraction of DNA sequence reads covering the variant position that contains the variant allele. This technique makes it possible to infer the subpopulations of tumor cells by counting the number of DNA sequence reads that contain a specific somatic mutation.

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. Normally, IDH enzymes help to break down nutrients and generate energy for cells. When mutated, IDH increases production of an oncometabolite 2-hydroxyglutarate (2HG) that alters the cells' epigenetic programming, thereby promoting cancer. 2HG has been found to be elevated in several tumor types. Agios believes that inhibition of the mutated IDH proteins may lead to clinical benefit for the subset of cancer patients whose tumors carry them.

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. Immature white blood cells known as myeloblasts, or "blasts" proliferate in the bone marrow rather than mature into normal blood cells. The decrease in normal blood cells can result in severe complications for patients including infections and dependence on blood product transfusions. AML incidence significantly increases with age, and according to the American Cancer Society, the median age of onset is 66. Less than 10 percent of U.S. AML patients are eligible for bone marrow transplant and 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 and IDH2 mutations are present in about 15 to 23 percent of AML cases.

About Agios
Agios is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic metabolic disorders 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.

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 Agios' product candidates targeting IDH mutations, including AG-120; Agios' plans for the further clinical development of AG-120; Agios' potential NDA submission for AG-120; 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; that a submitted NDA will be accepted; that an accepted NDA will be approved; 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’ Quarterly Report on Form 10-Q for the quarter ended September 30, 2016, 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.

Contacts

Investors:
Kendra Adams, 617-844-6407
Senior Director, Investor & Public Relations
Kendra.Adams@agios.com

Renee Leck, 617-649-8299
Senior Manager, Investor & Public Relations
Renee.Leck@agios.com

Media:
Dan Budwick, 973-271-6085
Senior Vice President, Media Relations
Pure Communications Inc.
dan@purecommunicationsinc.com

Agios Pharmaceuticals