FDA Grants Approval of TIBSOVO®, the First Oral, Targeted Therapy for Adult Patients with Relapsed/Refractory Acute Myeloid Leukemia and an IDH1 Mutation

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CAMBRIDGE, Mass., July 20, 2018 (GLOBE NEWSWIRE) -- - *Approval of TIBSOVO® was Based on Phase 1 Study Results, Including Rate and Duration of Complete Remission (CR) and CR with Partial Hematologic Recovery (CRh) and Rate of Conversion to Transfusion Independence[1]* -

TIBSOVO 250 mg bottle

TIBSOVO

- With Second IDHm Inhibitor Approved in Less Than A Year, Treatments Discovered and Developed by Agios Now Available for Relapsed/Refractory AML with an IDH1 or IDH2 Mutation -

- AML Patients with IDH1 and IDH2 Mutations Represent ~20% of All Patients with AML[2] -

- Company to Host Investor Conference Call Today at 1p.m. ET -

Agios Pharmaceuticals, Inc. (NASDAQ:AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today announced that TIBSOVO® (ivosidenib) was granted approval from the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (R/R AML) with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation as detected by an FDA approved test. TIBSOVO®, an oral, targeted inhibitor of the IDH1 enzyme, is the first and only FDA-approved therapy for patients with R/R AML and an IDH1 mutation[1].

“The FDA approval of TIBSOVO ® – our first wholly owned drug and the second approved medicine from our research platform in less than a year – is

an incredibly exciting milestone for our company and, importantly, for the approximately 6-10% of AML patients with an IDH1 mutation who have been waiting for new treatment options that work radically different than conventional chemotherapy," said David Schenkein, M.D., chief executive officer at Agios. "I want to thank the patients and their caregivers, nurses and physicians who participated in our clinical trials. With their support and the dedication of Agios' employees, we are well on our way to becoming a sustainable multi-product biopharmaceutical company delivering medicines that have the potential to change how serious diseases are treated."

AML is a cancer of the blood and bone marrow marked by rapid disease progression and is the most common acute leukemia affecting adults with approximately 20,000 new cases estimated in the U.S. each year.[3,4] The majority of patients with AML eventually relapse. Relapsed or refractory AML has a poor prognosis.[5] The five-year survival rate is approximately 27%.[3] For 6 to 10 percent of AML patients, the mutated IDH1 enzyme blocks normal blood stem cell differentiation, contributing to the genesis of acute leukemia.[2]

"AML patients who relapse or are refractory to available therapies have few, if any, treatment options," said Hagop M. Kantarjian, M.D., professor and chair of the Department of Leukemia at The University of Texas MD Anderson Cancer Center. "The clinical study demonstrated that TIBSOVO® has the potential to deliver strong, durable responses as a single agent and can help patients achieve and maintain transfusion independence. IDH inhibitors represent a new class of noncytotoxic, targeted therapies for AML patients with IDH mutations."

TIBSOVO® Safety and Efficacy Data[1]

The FDA approval was based on the clinical data from an open-label, single-arm, multicenter dose-escalation and expansion trial of adult patients with R/R AML and an IDH1 mutation (Study AG120-C-001, NCT02074839). TIBSOVO® was approved concurrently with the Abbott RealTi*m*e ™ IDH1 companion diagnostic test for selection of patients with R/R AML for treatment with TIBSOVO®.

The efficacy of TIBSOVO® was evaluated in 174 adult patients with R/R AML with an IDH1 mutation identified or confirmed by the Abbott RealTi*m*e ™ IDH1 assay. TIBSOVO® was given orally at a starting dose of 500 mg daily until disease progression, development of unacceptable toxicity, or undergoing hematopoietic stem cell transplantation. Patients had a median age of 67 years (range of 18 to 87) and received a median of two prior anticancer therapies (ranging from one to six). More than half (63%) were refractory to previous therapy and 33% had secondary AML. The primary endpoint is the combined complete remission (CR) and complete remission with partial hematologic improvement (CRh) rate. CRh is defined as <5% of blasts in the bone marrow, no evidence of disease and partial recovery of peripheral blood counts (platelets >50,000/microliter and ANC >500/microliter).

