Oral OTEZLA® (apremilast) Data Presented at EADV Show Improved Measures of Health-Related Quality of Life and Work Productivity in Patients with Moderate to Severe Plaque Psoriasis

Apremilast treatment resulted in improved health-related quality of life during 16 weeks of therapy in ESTEEM 2

Apremilast significantly increased work productivity and improved work limitations compared with placebo at week 16 in pooled analyses of ESTEEM 1 and 2

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene International Sàrl, a wholly-owned subsidiary of Celgene Corporation (NASDAQ: CELG) today announced that patient-reported health outcomes data for OTEZLA® (apremilast) were presented at the 23rd European Academy of Dermatology and Venereology (EADV) Congress in Amsterdam. The analyses from the phase III ESTEEM clinical trial program assessed the effect of apremilast on health-related quality of life measures and on work productivity/work limitation. Apremilast is the Company's oral, selective inhibitor of phosphodiesterase 4 (PDE4), for patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

A new analysis of the ESTEEM 2 trial demonstrated that treatment with apremilast 30 mg twice daily after 16 weeks significantly improved health-related quality of life compared with placebo. Significant improvement was seen in a variety of these standardized measures, including the Dermatology Quality of Life Index (DLQI), the Patient Health Questionnaire, the European Quality of Life 5 Dimensions Questionnaire and the Short-Form Health Survey mental component summary and physical component summary.

At Week 16, more than 70 percent of patients who received apremilast 30 mg twice daily achieved clinically meaningful improvement in DLQI of at least 5-points. Approximately half of patients treated with apremilast 30 mg twice daily also achieved at least a 50 percent improvement from baseline in the PASI-50 score versus placebo, along with a 5-point or greater DLQI improvement, thereby meeting treatment goal criteria from National Institute for Health and Care Excellence (NICE) and European S3 guidelines.

"Psoriasis can affect many aspects of patients' lives, including emotional health, day-to-day activities and functional and social skills," said Melinda Gooderham, MD, FRCPC, dermatologist and medical director at the Skin Centre for Dermatology, Peterborough, Ontario, Canada. "The results from this analysis showed improvement in important health-related outcomes indicating that patients taking apremilast could potentially see improvement in disease-related quality of life that is important to their overall well-being."

The results of a work productivity analysis of pooled data from 1250 patients from the ESTEEM 1 and 2 trials demonstrated that, compared with placebo, treatment with apremilast significantly increased work productivity (P=0.031) and reduced work limitations (P=0.035) at 16 weeks.

Patients in this study completed the Work Limitation Questionnaire (WLQ)—a 25-item questionnaire that assessed the degree to which employed individuals are experiencing on-the-job limitations due to their health problems as well as the health-related productivity loss—at baseline and week 16. Four categories of work limitations were used to calculate the WLQ index—physical demands, mental demands, time management demands and output demands. The WLQ scale scores were then converted into an estimate of productivity loss.

"The toll of psoriasis on patients, the healthcare system, and the economy is significant and underappreciated," said Scott Smith, President, Celgene Inflammation & Immunology. "These analyses further underscore the importance of continued investment in medical innovation to help patients live better, healthier and more productive lives."

Apremilast was approved on March 21, 2014, by the U.S. Food and Drug Administration (FDA) for the treatment of adults with active psoriatic arthritis and on September 23, 2014 for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. A New Drug Submission (NDS) based on the combined data from the PALACE 1, 2 and 3 trials for psoriatic arthritis was submitted to health authorities in Canada in the second quarter of 2013. A NDS for psoriasis in Canada as well as a combined psoriatic arthritis/plaque psoriasis Marketing Authorization Application
(MAA) in Europe were all submitted to health authorities in the fourth quarter of 2013.

The views expressed and the techniques presented by the speakers at the 23rd EADV Congress in Amsterdam, The Netherlands are not necessarily shared or endorsed by the European Academy of Dermatology and Venereology.

