Oral OTEZLA® (Apremilast) Showed Long-Term Clinical Benefits in Patients with Active Psoriatic Arthritis

Clinically meaningful improvements in measures of disease activity with OTEZLA seen at week 16 and were sustained for up to 52 weeks of treatment

OTEZLA demonstrated a consistent safety profile with no clinically meaningful changes in laboratory measurements across three PALACE phase III studies of 1,493 patients over 52 weeks

OTEZLA increased work productivity compared with placebo based on a separate 16-week analysis of PALACE 1

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene International Sàrl, a wholly-owned subsidiary of Celgene Corporation (NASDAQ:CELG), today announced results of additional analyses from the phase III clinical trials of OTEZLA, the Company's oral, selective inhibitor of phosphodiesterase 4 (PDE4). These included long-term (52-week) analyses from the PALACE 1, 2 and 3 trials of the impact of OTEZLA on psoriatic arthritis disease activity, safety and tolerability, in addition to a separate 16-week work productivity analysis from PALACE 1. The findings were presented at the European League Against Rheumatism Annual Congress (EULAR 2014) in Paris, France.

"People with psoriatic arthritis live with persistent symptoms of this painful disease," said Georg Schett, M.D., Ph.D., director of the Department of Internal Medicine III - Rheumatology and Immunology, University Hospital Erlangen, Germany. "These analyses of one-year data from the PALACE trials suggest that, based on the efficacy and safety data we've seen to-date, OTEZLA has the potential to help patients for the long-term management of manifestations of their psoriatic arthritis."

PALACE 1, PALACE 2 and PALACE 3: Measures of Disease Activity

Long-term (52-week) results from three studies demonstrated that treatment with OTEZLA improved measures of psoriatic arthritis disease activity, including tender and swollen joints, compared with placebo at 16 weeks. Disease activity was evaluated using the Disease Activity Score of 28 joint counts (DAS-28), as measured by the level of C-reactive protein (CRP), modified Psoriatic Arthritis Response Criteria (PsARC) response and good or moderate European League Against Rheumatism (EULAR) response. All three measurements of disease activity demonstrated sustained improvements through week 52 among patients who were continuously treated with OTEZLA.

PALACE 1, PALACE 2 and PALACE 3: Pooled 52-week Safety Data

Long-term safety results from an analysis of pooled data from the PALACE 1, 2 and 3 trials (including 1,493 patients) identified no new safety findings for patients with psoriatic arthritis who were treated with OTEZLA for up to 52 weeks, compared with the previously reported 24-week safety results. The nature, incidence and severity of adverse events (AEs) were comparable through the 24-week and 52-week periods.

Most AEs were mild or moderate in severity. Discontinuation due to AEs was low (OTEZLA 20 mg BID, 7.5 percent; OTEZLA 30 mg BID, 8.3 percent) and primarily occurred in the first 24 weeks of treatment. The incidence and severity of AEs were comparable through the 24-week and 52-week periods. The most commonly reported AEs were nausea, diarrhea, headache, upper respiratory tract infection and nasopharyngitis. Serious AEs occurred in 6.8 percent of patients receiving OTEZLA 20 mg BID and 7.2 percent of patients receiving OTEZLA 30 mg BID. One death occurred (OTEZLA 20 mg BID) due to multiorgan failure not suspected to be treatment-related.

Exposure-adjusted incidence rates per 100 subject years of major adverse cardiac events, serious infections, including opportunistic infections or malignancies, were comparable with those of placebo.

Similar to 24-week data previously reported from PALACE 1, 2 and 3, the 52-week data do not indicate a need for laboratory monitoring with OTEZLA treatment.

PALACE 1: Work Productivity
The results of a work productivity analysis of 261 patients from PALACE 1 demonstrated that treatment with OTEZLA increased work productivity and improved work limitations compared with placebo at 16 weeks. Patients in this study completed the Work Limitation Questionnaire (WLQ)—a 25-item questionnaire that assessed the impact of chronic health conditions on work performance and productivity—at baseline and week 16. Four categories of work limitations, physical demands, mental demands, time management demands and output demands, were used to calculate the WLQ index.

