European Commission Grants Marketing Authorization for Gilead's Zydelig® (Idelalisib) for the Treatment of Chronic Lymphocytic Leukemia and Follicular Lymphoma

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-- First-in-Class Oral Treatment for Two Incurable Blood Cancers --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Sep. 19, 2014-- Gilead Sciences, Inc. (Nasdaq:GILD) today announced that the European Commission has granted marketing authorization for Zydelig® (idelalisib), 150 mg tablets, a first-in-class oral treatment for two incurable blood cancers - chronic lymphocytic leukemia (CLL) and follicular lymphoma (FL). For the treatment of CLL, Zydelig has been approved for use in combination with rituximab for patients who have received at least one prior therapy; or as first-line treatment in the presence of 17p deletion or *TP53* mutation in patients unsuitable for chemo-immunotherapy. For the treatment of FL, Zydelig has been approved as a monotherapy in patients who are refractory to two prior lines of treatment. Zydelig inhibits PI3K delta, a protein that is overexpressed in many B-cell malignancies and plays a role in the viability, proliferation and migration of these cancer cells.

CLL and FL are slow-growing incurable blood cancers that can lead to life-threatening complications such as anemia, serious infection and bone marrow failure requiring treatment. The goal of therapy for patients with these cancers is to improve overall survival and quality of life.

"Although chemo-immunotherapy is initially used to treat both CLL and FL, relapse is common and many patients run out of treatment options to treat the disease as it progresses," said Peter Hillmen, PhD, Professor of Experimental Haematology and Honorary Consultant Haematologist at Leeds Teaching Hospitals NHS Trust. "Further, CLL patients with the 17p deletion or *TP53* mutation are not suitable for chemo-immunotherapy, requiring alternative first-line treatment options. Thus, Zydelig is a welcomed treatment option that offers a new approach in the management of these cancers."

A chromosome 17 deletion - del (17p) or a mutation in the *TP53* gene in CLL cells have been linked to poor prognosis and a more rapid disease progression. For these patients most conventional chemotherapy treatments are not effective and deliver poor responses of relatively short duration. Treatment options are limited for these patients.

"Zydelig represents an important therapeutic advance for patients living with CLL and FL," said John C. Martin, PhD, Chairman and Chief Executive Officer, Gilead Sciences. "Gilead is pleased to be making a difference in the lives of people living with these blood cancers and we are committed to helping ensure timely access to the treatment for patients who may benefit from therapy."

The approval of Zydelig 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 plus rituximab arm compared with the rituximab only treatment arm (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 approval in FL, the most common type of indolent non-Hodgkin lymphoma (iNHL), is supported by data from a single-arm Phase 2 study (Study 101-09) of Zydelig monotherapy in 125 iNHL patients refractory to rituximab and alkylating-agent-containing chemotherapy. In the 72 patients with FL in this study, Zydelig achieved an overall response rate of 54 percent and the median duration of response was not reached (range: 0.0, 14.8+ months). Results of Study 116 and Study 101-09 were published in *The New England Journal of Medicine* in March 2014.

Adverse drug reactions (including Grade ≥3) reported in clinical studies in patients with hematological malignancies

receiving Zydelig included infections, neutropenia, pneumonitis, diarrhea/colitis, increased transaminase (indicator of liver function), rash and pyrexia. For additional safety information, see the Summary of Product Characteristics at www.ema.europa.eu.

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 signalling is active in many B-cell leukemias and lymphomas, and by inhibiting the protein, Zydelig blocks several cellular signalling pathways that drive B-cell viability. In the EU, Zydelig is indicated in combination with rituximab for the treatment of adult patients with CLL who have received at least one prior therapy; or as first-line treatment in the presence of 17p deletion or *TP53* mutation in patients unsuitable for chemo-immunotherapy. Zydelig has also been approved as a monotherapy for the treatment of adult patients with FL that is refractory to two prior lines of treatment. Zydelig is administered orally twice-daily and is available as 150 mg and 100 mg dose strengths.

