

U.S. Food and Drug Administration Approves Gilead's Zydelig® (idelalisib) for Relapsed Chronic Lymphocytic Leukemia, Follicular Lymphoma and Small Lymphocytic Lymphoma

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-- 82 Percent Reduction in Risk of Disease Progression or Death When Combined with Rituximab Compared to Rituximab Alone in Patients with Relapsed Chronic Lymphocytic Leukemia --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Jul. 23, 2014-- Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the U.S. Food and Drug Administration (FDA) has approved Zydelig® (idelalisib) 150 mg tablets for the treatment of three B-cell blood cancers. Zydelig is indicated in combination with rituximab for patients with relapsed chronic lymphocytic leukemia (CLL) for whom rituximab alone would be considered appropriate therapy and as monotherapy for patients with relapsed follicular B-cell non-Hodgkin lymphoma (FL) and small lymphocytic lymphoma (SLL) who have received at least two prior systemic therapies. Accelerated approval was granted for FL and SLL based on overall response rate. Zydelig is a first-in-class inhibitor of PI3K delta, a protein that is over-expressed in many B-cell malignancies and plays a role in the viability, proliferation and migration of these cancer cells.

This press release has an accompanying Smart Marketing Page providing further details about the organization, products and services introduced below. You can access the Smart Marketing Page via the following link:

<http://smp.newshq.businesswire.com/pages/f89vj38d2m1w9d47j>.

"Zydelig is a much needed new treatment option for appropriate patients with CLL and these indolent lymphomas who have experienced relapses and have limited, if any, treatment options," said Bruce Cheson, MD, Professor of Medicine, Head of Hematology and Director of Hematology Research at Lombardi Comprehensive Cancer Center at Georgetown University, and a principal investigator on the Zydelig pivotal Phase 3 trial in CLL. "In clinical studies among patients with relapsed CLL, FL and SLL, Zydelig produced strong responses, including a significant improvement in progression-free survival in CLL. I believe it helps fill a significant unmet need for these patients."

Over 200,000 Americans are living with CLL, FL or SLL, slow-growing incurable blood cancers that can lead to life-threatening complications such as anemia, serious infection and bone marrow failure requiring treatment. Relapse commonly occurs after initial chemoimmunotherapy and many patients with relapsed CLL, FL or SLL are unable to tolerate chemotherapy, which may limit their treatment options.

"Gilead is committed to the development of novel cancer therapies and we are proud to have this opportunity to make a difference in the lives of people living with these cancers," said John C. Martin, PhD, Chairman and Chief Executive Officer, Gilead Sciences. "We extend our thanks to the many physicians and patients who participated in Zydelig clinical trials, and are now focused on making this medicine available to patients as expeditiously as possible."

The product's approval in CLL is supported primarily by data from a randomized, placebo-controlled Phase 3 trial (Study 116) of Zydelig plus rituximab in 220 patients with relapsed CLL who were not able to tolerate standard chemotherapy. Study 116 was stopped early in October 2013 by an independent Data Monitoring Committee due to a highly statistically significant benefit in progression-free survival (PFS) in the Zydelig arm as compared to those receiving rituximab alone (hazard ratio = 0.18 (95 percent CI: 0.10, 0.32), $p < 0.0001$). Median PFS was not reached in the Zydelig plus rituximab arm (95 percent CI: 10.7 months, NR) and was 5.5 months in the placebo plus rituximab arm (95 percent CI: 3.8, 7.1). The FDA granted Zydelig a Breakthrough Therapy designation for relapsed CLL, a designation granted to drug candidates that may offer major advances in treatment over existing options.

Zydelig's accelerated approval in FL and SLL, two types of indolent non-Hodgkin lymphoma, is supported by data from a single-arm Phase 2 study (Study 101-09) of Zydelig monotherapy in patients refractory to rituximab and alkylating-agent-containing chemotherapy (FL: $n=72$; SLL: $n=26$). In the study, Zydelig achieved an overall response rate of 54 percent (range: 42-66 percent) and 58 percent (range: 37-77 percent), respectively, in FL and SLL patients. Of the

responses seen in FL patients, 8 percent (n=6) were complete responses; all 15 responses in SLL patients were partial responses. The median duration of response was 11.9 months in SLL patients (range: 0.0, 14.7 months) and median duration of response was not reached in FL patients (range: 0.0, 14.8 months). Improvement in patient survival or disease related symptoms has not been established in these indications. Results of Study 116 and Study 101-09 were published in *The New England Journal of Medicine* in March 2014.

Zydelig has a **BOXED WARNING** in its product label regarding the risks of fatal and serious toxicities: hepatic, severe diarrhea, colitis, pneumonitis and intestinal perforation; see below for Important Safety Information, including contraindications and warnings and precautions.

