



AgiOS Announces FDA Acceptance of Supplemental New Drug Application for TIBSOVO® (ivosidenib) for the Treatment of Patients with Newly Diagnosed Acute Myeloid Leukemia with an IDH1 Mutation Not Eligible for Standard Therapy

February 20, 2019

– PDUFA Date Set for June 21, 2019 –

CAMBRIDGE, Mass., Feb. 20, 2019 (GLOBE NEWSWIRE) -- Agios Pharmaceuticals, Inc. (NASDAQ:AGIO), a leader in the field of cellular metabolism to treat cancer and rare genetic diseases, today announced that the U.S. Food and Drug Administration (FDA) has accepted the company's supplemental New Drug Application (sNDA) for TIBSOVO® (ivosidenib) for the treatment of patients with newly diagnosed acute myeloid leukemia (AML) with an isocitrate dehydrogenase 1 (IDH1) mutation who are not eligible for standard therapy.

The sNDA was granted Priority Review and has been given a Prescription Drug User Fee Act (PDUFA) action date of June 21, 2019. The FDA's Priority Review status accelerates the review time from 10 months to a goal of six months from the day of filing acceptance and is given to drugs that may offer major advances in treatment or may provide a treatment where no adequate therapy exists. In addition, the FDA accepted the TIBSOVO® sNDA under its Real-Time Oncology Review pilot program, which aims to make the review of oncology drugs more efficient by allowing the FDA access to clinical trial data before the information is formally submitted to the agency.

"In less than seven months since TIBSOVO's approval in relapsed or refractory AML, we are pleased to be working with the FDA to expand its labeled indication into the frontline setting," said Chris Bowden, M.D., chief medical officer of Agios. "Patients with newly diagnosed AML who are not eligible for standard treatments, such as intensive and non-intensive chemotherapy, are currently offered only palliative care. There is tremendous need for new treatment options, and we believe AML patients with IDH1 mutations have the potential to benefit from this targeted therapy."

TIBSOVO® is a first-in-class, oral, targeted inhibitor of mutant IDH1. The sNDA submission is based on results from the untreated AML patients from the Phase 1 dose-escalation and expansion study of ivosidenib in patients with newly diagnosed AML ineligible for standard treatment. Data from the untreated AML portion of this study were presented at the 2018 American Society of Hematology (ASH) Annual Meeting.

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-HT₃ 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 ($\geq 20\%$) 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 \geq Grade 3 adverse reactions ($\geq 5\%$) were electrocardiogram QT prolonged (10%), dyspnea (9%), leukocytosis (8%), tumor lysis syndrome (6%), and differentiation syndrome (5%).
- Serious adverse reactions ($\geq 5\%$) 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. Undifferentiated blast cells proliferate in the bone marrow rather than mature into normal blood cells. AML incidence significantly increases with age, and the median age of diagnosis is 68. 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 27 percent. IDH1 mutations are present in about 6 to 10 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 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 Agios' expectations for the FDA's review of its sNDA for TIBSOVO[®] (ivosidenib). The words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" 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, the FDA's acceptance of Agios's sNDA for TIBSOVO[®] is not a guarantee of approval. 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: risks associated with the regulatory review process generally; the risk that the FDA may determine that the data included in the sNDA are insufficient for approval and that the Company must conduct additional clinical trials, or nonclinical or other studies, before the sNDA can be approved; the risk that the results of previously conducted studies involving TIBSOVO[®] will not be repeated or observed in ongoing or future studies or following commercial launch, if the sNDA is approved; and risks associated with the Company's dependence on third parties with respect to regulatory matters for TIBSOVO[®]. 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.

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