



# U.S. FDA Approves DAURISMO™ (glasdegib) for Adult Patients with Newly-Diagnosed Acute Myeloid Leukemia (AML) for Whom Intensive Chemotherapy is Not an Option

Wednesday, November 21, 2018 - 08:40am

DAURISMO is the first and only Hedgehog pathway inhibitor approved for the treatment of AML. In a randomized Phase 2 trial, DAURISMO plus low-dose chemotherapy significantly improved median overall survival in patients who were not able to receive intensive chemotherapy due to age or comorbidities – a difficult-to-treat patient population.

Pfizer Inc. (NYSE:PFE) today announced that the U.S. Food and Drug Administration (FDA) approved DAURISMO™ (glasdegib), a once-daily oral medicine, for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adult patients who are 75 years or older or who have comorbidities that preclude use of intensive induction chemotherapy. DAURISMO is taken in combination with low-dose cytarabine (LDAC), a type of chemotherapy. DAURISMO has not been studied in patients with severe renal impairment or moderate-to-severe hepatic impairment.<sup>1</sup>

AML is a rapidly progressing bone marrow cancer with poor survival rates compared to other leukemias.<sup>2</sup> The standard of care for people with AML is intensive chemotherapy; however, for many elderly patients with AML, as well as those who have certain health conditions prior to receiving their diagnosis, intensive treatment is not an option.<sup>3</sup> Historically, a majority of these individuals do not receive treatment and face a poor prognosis.<sup>4</sup>

“As our second medicine approved in the last 14 months for patients with acute myeloid leukemia, DAURISMO reinforces our commitment to delivering new medicines to patients living with some of the most difficult-to-treat cancers, especially those for which there are limited treatment options available,” said Andy Schmeltz, Global President, Pfizer Oncology. “We are proud to now offer these patients for whom intensive chemotherapy is not an option a new oral medicine, taken in combination with low-dose chemotherapy, that may improve their chances of survival.”

DAURISMO is the first and only FDA-approved Hedgehog pathway inhibitor for AML. The Hedgehog signaling pathway plays an essential role in embryogenesis, the process by which human embryos are developed. In adults, however, abnormal activation of this pathway is thought to contribute to the development and persistence of cancer stem cells. Preclinical studies have shown that disruption of this pathway can impair the development and survival of these cancer stem cells.<sup>5,6</sup>

“The randomized Phase 2 study, which formed the basis for today’s approval, included patients with cardiac disease or mild to moderate kidney disease, who are often excluded from clinical trials,” said Jorge Cortes, M.D., deputy chair and professor of medicine in the Department of Leukemia, University of Texas, MD Anderson Cancer Center. “In the trial, DAURISMO plus low-dose chemotherapy reduced the risk of death during the study period by 54 percent compared to chemotherapy alone. This provides a much-needed treatment for those patients for whom intensive chemotherapy is not an option.”

In the pivotal, randomized, international Phase 2 BRIGHT 1003 trial, 115 patients with newly diagnosed AML were randomized 2:1 to receive DAURISMO plus LDAC or LDAC alone. Of the 77 patients treated with DAURISMO plus LDAC, more than half (51%, 39 patients) had secondary AML, or AML that develops as a result of prior blood/bone marrow conditions or previous anticancer therapy. Eleven of the 39 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. Median overall survival was 8.3 months (95% CI: 4.4,12.2) for patients treated with DAURISMO plus LDAC compared with 4.3 months (95% CI: 1.9, 5.7) for patients treated with LDAC alone. This difference represented a 54 percent reduction in the risk of death for patients treated with DAURISMO plus LDAC (HR: 0.46, 95% CI: 0.30, 0.71, one-sided p-value 0.0002).<sup>1</sup>