About ESTEEM 1 and 2

ESTEEM 1 and 2 are two large pivotal phase III randomized, placebo-controlled studies evaluating apremilast in patients with a diagnosis of moderate to severe plaque psoriasis for at least 12 months prior to screening, and who were also candidates for phototherapy or systemic therapy. Approximately 1,257 patients were randomized 2:1 to receive either apremilast 30 mg twice daily or placebo after an initial five-day titration period, for the first 16 weeks, followed by a maintenance phase from weeks 16-32 in which placebo patients were switched to apremilast 30 mg twice daily through week 32, and a randomized withdrawal phase for responders from week 32 to week 52 based on their initial apremilast randomization and Psoriasis Area and Severity Index (PASI)-75 response. Approximately 30 percent of all patients had received prior phototherapy and 54 percent had received prior conventional systemic and/or biologic therapy. Approximately one-third of patients had not received prior phototherapy, conventional systemic nor biologic therapy. A total of 18 percent of patients had a history of psoriatic arthritis.

About Apremilast

Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels which is thought to indirectly modulate the production of inflammatory mediators. The specific mechanism(s) by which apremilast exerts its therapeutic action in psoriasis or psoriatic arthritis is not well defined.

INDICATIONS

Apremilast is indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Apremilast is also indicated for the treatment of adult patients with active psoriatic arthritis.

IMPORTANT SAFETY INFORMATION

Contraindications

Apremilast is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation.

Warnings and Precautions

Depression: Treatment with apremilast is associated with an increase in adverse reactions of depression. During clinical trials, 1.3% (12/920) of patients treated with apremilast reported depression compared to 0.4% (2/506) on placebo; 0.1% (1/1308) of apremilast patients discontinued treatment due to depression compared with none on placebo (0/506). Depression was reported as serious in 0.1% (1/1308) of patients exposed to apremilast, compared to none in placebo-treated patients (0/506). Suicidal behavior was observed in 0.1% (1/1308) of patients on apremilast, compared to 0.2% (1/506) on placebo. One patient treated with apremilast attempted suicide; one patient on placebo committed suicide.

Carefully weigh the risks and benefits of treatment with apremilast for patients with a history of depression and/or suicidal thoughts/behavior, or in patients who develop such symptoms while on apremilast. Patients, caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and they should contact their healthcare provider if such changes occur.

Weight Decrease: Body weight loss of 5-10% occurred in 12% (96/784) of patients treated with apremilast and in 5% (19/382) of patients treated with placebo. Body weight loss of ≥10% occurred in 2% (16/784) of patients treated with apremilast compared to 1% (3/382) of patients treated with placebo. Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of apremilast.

Drug Interactions: Apremilast exposure was decreased when apremilast was co-administered with rifampin, a strong CYP450 enzyme inducer; loss of apremilast efficacy may occur. Concomitant use of apremilast with CYP450 enzyme inducers (eg, rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended.

Adverse Reactions
Adverse reactions reported in ≥5% of patients were (apremilast%, placebo%): diarrhea (17, 6), nausea (17, 7), upper respiratory tract infection (9, 6), tension headache (8, 4), and headache (6, 4).

**Use in Specific Populations**

Pregnancy and Nursing Mothers: apremilast is Pregnancy Category C; it has not been studied in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether apremilast or its metabolites are present in human milk. Caution should be exercised when apremilast is administered to a nursing woman.

Renal Impairment: apremilast dosage should be reduced in patients with severe renal impairment (creatinine clearance less than 30 mL/min); for details, see Dosage and Administration, Section 2, in the Full Prescribing Information.

Please [click here](#) for Full Prescribing Information.

**About Psoriasis**

Psoriasis is an immune-mediated, non-contagious chronic inflammatory skin disorder of unknown cause. The disorder is a chronic recurring condition which varies in severity from minor localized patches to complete body coverage. Plaque psoriasis is the most common type of psoriasis. About 80 percent of people who develop psoriasis have plaque psoriasis, which appears as patches of raised, reddish skin covered by silvery-white scales. These patches, or plaques, frequently form on the elbows, knees, lower back, and scalp. Psoriasis occurs nearly equally in males and females. Psoriasis is believed to be most common in Caucasians and slightly less common in other ethnic groups. Worldwide, psoriasis is most common in Scandinavia and other parts of northern Europe. An estimated 125 million people worldwide have psoriasis. To learn more about the role of PDE4 in inflammatory diseases, go to [www.discoverpde4.com](http://www.discoverpde4.com).

**About Celgene**

Celgene International Sàrl, located in Boudry, Switzerland, is a wholly-owned subsidiary and international headquarters of Celgene Corporation. Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global pharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through gene and protein regulation. For more information, please visit [www.celgene.com](http://www.celgene.com).

**Forward-Looking Statements**

This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in our Annual Report on Form 10-K and other reports filed with the Securities and Exchange Commission.

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