Pfizer Logo

European Commission Approves DAURISMO™ (glasdegib) for Certain Adult Patients with Newly Diagnosed Acute Myeloid Leukemia (AML)

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NEW YORK, N.Y., June 29, 2020 – Pfizer Inc. (NYSE:PFE) today announced that the European Commission approved DAURISMO™ (glasdegib), a Hedgehog pathway inhibitor, in combination with low-dose cytarabine (LDAC), a type of chemotherapy, for the treatment of newly diagnosed (de novo or secondary) acute myeloid leukemia (AML) in adult patients who are not candidates for standard chemotherapy. The approval follows the medicine's positive opinion from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) earlier this year, as well as the medicine's approval by the U.S. Food and Drug Administration (FDA) in November 2018.

"The standard of care for people with acute myeloid leukemia is intensive chemotherapy, however, this is not an option for many elderly people and those who have certain health conditions prior to receiving their diagnosis," said Masum Hossain, Regional President, Oncology International Developed Markets at Pfizer. "Through the European Commission approval of DAURISMO, we are proud to further deliver on our decades long commitment to people living with blood cancers by offering this new treatment option for certain patients in Europe with acute myeloid leukemia, who previously had limited treatment options."

The European Commission's approval of DAURISMO is based on results from the Phase 2 BRIGHT 1003 trial, which showed DAURISMO nearly doubled median overall survival compared to LDAC alone (8.3 months vs. 4.3 months, HR 0.463, 95% CI [0.299,0.717]) in patients with previously untreated (de novo or secondary) AML who were not eligible for intensive chemotherapy. The difference represented a 54 percent reduction in the risk of death for patients treated with DAURISMO plus LDAC (HR: 0.463, 95% CI: 0.299, 0.717, one-sided p-value 0.0002).[1]

"The BRIGHT 1003 trial demonstrated that DAURISMO in combination with low-dose cytarabine nearly doubled overall survival compared to low-dose cytarabine alone," said Dr. Pau Montesinos, M.D., Ph.D., attending physician at the University Hospital La Fe in Valencia, Spain. "People with previously untreated acute myeloid leukemia who cannot withstand intensive chemotherapy are in urgent need of new options and I look forward to using this new therapy that may extend survival for appropriate patients."

In the Phase 2 BRIGHT 1003 trial, 116 patients with previously untreated de novo or secondary AML who were not eligible to receive intensive chemotherapy were randomized 2:1 to receive DAURISMO plus LDAC or LDAC alone. Of the 78 patients treated with DAURISMO plus LDAC, more than half (51%, 40 patients) had secondary AML, or AML that develops as a result of prior blood/bone marrow conditions or previous anticancer therapy. Eleven of the 40 patients with secondary AML received prior treatment with a hypomethylating agent; historically, the prognosis is poor for these patients and treatment options have been limited to clinical trials or

palliative care.

The most frequently (?20%) reported adverse reactions in patients receiving DAURISMO were anemia (45.2%), hemorrhages (45.2%), febrile neutropenia (35.7%), nausea (35.7%), decreased appetite (33.3%), fatigue (30.9%), muscle spasms (30.9%), thrombocytopenia (30.9%), pyrexia (29.7%), diarrhea (28.5%), pneumonia (28.5%), dysgeusia (26.1%), oedema peripheral (26.1%), constipation (25.0%), abdominal pain (25.0%), rash (25.0%), dyspnea (25.0%) vomiting (21.4%), and weight decreased (20.2%). The most frequently reported adverse reactions leading to dose reductions in patients receiving DAURISMO were muscle spasms (4.7%), fatigue (3.5%), febrile neutropenia (3.5%), anemia (2.3%), thrombocytopenia (2.3%), and electrocardiogram QT prolonged (2.3%). The most frequently reported adverse reactions leading to permanent discontinuation in patients receiving DAURISMO were pneumonia (5.9%), febrile neutropenia (3.5%), and nausea (2.3%).[1]