The U.S. labeling for DAURISMO includes a boxed warning for embryo-fetal toxicity. The most frequently ( $\geq 20\%$  of patients) reported adverse events (AEs) in patients treated with DAURISMO plus LDAC compared to LDAC alone in first 90 days of therapy were

anemia (43% vs 42%), fatigue (36% vs 32%), hemorrhage (36% vs 42%), febrile neutropenia (31% vs 22%), musculoskeletal pain (30% vs 17%), nausea (29% vs 12%), edema (30% vs 20%), thrombocytopenia (30% vs 27%), dyspnea (23% vs 24%), decreased appetite (21% vs 7%), dysgeusia (21% vs 2%), mucositis (21% vs 12%), constipation (20% vs 12%) and rash (20% vs 7%).<sup>1</sup> Serious adverse reactions were reported in 79% of patients treated in the DAURISMO plus LDAC arm. The most common ( $\geq 5\%$ ) serious adverse reactions in patients receiving DAURISMO plus LDAC were febrile neutropenia (29%), pneumonia (23%), hemorrhage (12%), anemia (7%) and sepsis (7%).<sup>1</sup>

“DAURISMO, a Hedgehog pathway inhibitor, was discovered in Pfizer laboratories and exemplifies our continued commitment to developing medicines that have the potential to advance cancer therapeutics,” said Mace Rothenberg, M.D., Chief Development Officer, Oncology, Pfizer Global Product Development. “We are delighted by today’s approval of DAURISMO by the FDA, and are working to gain greater understanding of its role in treating patients with acute myeloid leukemia. The ongoing Phase 3 BRIGHT trials are evaluating DAURISMO in combination with other agents commonly used to treat patients with acute myeloid leukemia, in an effort to understand the full potential of this medicine against this aggressive leukemia.”

Pfizer is committed to ensuring that patients who are prescribed DAURISMO have access to this innovative therapy. Patients in the U.S. have access to Pfizer Oncology Together™, which offers personalized support and financial assistance resources to help patients access their prescribed Pfizer Oncology medications.

The full Prescribing Information, including BOXED WARNING, for DAURISMO can be found [here](#).

#### IMPORTANT DAURISMO 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. 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 (incidence  $\geq 20\%$ ) are anemia, fatigue, hemorrhage, febrile neutropenia, musculoskeletal pain, nausea, edema, thrombocytopenia, dyspnea, decreased appetite, dysgeusia, mucositis, constipation, and rash.

**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 CYP3A4 inducers should be avoided due to decreased DAURISMO plasma concentrations, which may reduce efficacy.

**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.

### About DAURISMO™ (glasdegib)

DAURISMO is a once-daily oral Hedgehog pathway inhibitor, taken 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.<sup>1</sup> DAURISMO has not been studied in patients with severe renal impairment or moderate-to-severe hepatic impairment. As an oral therapy, which is taken with subcutaneous

LDAC, DAURISMO offers the flexibility for patients to receive this treatment regimen at home or in the outpatient setting.

DAURISMO was discovered in Pfizer's U.S. laboratories and we utilize state-of-the-art continuous manufacturing to produce this treatment.

DAURISMO is not approved for any indication in any market outside the U.S.

### About the BRIGHT Clinical Trials

BRIGHT AML 1019 (NCT03416179) consists of two randomized, placebo-controlled Phase 3 trials evaluating the addition of DAURISMO to intensive or non-intensive chemotherapy in patients with newly diagnosed AML. In the first study, patients with AML will be randomized to receive DAURISMO plus cytarabine and daunorubicin, an intensive chemotherapy regimen, or placebo plus cytarabine and daunorubicin. In the second study, patients with AML for whom intensive chemotherapy is not an option will be randomized to receive DAURISMO plus azacitidine, a hypomethylating agent, or placebo plus azacitidine.

A separate Phase 1b BRIGHT 1012 study (NCT02367456) has also been expanded to evaluate DAURISMO in combination with azacitidine in patients with previously untreated high-risk myelodysplastic syndromes (MDS) or AML. These trials are currently enrolling patients.

