Agios Outlines Key Clinical Development & Research Strategies

October 16, 2015

- Phase 3 Study of AG-221 in Relapsed/Refractory IDH2 Mutant Acute Myeloid Leukemia (IDHENTIFY) Initiated -

- Frontline Combination Development Strategy for AG-221 and AG-120 Announced -

- Second Pyruvate Kinase-R Activator AG-519 Entering Clinical Development -

- Company to Webcast Today's R&D Day -

CAMBRIDGE, Mass., Oct. 16, 2015 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals (NASDAQ:AGIO) announced its clinical development strategy for the company's lead cancer metabolism and rare genetic metabolic disorders programs, along with insights into emerging research at its R&D Day today.

"With our lead IDH programs progressing through Phase 1 expansion cohorts and the initiation of the Phase 3 AG-221 study with our collaboration partner Celgene, we are moving closer to our goal of providing people with advanced AML with transformational new medicines as quickly as possible," said David Schenkein, M.D., chief executive officer at Agios. "We will share our long-term vision for these programs at today's R&D Day, as we hope to one day provide benefit to every patient diagnosed with an IDH mutant-positive cancer."

"At our core, Agios is a research-driven organization, and I'm proud that our scientists have discovered AG-519, a novel PK activator, which represents our fifth new investigational medicine in just seven years. We continue to conduct research that we believe will enable us to make important advances for patients," Dr. Schenkein continued.

IDH Program Updates

In clinical studies to date, AG-221 and AG-120, which target mutated IDH2 and IDH1, respectively, have demonstrated positive clinical single-agent activity with durable complete and partial responses and manageable safety profiles in patients with AML. Together with our collaboration partner Celgene, Agios remains committed to bringing AG-221 and AG-120 to patients as quickly and efficiently as possible by leveraging a clinical development strategy that maximizes both speed and breadth.

Agios today announced clinical development updates for AG-221 and AG-120 in AML, including:

- Initiation of the AG-221 Phase 3 Study: The IDHENTIFY study of AG-221 is a Phase 3, international, multi-center, open-label, randomized clinical trial designed to compare the efficacy and safety of AG-221 versus conventional care regimens in patients 60 years or older with IDH2 mutant-positive AML that is refractory to or relapsed after second- or third-line therapy. Additional details can be found below and on www.clinicaltrials.gov. This study is being conducted by Celgene.
- Novel Design of the AG-221 and AG-120 Frontline Trials in AML:
    - For Newly Diagnosed AML Patients Eligible for Intensive Chemotherapy: A Phase 1b combination study of either AG-221 or AG-120 with standard induction (7+3, Ara-C and idarubicin/daunorubicin) and consolidation (Ara-C, or mitoxantrone with etoposide) chemotherapy is planned for initiation by the end of 2015.
    - For Newly Diagnosed AML Patients Not Eligible for Intensive Chemotherapy: A Phase 1/2 combination study of either AG-221 or AG-120 with VIDAZA® (azacitidine) is planned for initiation in the first quarter of 2016. This study has a Phase 1 component to determine the safety of the combinations, followed by a Phase 2 randomized component evaluating the safety and clinical activity of each investigational combination versus single-agent VIDAZA® using a primary endpoint of overall response rate.
- ASH Data Presentations: New data from the ongoing Phase 1 dose-escalation and expansion studies of AG-221 and AG-120 in advanced hematologic malignancies have been accepted for presentation at the American Society of Hematology (ASH) Annual Meeting and Exhibition taking place December 5-8, 2015 in Orlando.
- EORTC-NCI-AACR Data Presentation: The first data from the ongoing Phase 1 trial of AG-120 in advanced IDH1-mutant positive solid tumors have been accepted for oral presentation at EORTC-NCI-AACR International Conference on Molecular Targets and Cancer Therapeutics taking place November 5-9, 2015 in Boston.