In this trial, TIBSOVO® demonstrated:

- CR+CRh rate of 32.8% (57 of 174 patients) (95% CI: 25.8, 40.3).
- The CR rate was 24.7% (43 of 174 patients) (95% CI 18.5, 31.8) and the CRh rate was 8% (14 of 174 patients) (95% CI 4.5, 13.1).
- Median duration of CR+CRh was 8.2 months (95% CI: range 5.6, 12 months).
- For patients who achieved a CR or CRh, the median time to best response of CR or CRh was 2.0 months (range, 0.9 to 5.6 months).
- Among the 110 patients who were dependent on red blood cell (RBC) and/or platelet transfusions at baseline, 41 (37.3%) became independent of RBC and platelet transfusions during any 56-day post-baseline period.
- Of the 64 patients who were independent of both RBC and platelet transfusions at baseline, 38 (59.4%) remained transfusion independent during any 56-day post-baseline period.
- Twenty-one of the 174 patients (12%) went on to stem cell transplant following TIBSOVO® treatment.

The safety profile of single-agent TIBSOVO® was evaluated in 179 patients with R/R AML with an IDH1 mutation treated with a dose of 500 mg daily. The median duration of exposure to TIBSOVO® was 3.9 months (range 0.1 to 39.5 months). In the clinical trial, 19% (34/179) of patients treated with TIBSOVO® experienced differentiation syndrome, which can be fatal if not treated. QTc interval prolongation and Guillain-Barré Syndrome occurred in patients treated with TIBSOVO®. The most common adverse reactions (≥20%) of any grade were fatigue, leukocytosis, arthralgia, diarrhea, dyspnea, edema, nausea, mucositis, electrocardiogram QT prolonged, rash, pyrexia, cough and constipation. The most frequent serious adverse reactions (≥5%) were differentiation syndrome (10%), leukocytosis (10%) and electrocardiogram QT prolonged (7%).

About TIBSOVO® (ivosidenib)

TIBSOVO® (ivosidenib) is an isocitrate dehydrogenase-1 (IDH1) inhibitor indicated for the treatment of adult patients with relapsed or refractory acute myeloid leukemia (AML) with a susceptible IDH1 mutation as detected by an FDA-approved test. For more information, visit TIBSOVO.com.

IMPORTANT SAFETY INFORMATION

WARNING: DIFFERENTIATION SYNDROME

Patients treated with TIBSOVO have experienced symptoms of differentiation syndrome, which can be fatal if not treated. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, and hepatic, renal, or multi-organ dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

WARNINGS AND PRECAUTIONS

Differentiation Syndrome: See Boxed WARNING. In the clinical trial, 19% (34/179) of patients with relapsed or refractory AML treated with

TIBSOVO experienced differentiation syndrome. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal if not treated. Symptoms of differentiation syndrome in patients treated with TIBSOVO included noninfectious leukocytosis, peripheral edema, pyrexia, dyspnea, pleural effusion, hypotension, hypoxia, pulmonary edema, pneumonitis, pericardial effusion, rash, fluid overload, tumor lysis syndrome, and creatinine increased. Of the 34 patients who experienced differentiation syndrome, 27 (79%) recovered after treatment or after dose interruption of TIBSOVO. Differentiation syndrome occurred as early as 1 day and up to 3 months after TIBSOVO initiation and has been observed with or without concomitant leukocytosis.

If differentiation syndrome is suspected, initiate dexamethasone 10 mg IV every 12 hours (or an equivalent dose of an alternative oral or IV corticosteroid) and hemodynamic monitoring until improvement. If concomitant noninfectious leukocytosis is observed, initiate treatment with hydroxyurea or leukapheresis, as clinically indicated. Taper corticosteroids and hydroxyurea after resolution of symptoms and administer corticosteroids for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid and/or hydroxyurea treatment. If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, interrupt TIBSOVO until signs and symptoms are no longer severe.