About PALACE Program

PALACE 1, 2 and 3 are the pivotal phase III multi-center, double-blind, placebo-controlled, parallel-group studies with two active-treatment groups. Across these studies, approximately 1,500 patients were randomized 1:1:1 to receive either OTEZLA 20 mg twice daily, OTEZLA 30 mg twice daily or identically-appearing placebo, for 16 weeks. At week 16, some placebo-treated patients were randomized to one of the two OTEZLA groups, while others remained on placebo through week 24. After week 24, patients began a subsequent long term, open-label, active treatment phase. The PALACE 1, 2 and 3 studies included a wide spectrum of patients with active psoriatic arthritis, including those who had been previously treated with oral disease-modifying antirheumatic drugs (DMARDs), and/or biologics, with some patients who had previously failed a tumor necrosis factor (TNF) blocker.

The primary endpoint of the PALACE 1, 2, and 3 studies was the modified American College of Rheumatology criteria for 20 percent improvement (ACR20) at week 16. Secondary endpoints included other measures of signs and symptoms of psoriatic arthritis, physical functioning, and patient-reported outcomes.

Taken together, the PALACE program is the largest psoriatic arthritis program to date intended for regulatory submission.

OTEZLA was approved on March 21, 2014 by the U.S. Food and Drug Administration (FDA) for the treatment of adults with active psoriatic arthritis. A combined psoriatic arthritis/psoriasis Marketing Authorization Application (MAA) in Europe was submitted to health authorities in the fourth quarter of 2013.

To learn more about OTEZLA visit www.otezla.com.

About OTEZLA

OTEZLA is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels.

Important Safety Information

INDICATION

OTEZLA® (apremilast) is indicated for the treatment of adult patients with active psoriatic arthritis.

IMPORTANT SAFETY INFORMATION

Contraindications

OTEZLA 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 OTEZLA is associated with an increase in adverse reactions of depression. During clinical trials, 1.0% (10/998) of patients treated with OTEZLA reported depression or depressed mood compared to 0.8% (4/495) treated with placebo; 0.3% (4/1441) of patients treated with OTEZLA discontinued treatment due to depression or depressed mood compared with none in placebo treated patients (0/495). Depression was reported as serious in 0.2% (3/1441) of patients exposed to OTEZLA, compared to none in placebo treated patients (0/495). Suicidal ideation and behavior were observed in 0.2% (3/1441) of patients on OTEZLA, compared to none on placebo (0/495). Two patients who received placebo committed suicide compared to none on OTEZLA.

Carefully weigh the risks and benefits of treatment with OTEZLA for patients with a history of depression and/or suicidal thoughts/behavior, or in patients who develop such symptoms while on OTEZLA. 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% was reported in 10% of patients taking OTEZLA and in 3.3% of patients taking
placebo. Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of OTEZLA.

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

**Adverse Reactions**

Adverse reactions reported in at least 2% of patients taking OTEZLA, that occurred at a frequency at least 1% higher than that observed in patients taking placebo, for up to 16 weeks (after the initial 5-day titration), were (OTEZLA%, placebo%): diarrhea (7.7, 1.6); nausea (8.9, 3.1); headache (5.9, 2.2); upper respiratory tract infection (3.9, 1.8); vomiting (3.2, 0.4); nasopharyngitis (2.6, 1.6); upper abdominal pain (2.0, 0.2).

**Use in Specific Populations**

Pregnancy and Nursing Mothers: OTEZLA 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 OTEZLA is administered to a nursing woman.

Renal Impairment: OTEZLA 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 Psoriatic Arthritis**

Psoriatic arthritis is a painful, chronic inflammatory disease characterized by pain, stiffness, swelling and tenderness of the joints, inflammation of specific ligaments and tendons, and decrease in physical functioning. It is estimated that nearly 38 million people worldwide have psoriatic arthritis. Psoriatic arthritis can impact day-to-day activities and has been reported to increase work disability. Common signs and symptoms of psoriatic arthritis include pain, stiffness, and swelling in joints. To learn more about psoriatic arthritis, go to [www.discoverpsa.com](http://www.discoverpsa.com). 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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