Important EU Safety Information

Contraindications: Hypersensitivity to the active substance or to any excipients listed in the Zydelig summary of product characteristics.

Special warnings and precautions for use: The summary of product characteristics of co-prescribed medicinal products should be consulted before starting therapy with Zydelig.

Transaminase elevations

Elevations in ALT and AST of Grade 3 and 4 (> 5 x ULN) have been observed in clinical studies of Zydelig. These laboratory findings were generally observed within the first 12 weeks of treatment, were generally asymptomatic, and were reversible with dose interruption. Most patients resumed treatment at a lower dose without recurrence. ALT, AST, and total bilirubin must be monitored in all patients every 2 weeks for the first 3 months of treatment, then as clinically indicated. If Grade 2 or higher elevations in ALT and/or AST are observed, patients must be monitored weekly until the values return to Grade 1 or below.

Diarrhoea/colitis

Cases of severe drug-related colitis occurred relatively late (months) after the start of therapy, sometimes with rapid aggravation, but resolved within a few weeks with dose interruption and additional symptomatic treatment (e.g., anti-inflammatory agents such as enteric budesonide).

There is very limited experience from the treatment of patients with a history of inflammatory bowel disease.

Pneumonitis

Cases of pneumonitis have been reported in clinical studies with Zydelig. Patients presenting with serious lung events that do not respond to conventional antimicrobial therapy should be assessed for drug-induced pneumonitis. If pneumonitis is suspected, Zydelig should be interrupted and the patient treated accordingly. Treatment must be discontinued for moderate or severe symptomatic pneumonitis.

CYP3A inducers

Zydelig exposure may be reduced when co-administered with CYP3A inducers such as rifampicin, phenytoin, St. John’s wort (*Hypericum perforatum*), or carbamazepine. Since a reduction in Zydelig plasma concentrations may result in decreased efficacy, co-administration of Zydelig with moderate or strong CYP3A inducers should be avoided.

CYP3A substrates

The primary metabolite of Zydelig, GS-563117, is a strong CYP3A4 inhibitor. Thus, Zydelig has the potential to interact with medicinal products that are metabolized by CYP3A, which may lead to increased serum concentrations of the other product. When Zydelig is co-administered with other medicinal products, the Summary of Product Characteristics (SmPC) for the other product must be consulted for the recommendations regarding co-administration with CYP3A4 inhibitors. Concomitant treatment of Zydelig with CYP3A substrates with serious and/or life-threatening adverse reactions (e.g., alfuzosin, amiodarone, cisapride, pimozide, quinidine, ergotamine, dihydroergotamine, quetiapine, lovastatin, simvastatin, sildenafil, midazolam, triazolam) should be avoided and alternative medicinal products that are less sensitive to CYP3A4 inhibition should be used if possible.

Hepatic impairment

Intensified monitoring of adverse reactions is recommended in patients with impaired hepatic function as exposure is expected to be increased in this population, in particular in patients with severe hepatic impairment. No patients with severe hepatic impairment were included in clinical studies of Zydelig. Caution is recommended when administering Zydelig in this population.

Chronic hepatitis

Zydelig has not been studied in patients with chronic active hepatitis including viral hepatitis. Caution should be exercised when administering Zydelig in patients with active hepatitis.

Women of childbearing potential

Women of childbearing potential must use highly effective contraception while taking Zydelig and for 1 month after stopping treatment. Women using hormonal contraceptives should add a barrier method as a second form of contraception since it is currently unknown whether Zydelig may reduce the effectiveness of hormonal contraceptives.

[Only for 100 mg strength]

Excipients

Zydelig contains the azo colouring agent sunset yellow FCF (E110), which may cause allergic reactions.

For the Summary of Product Characteristics, please visit www.ema.europa.eu.

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. 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 June 30, 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.

Zydelig is a registered trademark of Gilead Sciences, Inc.

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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