QTc Interval Prolongation: Patients treated with TIBSOVO can develop QT (QTc) prolongation and ventricular arrhythmias. One patient developed ventricular fibrillation attributed to TIBSOVO. Concomitant use of TIBSOVO with drugs known to prolong the QTc interval (e.g., anti-arrhythmic medicines, fluoroquinolones, triazole anti-fungals, 5-HT_3 receptor antagonists) and CYP3A4 inhibitors may increase the risk of QTc interval prolongation. Conduct monitoring of electrocardiograms (ECGs) and electrolytes. In patients with congenital long QTc syndrome, congestive heart failure, electrolyte abnormalities, or in those who are taking medications known to prolong the QTc interval, more frequent monitoring may be necessary.

Interrupt TIBSOVO if QTc increases to greater than 480 msec and less than 500 msec. Interrupt and reduce TIBSOVO if QTc increases to greater than 500 msec. Permanently discontinue TIBSOVO in patients who develop QTc interval prolongation with signs or symptoms of life-threatening arrhythmia.

Guillain-Barré Syndrome: Guillain-Barré syndrome occurred in <1% (2/258) of patients treated with TIBSOVO in the clinical study. Monitor patients taking TIBSOVO for onset of new signs or symptoms of motor and/or sensory neuropathy such as unilateral or bilateral weakness, sensory alterations, paresthesias, or difficulty breathing. Permanently discontinue TIBSOVO in patients who are diagnosed with Guillain-Barré syndrome.

ADVERSE REACTIONS

- The most common adverse reactions (≥20%) of any grade were fatigue (39%), leukocytosis (38%), arthralgia (36%), diarrhea (34%), dyspnea (33%), edema (32%), nausea (31%), mucositis (28%), electrocardiogram QT prolonged (26%), rash (26%), pyrexia (23%), cough (22%), and constipation (20%).
- The most frequently reported ≥Grade 3 adverse reactions (≥5%) were electrocardiogram QT prolonged (10%), dyspnea (9%), leukocytosis (8%), tumor lysis syndrome (6%), and differentiation syndrome (5%).
- Serious adverse reactions (≥5%) were differentiation syndrome (10%), leukocytosis (10%), and electrocardiogram QT prolonged (7%). There was one case of progressive multifocal leukoencephalopathy (PML).

DRUG INTERACTIONS

Strong or Moderate CYP3A4 Inhibitors: Reduce TIBSOVO dose with strong CYP3A4 inhibitors. Monitor patients for increased risk of QTc interval prolongation.

Strong CYP3A4 Inducers: Avoid concomitant use with TIBSOVO.

Sensitive CYP3A4 Substrates: Avoid concomitant use with TIBSOVO.

QTc Prolonging Drugs: Avoid concomitant use with TIBSOVO. If co-administration is unavoidable, monitor patients for increased risk of QTc interval prolongation.

LACTATION

Many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed children, advise women not to breastfeed during treatment with TIBSOVO and for at least 1 month after the last dose.

Please see full Prescribing Information, including Boxed WARNING.

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.[4] Undifferentiated blast cells proliferate in the bone marrow rather than mature into normal blood cells.[4] AML incidence significantly increases with age, and the median age of diagnosis is 68.[3] The vast majority of patients do not respond to chemotherapy and progress to relapsed/refractory AML.[5] The five-year survival rate for AML is approximately 27 percent.[3] IDH1 mutations are present in about 6 to 10 percent of AML cases.[2]

Conference Call Information

Agios will host a conference call and live webcast with slides today at 1p.m. ET to discuss the FDA approval of TIBSOVO®. To participate in the conference call, please dial 1-877-377-7098 (domestic) or 1-631-291-4547 (international) and referring to conference ID 2065849. The live webcast can be accessed under “Events & Presentations” in the Investors section of the company's website at www.agios.com. The archived webcast will be available on the company's website beginning approximately two hours after the event.

About myAgios™ Patient Support Services

myAgios™ Patient Support Services is an expansive program that helps patients with access, reimbursement, and financial assistance for TIBSOVO® (ivosidenib). Healthcare providers and pharmacists can enroll patients at myAgios.com/enroll.

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 two approved oncology precision medicines and multiple first-in-class investigational therapies 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' products, including TIBSOVO® (ivosidenib), and its strategic plans and focus. The words “estimate,” “may,” “milestone,” “potential,” 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 development of any of Agios' product candidates will successfully continue, or 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 CStone Pharmaceuticals; 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.

References

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