### About Pfizer Hematology

Pfizer's commitment to hematologic malignancies began in 2012 with the approval of our treatment for chronic myeloid leukemia (CML). Since then, we've continued to expand our hematology portfolio to meet the needs of patients with acute lymphoblastic leukemia (ALL) and AML. We now have four products approved for leukemia in different countries around the world, including three in the past two years. Together with the community, Pfizer aims to overcome the challenges of hematologic cancers and translate breakthrough science into meaningful treatment advances for patients.

### About Pfizer Oncology

At Pfizer Oncology, we are committed to advancing medicines wherever we believe we can make a meaningful difference on the lives of patients. Today, Pfizer Oncology has an industry-leading portfolio of 14 approved cancer medicines across 22 indications, including breast, prostate, kidney, lung and hematology. We also have two oncology biosimilar medicines approved globally and several assets in mid to late-stage

development for the treatment of cancer or as supportive care. Pfizer Oncology is striving to change the trajectory of cancer.

Pfizer Inc.: Working together for a healthier world®

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. Our global portfolio includes medicines and vaccines as well as many of the world's best-known consumer health care products. 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](http://www.pfizer.com). In addition, to learn more, please visit us on [www.pfizer.com](http://www.pfizer.com) and follow us on Twitter at @Pfizer and @Pfizer\_News, LinkedIn, YouTube, and like us on Facebook at [Facebook.com/Pfizer](https://www.facebook.com/Pfizer).

**DISCLOSURE NOTICE:** The information contained in this release is as of November 21, 2018. 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 DAURISMO (glasdegib) and Pfizer Oncology, including their potential benefits, that involves 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 trial commencement and completion dates and regulatory submission dates, as well as the possibility of unfavorable clinical trial results, including unfavorable new clinical data and additional analyses of existing clinical data; the risk that clinical trial data are subject to differing interpretations, and, even when we view data as sufficient to support the safety and/or effectiveness of a product candidate, regulatory authorities may not share our views and may require additional data or may deny approval altogether; whether regulatory authorities will be satisfied with the design of and results from our clinical studies; whether and when drug applications may be filed in any other jurisdictions for

DAURISMO, for any additional indications for DAURISMO or for any other oncology products; whether and when any such applications may be approved by regulatory authorities, which will depend on the assessment by such regulatory authorities of the benefit-risk profile suggested by the totality the efficacy and safety information submitted, and, if approved, whether DAURISMO or any such other oncology products will be commercially successful; decisions by regulatory authorities regarding labeling and other matters that could affect the availability or commercial potential of DAURISMO or any other oncology products; 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, 2017 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](http://www.sec.gov) and [www.pfizer.com](http://www.pfizer.com).

---

1 DAURISMOTM (glasdegib) Prescribing Information. New York. NY: Pfizer Inc: 2018.

2 SEER Cancer Stat Facts: Acute Myeloid Leukemia. National Cancer Institute. Bethesda, MD, April 2017. Available at: <http://seer.cancer.gov/statfacts/html/amyl.html>. Accessed November 7, 2018.

3 Dohner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. *Blood*. 2017;129:424-447.

4 Medeiros BC, Satram-Hoang S, Hurst D, Hoang KQ, Momin F, Reyes C. Big data analysis of treatment patterns and outcomes among elderly acute myeloid leukemia patients in the United States. *Ann Hematol*. 2015;94:1127-1138. doi:10.1007/s00277-015-2351-x.

5 Irvine DA, Copland M. Targeting hedgehog in hematologic malignancy. *Blood*. 2012;119(10):2196-2204. doi:10.1182/blood-2011-10-383752.

6 Laranjeira ABA, Yang SX. Therapeutic target discovery and drug development in cancer stem cells for leukemia and lymphoma: from bench to the clinic. *Expert Opinion on Drug Discovery*. 2016;11(11):1071-1080. doi:10.1080/17460441.2016.1236785.

Pfizer Media Contact: Jessica Smith, 212-733-6213 [Jessica.M.Smith@pfizer.com](mailto:Jessica.M.Smith@pfizer.com) or Pfizer  
Investor Contact: Ryan Crowe, 212-733-8160 [Ryan.Crowe@pfizer.com](mailto:Ryan.Crowe@pfizer.com)