About DAURISMO™ (glasdegib)

DAURISMO is a once-daily oral Hedgehog pathway inhibitor, taken in combination with LDAC. In the EU, DAURISMO is approved in combination with LDAC for the treatment of newly diagnosed (de novo or secondary) acute myeloid leukemia (AML) in adult patients who are not candidates for standard chemotherapy. 1 In the U.S. and Canada, DAURISMO is approved in combination with LDAC for the treatment of newly diagnosed AML in adult patients who are 75 years or older or who have comorbidities that preclude use of intensive induction chemotherapy.[2,3]

IMPORTANT DAURISMO™ (Glasdegib) SAFETY INFORMATION FROM THE U.S. PRESCRIBING INFORMATION

WARNING: EMBRYO-FETAL TOXICITY: DAURISMO can cause embryo-fetal death or severe birth defects when administered to a pregnant woman. DAURISMO is embryotoxic, fetotoxic, and teratogenic in animals. Conduct pregnancy testing in females of reproductive potential prior to initiation of DAURISMO treatment. Advise females of reproductive potential to use effective contraception during treatment with DAURISMO and for at least 30 days after the last dose. Advise males of the potential risk of DAURISMO exposure through semen and to use condoms with a pregnant partner or a female partner of reproductive potential during treatment with DAURISMO and for at least 30 days after the last dose to avoid potential drug exposure.

Blood Donation: Advise patients not to donate blood or blood products while taking DAURISMO and for at least 30 days after the last dose, because their blood or blood products might be given to a female of reproductive potential.

QTc Interval Prolongation: Patients treated with DAURISMO can develop QTc prolongation and ventricular arrhythmias, including ventricular fibrillation and ventricular tachycardia. Of the 98 evaluable patients treated with DAURISMO 100 mg in combination with low-dose cytarabine in the clinical trial, 5% were found to have a QTc interval greater than 500 ms and 4% of patients had an increase from baseline QTc greater than 60 ms. The clinical trial excluded patients with baseline QTc of greater than 470 ms or with a history of long QT syndrome or uncontrolled cardiovascular disease. Monitor electrocardiograms (ECGs) and electrolytes.

Concomitant use of DAURISMO with drugs known to prolong the QTc interval and CYP3A4 inhibitors may increase the risk of QTc interval prolongation. In patients with congenital long QT syndrome, congestive heart failure, electrolyte abnormalities, or those who are taking medications known to prolong the QTc interval, more frequent ECG monitoring is recommended. Interrupt DAURISMO if QTc interval is >500 ms and discontinue permanently for patients who develop QTc interval prolongation with signs or symptoms of life-threatening arrhythmia.

Adverse Reactions: Most common adverse reactions associated with DAURISMO (incidence ?20%) were anemia (43%), fatigue (36%), hemorrhage (36%), febrile neutropenia (31%), musculoskeletal pain (30%), edema (30%), thrombocytopenia (30%), nausea (29%), dyspnea (23%), decreased appetite (21%), dysgeusia (21%), mucositis (21%), constipation (20%), and rash (20%).

Drug Interactions: Co-administration with strong CYP3A4 inhibitors increased DAURISMO plasma concentrations, which may increase the risk of adverse reactions including QTc interval prolongation. Consider alternative therapies that are not strong CYP3A4 inhibitors during treatment with DAURISMO and monitor patients for increased risk of adverse reactions including QTc interval prolongation. Strong and moderate CYP3A4 inducers should be avoided due to decreased DAURISMO plasma concentrations, which may reduce efficacy. If concomitant use of moderate CYP3A4 inducers cannot be avoided, increase the DAURISMO dosage to 200 mg once daily (if the patient is taking 100 mg) and 100 mg once daily (if the patient is taking 50 mg) as tolerated. Co-administration of DAURISMO with QTc-prolonging drugs may increase the risk of QTc interval prolongation. Avoid co-administration of QTc-prolonging drugs with DAURISMO or replace with alternative therapies. If co-administration of a QTc-prolonging drug is unavoidable, monitor patients for increased risk of QTc interval prolongation.

