One Year Data from Phase III Study Evaluating Oral OTEZLA® (apremilast) or Injectable etanercept versus Placebo in Patients with Moderate to Severe Plaque Psoriasis Presented at EADV

Improvements in PASI scores and disease-related quality of life observed at week 16 were maintained at week 52 in patients randomized to OTEZLA at baseline and in patients who switched from etanercept to OTEZLA at week 16.

An exploratory analysis suggested improvements in itching observed at week 16 were also maintained at week 52 in patients in both groups.

No new safety signals or clinically meaningful changes in laboratory values for OTEZLA identified through week 52.

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene International Sàrl, a wholly owned subsidiary of Celgene Corporation (NASDAQ: CELG), today announced that results from its ongoing phase III LIBERATE™ trial evaluating Otezla® (apremilast), the Company's oral, selective inhibitor of phosphodiesterase 4 (PDE4), in patients with moderate to severe plaque psoriasis were presented as a late-breaker at the 24th European Academy of Dermatology and Venereology (EADV) Congress in Copenhagen, Denmark, October 7-11, 2015.

"Many patients with moderate to severe plaque psoriasis need treatment options that can help in managing multiple facets of the disease, including itching and impact on disease-related quality of life," said Kristian Reich, M.D., SCIderm Research Institute and Dermatologikum Hamburg, Germany. "The encouraging findings presented at EADV add to the growing body of data which suggest that treatment benefits observed with OTEZLA at week 16 are maintained through week 52 of treatment."

The LIBERATE study evaluated the clinical efficacy and safety of either oral OTEZLA 30 mg twice daily or weekly subcutaneous (SC) etanercept 50 mg compared with placebo at week 16 in 250 patients who had no prior exposure to a biological therapy. It also examined the relative safety of a switch from etanercept to OTEZLA after week 16 during an open label extension phase. Primary findings were previously presented at the 73rd Annual Meeting of the American Academy of Dermatology (AAD) in San Francisco, California. LIBERATE was not designed or powered to directly compare OTEZLA to etanercept.

As shown at AAD, at week 16, 40 percent (33/83) of patients receiving OTEZLA 30 mg twice daily demonstrated statistically significant and clinically meaningful improvements compared with 12 percent (10/84) of patients on placebo in the primary endpoint, Psoriasis Area and Severity Index (PASI)-75 response (P < 0.0001). Statistical significance was also achieved for patients receiving weekly injections of etanercept 50 mg compared with placebo [48 percent (n=40/83) vs. 12 percent (n=10/84), respectively, P < 0.0001].

New findings presented at EADV showed that 51 percent (42/83) of patients randomized to OTEZLA at baseline and 55 percent of patients who switched from etanercept to OTEZLA at week 16 (46/83) achieved PASI-75 at week 52.

Based on an exploratory analysis, OTEZLA also improved pruritus (itching), one of the most common and bothersome symptoms of psoriasis, as measured by a visual analog scale (0 mm=no itch at all; 100 mm=worst itch imaginable). Significantly greater improvements in itching scores were seen at week 16 for patients treated with OTEZLA 30 mg twice daily (decrease of 38 mm; 95% confidence interval [CI]: -45 to -31 mm) compared with placebo (decrease of 26 mm; CI: -34 to -19 mm). Improvement in pruritus was observed as early as week 2 in patients receiving OTEZLA. Lower itching scores were also observed in patients who received weekly injections of etanercept 50 mg from baseline to week 16.

Improvements in itching were maintained from week 16 to week 52 (decrease of 36 mm) in patients who received OTEZLA from baseline and in patients who switched from etanercept to OTEZLA at week 16 (decrease of 35 mm).

Treatment with OTEZLA 30 mg twice daily also significantly improved disease-related quality of life (a secondary endpoint) at week 16 compared with placebo. OTEZLA showed a mean improvement from baseline in total Dermatology Life Quality Index...
(DLQI) score (decrease of 8.7; CI: -10.5 to -6.9) vs. placebo (decrease of 4.9; CI: -6.1 to -3.7) at week 16. A decrease in total DLQI scores was also observed for patients who received weekly injections of etanercept 50 mg from baseline to week 16.