Pyruvate Kinase (PK) Deficiency Program Updates

Agios is pioneering the development of its small molecule enzyme activators in PK deficiency, a rare genetic metabolic disorder with no disease-altering therapies.

- AG-348: AG-348, a first-in-class orally available, potent, selective small molecule activator of pyruvate kinase-R (PKR), is on track and enrolling in DRIVE PK, a global Phase 2, open-label safety and efficacy trial in adult, transfusion-independent patients with PK deficiency.
- AG-519: Agios announced today the development of its second PKR activator, AG-519. This program provides clinical

development optionality for our PK activator portfolio and potentially opportunities in other hemolytic anemias where PK activation may be therapeutic. The development plan for AG-519 includes a placebo-controlled Phase 1 study in healthy volunteers, which is planned for the first quarter of 2016. This study will be an integrated single ascending dose (SAD) and multiple ascending dose (MAD) trial.

Research Program Updates

Agios has advanced and led the emerging field of cancer metabolism with its novel IDH1 and IDH2 programs, demonstrating significant potential benefit for AML patients whose cancers carry these mutations. Agios' work in IDH exemplifies the company's strategy of targeting metabolic vulnerabilities. The company continues to discover novel metabolic targets that meet a high bar for future development. Today at its R&D day, Agios will describe:

- Its precision medicine strategy to discover novel cancer metabolism targets.
- Novel research approach to rare genetic diseases using allosteric modulation to correct the underlying dysfunction in metabolic pathways.
- The potential for PKR activators to provide clinical benefit in other indications, such as beta-thalassemia.

Webcast

A live webcast of the company's R&D Day will begin today at 9:00 a.m. ET and can be accessed under "Events & Presentations" in the Investors and Media section of the company's website at www.agios.com. A replay of the webcast will be archived on the Agios website for 30 days following the presentation.

About the IDHENTIFY Phase 3 Study of AG-221

The Phase 3, international, multicenter, open-label, randomized clinical trial is designed to compare the efficacy and safety of AG-221 versus conventional care regiments in subjects 60 years or older with IDH2 mutant-positive AML refractory to or relapsed after second- or third-line therapy. Patients will be randomly assigned to receive either AG-221, 100 mg orally once a day for 28 days, or one of the conventional care regiments. The conventional treatment options include best supportive care only, azacitidine, low-dose cytarabine or intermediate-dose cytarabine. The primary endpoint of the trial is overall survival. The study is expected to enroll approximately 280 patients and is being conducted by Celgene. Please refer to www.clinicaltrials.gov for additional clinical trial details.

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. 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 AG-348 and PK Deficiency

PKD is a rare inherited disease resulting from mutations in the PKR enzyme that result in hemolytic anemia, which is the accelerated destruction of red blood cells. The mutations in the PKR enzymes cause a deficit in cellular energy within the red blood cell, as evidenced by a decline in the energy metabolite ATP and a build-up of the metabolite 2,3-DPG. Agios scientists have previously reported that AG-348 is a potent activator of the wild-type and mutated PKR enzymes, resulting in restoration of ATP levels and a decrease in 2,3-DPG levels in patient blood *ex vivo*. The current standard of care for PK deficiency is supportive, including blood transfusions, splenectomy, chelation therapy to address iron overload and/or interventions for other treatment- and disease-related morbidities. Currently, there is no approved therapy to treat the underlying cause of PKD. AG-348, a first-in-class orally available, potent, selective small molecule activator of PKR, was discovered by Agios scientists, and the company retains worldwide development and commercialization rights.

About Agios

Agios is focused on discovering and developing novel investigational medicines to treat cancer and rare genetic disorders of metabolism 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 IDH1/IDH2 or pyruvate kinase-R mutations, including AG-221, AG-120, AG-881, AG-348 and AG-519; its plans and timelines for the clinical development of AG-221, AG-120, AG-348 and AG-519; its plans regarding future data presentations; and the benefit of its strategic plans and focus. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "potential," "hope," "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 June 30, 2015, 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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