FDA has also approved a risk evaluation and mitigation strategy (REMS) for Zydelig. The purpose of the Zydelig REMS is to inform healthcare providers of the serious risks of hepatotoxicity, severe diarrhea, colitis, pneumonitis and intestinal perforation. Additional information about the Zydelig REMS program can be found at www.ZydeligREMS.com.

The most common adverse reactions (incidence ≥ 20 percent; all grades) in patients given Zydelig with or without rituximab are diarrhea, pyrexia, fatigue, nausea, cough, abdominal pain, chills and rash. The most common lab abnormalities (incidence ≥ 30 percent; all grades) in clinical studies were neutropenia, hypertriglyceridemia, hyperglycemia and ALT/AST elevations (indicators of liver function).

U.S. Patient Support Program

Gilead is committed to ensuring that patients with CLL, FL and SLL can access Zydelig and has launched Zydelig AccessConnectSM to provide assistance to appropriate patients who are uninsured, underinsured or who need financial assistance to pay for the medicine. The program consists of an integrated offering of support services for patients and providers, including:

- Access to dedicated case specialists to help patients and their providers with insurance-related needs, including identifying coverage options.
- The Zydelig Co-pay Coupon Program, which provides co-pay assistance for eligible patients with private insurance who need assistance paying for out-of-pocket medication costs. Most patients will pay no more than \$5 per monthly co-pay.
- Gilead will provide support to independent non-profit organizations that provide assistance for eligible federally-insured and privately-insured patients who need help covering out-of-pocket medication costs.
- Eligible patients who have been prescribed Zydelig for an FDA-approved indication and who are experiencing insurance coverage delays greater than five business days may receive a 30-day supply of Zydelig while coverage is established.
- Patients enrolled into Zydelig AccessConnect will receive the support needed to connect with a specialty pharmacy based on the policies of their individual health plan.
- The AccessConnect Patient Assistance Program will provide Zydelig at no charge for eligible patients with no other insurance options.

Information about how to apply for any of these forms of assistance, and more information on authorized distributors and specialty pharmacies can be found at www.zydeligaccessconnect.com or by calling 1-844-6ACCESS (1-844-622-2377) between 8 a.m. and 8 p.m. ET.

About Zydelig (idelalisib)

Zydelig is an oral inhibitor of phosphoinositide 3-kinase (PI3K) delta, a protein that plays a role in the activation, proliferation and viability of B cells, a critical component of the immune system. PI3K delta signaling is active in many B-cell leukemias and lymphomas, and by inhibiting the protein, Zydelig blocks several cellular signaling pathways that drive B-cell viability. Zydelig is indicated in combination with rituximab for the treatment of relapsed chronic lymphocytic leukemia in patients for whom rituximab alone would be considered appropriate therapy due to other co-morbidities and

as monotherapy for relapsed follicular B-cell non-Hodgkin lymphoma (FL) and relapsed small lymphocytic lymphoma (SLL) in patients who have received at least two prior therapies. The FL and SLL indications were granted accelerated approval based on overall response rate; improvement in patient survival or disease related symptoms has not been established in these indications. Continued approval for these indications is contingent upon verification of clinical benefit in confirmatory trials. Zydelig is available as 150 mg and 100 mg tablets, administered orally twice-daily; 150 mg is the recommended starting dose (see Important Safety Information below for dose modification instructions).

Important Safety Information

BOXED WARNING: FATAL and SERIOUS TOXICITIES: HEPATIC, SEVERE DIARRHEA, COLITIS, PNEUMONITIS and INTESTINAL PERFORATION

- **Fatal and/or serious hepatotoxicity occurred in 14 percent of Zydelig-treated patients. Monitor hepatic function prior to and during treatment. Interrupt and then reduce or discontinue Zydelig as recommended.**
- **Fatal, serious, and/or severe diarrhea or colitis occurred in 14 percent of Zydelig-treated patients. Monitor for the development of severe diarrhea or colitis. Interrupt and then reduce or discontinue Zydelig as recommended.**
- **Fatal and serious pneumonitis can occur. Monitor for pulmonary symptoms and bilateral interstitial infiltrates. Interrupt or discontinue Zydelig as recommended.**
- **Fatal and serious intestinal perforation can occur in Zydelig-treated patients. Discontinue Zydelig for intestinal perforation.**

Contraindications

- **History of serious allergic reactions**, including anaphylaxis and toxic epidermal necrolysis (TEN)