Lactation: Because of the potential for serious adverse reactions from DAURISMO in a breastfed child, advise women who are taking DAURISMO not to breastfeed or provide breast milk to infants or children during treatment and for at least 30 days after the last dose.

Renal Impairment: No dosage modification is recommended for patients with mild to severe renal impairment. Monitor patients with severe renal impairment (eGFR 15 to 29 mL/min) for increased risk of adverse reactions, including QTc interval prolongation, due to increased glasdegib concentrations.

About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference in the lives of people living with cancer. Today, we have an industry-leading portfolio of 23 approved innovative cancer medicines and biosimilars across more than 30 indications, including breast, genitourinary, colorectal, blood and lung cancers, as well as melanoma.

Pfizer Inc.: Breakthroughs that change patients' lives

At Pfizer, we apply science and our global resources to bring therapies to people that extend and significantly improve their lives. We strive to set the standard for quality, safety and value in the discovery, development and manufacture of health care products, including innovative medicines and vaccines. Every day, Pfizer colleagues work across developed and emerging markets to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. Consistent with our responsibility as one of the world's premier innovative biopharmaceutical companies, we collaborate with health care providers, governments and local communities to support and expand access to reliable, affordable health care around the world. For more than 150 years, we have worked to make a difference for all who rely on us. We routinely post information that may be important to investors on our website at www.pfizer.com. In addition, to learn more, please visit us on www.pfizer.com and follow us on Twitter at @Pfizer and @Pfizer_News, LinkedIn, YouTube and like us on Facebook at Facebook.com/Pfizer.

DISCLOSURE NOTICE: The information contained in this release is as of June 29, 2020. Pfizer assumes no obligation to update forward-looking statements contained in this release as the result of new information or future events or developments.

This release contains forward-looking information about DAURISMOTM (glasdegib)and Pfizer Oncology, including their potential benefits, that involve substantial risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statements. Risks and uncertainties include, among other things, uncertainties regarding the commercial success of DAURISMO; the uncertainties inherent in research and development, including the ability to meet anticipated clinical endpoints, commencement and/or completion dates for our clinical trials, regulatory submission dates, regulatory approval dates and/or launch dates, as well as the possibility of unfavorable new clinical data and further analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations and assessments by regulatory authorities; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when applications for DAURISMO may be filed in any other jurisdictions; for any additional indications for DAURISMO or for any other oncology products; whether and when any such applications for DAURISMO that may be pending or filed may be approved by regulatory authorities, which will depend on myriad factors, including making a determination as to whether the product's benefits outweigh its known risks and determination of the product's efficacy and, if approved, whether DAURISMO will be commercially successful; decisions by regulatory authorities impacting labeling, manufacturing processes, safety and/or other matters that could affect the availability or commercial potential of DAURISMO; uncertainties regarding the impact of COVID-19 on our business, operations and financial results; and competitive developments.

A further description of risks and uncertainties can be found in Pfizer's Annual Report on Form 10-K for the fiscal year ended December 31, 2019 and in its subsequent reports on Form 10-Q, including in the sections thereof captioned "Risk Factors" and "Forward-Looking Information and Factors That May Affect Future Results", as well as in its subsequent reports on Form 8-K, all of which are filed with the U.S. Securities and Exchange Commission and available at www.sec.gov and www.pfizer.com.

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[1] DAURISMO™ (glasdegib) Summary of Product Characteristics.

[2] DAURISMO™ (glasdegib) Prescribing Information. New York. NY: Pfizer Inc: 2020.

[3] DAURISMO™ (glasdegib) Patient Medication Information. Kirkland. QC : Pfizer Canada ULC: 2020.

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