Warnings and Precautions

- **Hepatotoxicity:** Findings were generally observed within the first 12 weeks of treatment and reversed with dose interruption. Upon rechallenge at a lower dose, ALT/AST elevations recurred in 26 percent of patients. In all patients, monitor ALT/AST every 2 weeks for the first 3 months, every 4 weeks for the next 3 months, and every 1 to 3 months thereafter. If ALT/AST is $>3x$ upper limit of normal (ULN), monitor for liver toxicity weekly. If ALT/AST is $>5x$ ULN, withhold Zydelig and monitor ALT/AST and total bilirubin weekly until resolved. Discontinue Zydelig for recurrent hepatotoxicity. Avoid concurrent use with other hepatotoxic drugs.
- **Severe diarrhea or colitis:** Grade 3+ diarrhea can occur at any time and responds poorly to antimotility agents. Avoid concurrent use with other drugs that cause diarrhea.
- **Pneumonitis:** Evaluate for pneumonitis in patients presenting with pulmonary symptoms such as cough, dyspnea, hypoxia, interstitial infiltrates on radiologic exam, or oxygen saturation decline by ≥ 5 percent.
- **Intestinal perforation:** Advise patients to promptly report any new or worsening abdominal pain, chills, fever, nausea, or vomiting.
- **Severe cutaneous reactions:** One case of TEN occurred in a study of Zydelig in combination with rituximab and bendamustine. Other severe or life-threatening (grade ≥ 3) cutaneous reactions have been reported. Monitor patients for the development of severe cutaneous reactions and discontinue Zydelig if a reaction occurs.
- **Anaphylaxis:** Serious allergic reactions including anaphylaxis have been reported. Discontinue Zydelig permanently and institute appropriate supportive measures if a reaction occurs.
- **Neutropenia:** Treatment-emergent grade 3-4 neutropenia occurred in 31 percent of Zydelig-treated patients in clinical trials. In all patients, monitor blood counts \geq every 2 weeks for the first 3 months. In patients with neutrophil counts <1.0 Gi/L, monitor weekly.
- **Embryo-fetal toxicity:** Zydelig may cause fetal harm. Women who are or become pregnant while taking Zydelig should be apprised of the potential hazard to the fetus. Advise women to avoid pregnancy while taking Zydelig and to use effective contraception during and at least 1 month after treatment with Zydelig.

Adverse Reactions

- **Most common adverse reactions** (incidence approximately 20 percent; all grades) in clinical studies, when used alone or in combination with rituximab, were diarrhea, pyrexia, fatigue, nausea, cough, pneumonia, abdominal pain, chills and rash.
- **Most frequent serious adverse reactions (SAR)** in clinical studies in combination with rituximab were pneumonia (17 percent), pyrexia (9 percent), sepsis (8 percent), febrile neutropenia (5 percent), and diarrhea (5 percent); SAR were reported in 49 percent of patients and 10 percent of patients discontinued due to adverse reactions. Most frequent SAR in clinical studies when used alone were pneumonia (15 percent), diarrhea (11 percent) and pyrexia (9 percent); SAR were reported in 50 percent of patients and 53 percent of patients discontinued or interrupted therapy due to adverse reactions.
- **Most common lab abnormalities** (incidence approximately 30 percent; all grades) in clinical studies were neutropenia, hypertriglyceridemia, hyperglycemia and ALT/AST elevations.

Drug Interactions

- **CYP3A inducers:** Avoid coadministration with strong CYP3A inducers.
- **CYP3A inhibitors:** When coadministered with strong CYP3A inhibitors, monitor closely for Zydelig toxicity.
- **CYP3A substrates:** Avoid coadministration with CYP3A substrates.

Dosage and Administration

- **Adult starting dose:** One 150 mg tablet twice daily, swallowed whole with or without food. Continue treatment until disease progression or unacceptable toxicity. The safe dosing regimen for patients who require treatment longer than several months is unknown.
- **Dose modification:** Consult the Zydelig full Prescribing Information for dose modification and monitoring recommendations for the following specific toxicities: pneumonitis, ALT/AST elevations, bilirubin elevations, diarrhea, neutropenia and thrombocytopenia. For other severe or life-threatening toxicities, withhold Zydelig until toxicity is resolved and reduce the dose to 100 mg, twice daily, upon resuming treatment. If severe or life-threatening toxicities recur upon rechallenge, Zydelig should be permanently discontinued.

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North and South America, Europe and Asia Pacific.

Forward-Looking Statement

This press release includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the risk that physicians and patients may not see advantages of Zydelig over other therapies and may therefore be reluctant to prescribe the product. In addition, European and other regulatory agencies may not approve Zydelig in the currently anticipated timelines or at all, and any marketing approvals, if granted, may have significant limitations on its use. Further, additional studies of Zydelig may produce unfavorable results. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended March 31, 2014, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

U.S. full prescribing information, including **BOXED WARNING** for Zydlig is available at www.gilead.com.

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For more information on Gilead Sciences, please visit the company's website at www.gilead.com, follow Gilead on Twitter (@GileadSciences) or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

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Gilead Sciences, Inc.

Patrick O'Brien, 650-522-1936 (Investors)

Nathan Kaiser, 650-522-1853 (Media)