Total DLQI scores were maintained from week 16 to week 52 in patients who received OTEZLA from baseline (decrease of 8.9; CI: -10.8 to -7.0) and in patients who switched from etanercept to OTEZLA at week 16 (decrease of 8.0; CI: -9.7 to -6.4).

The safety and tolerability data for OTEZLA observed in the LIBERATE study were generally consistent with previously reported data from six other phase III studies of OTEZLA in psoriasis or psoriatic arthritis; no new safety signals were observed. Adverse events reported in at least five percent of patients taking OTEZLA in the LIBERATE study were diarrhea, nausea, upper respiratory tract infection, nasopharyngitis, headache and tension headache. No new safety or tolerability issues were observed through week 52 in patients who switched from etanercept to OTEZLA at week 16.

The LIBERATE study is ongoing.

The views expressed and the techniques presented by the speakers at the 24th EADV Congress in Copenhagen, Denmark are not necessarily shared or endorsed by the European Academy of Dermatology and Venereology.

About LIBERATE

LIBERATE (PSOR-010; Evaluatiion from a PlaceBo-controllEd Study of ORal ApremilasT and Etanercept in Plaque Psoriasis) is a phase IIIb, multicenter, randomized, placebo-controlled, double-blind, double-dummy study of the efficacy and safety of OTEZLA, etanercept and placebo, in subjects with moderate to severe plaque psoriasis. The primary objective of the LIBERATE study was to evaluate the clinical efficacy and safety of oral OTEZLA 30 mg twice daily compared with placebo at week 16. Secondary objectives of the study included: the evaluation of the clinical efficacy and safety of etanercept 50 mg SC once weekly (QW) compared with placebo at week 16 and the evaluation of the relative safety of a crossover from etanercept to OTEZLA 30 mg twice daily, as compared with OTEZLA dosed since week 0, after week 16. Subjects were required to have inadequate response, intolerance or contraindication to at least one conventional systemic agent and no prior exposure to biologics. The study enrolled 250 subjects who were randomized 1:1:1 to receive OTEZLA 30 mg twice daily, etanercept 50 mg QW or placebo, for 16 weeks. Following the first 16 weeks, all subjects were switched to (or continued on) OTEZLA 30 mg twice daily through week 104. The primary endpoint was the proportion of subjects with either OTEZLA 30 mg twice daily or placebo who achieved PASI-75 at week 16. Secondary endpoints included other measures of disease activity and quality of life for the comparison of OTEZLA 30 mg twice daily versus placebo and the comparison of etanercept 50 mg SC QW versus placebo.

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 which is thought to indirectly modulate the production of inflammatory mediators. The specific mechanism(s) by which OTEZLA exerts its therapeutic action in patients with psoriasis or psoriatic arthritis is not well defined.

OTEZLA is approved:

- In the European Union:
  - For the treatment of moderate-to-severe chronic plaque psoriasis in adult patients who failed to respond to or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, methotrexate or psoralen and ultraviolet-A light (PUVA)
  - Alone or in combination with Disease Modifying Antirheumatic Drugs (DMARDs), for the treatment of active psoriatic arthritis (PsA) in adult patients who have had an inadequate response or who have been intolerant to a prior DMARD therapy

- In Switzerland:
  - For the treatment of adult patients with moderate to severe plaque psoriasis who have not responded to another systemic therapy or do not tolerate such therapy or where such therapy is contraindicated
  - As monotherapy or in combination with disease-modifying anti-rheumatic drugs (DMARDs) for the treatment of active psoriatic arthritis in adults who have not responded to a previous DMARD therapy, who have not tolerated it, or where DMARD therapy is contraindicated

- In the U.S.:
  - For the treatment of adults with active psoriatic arthritis
  - For the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy

- In Canada:
For the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy

For the treatment of active psoriatic arthritis, alone or in combination with methotrexate, in adult patients who have had an inadequate response, intolerance or contraindication to a prior disease-modifying anti-rheumatic drug (DMARD).

• In Australia:
  • For the treatment of signs and symptoms of active psoriatic arthritis in adult patients
  • For the treatment of adult patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy

**Important Safety Information (based on US labeling)**

**Contraindications**

Otezla® (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 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 (eg, 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 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. An estimated 125 million people worldwide have psoriasis. To learn more about the role of PDE4 in inflammatory diseases, go to 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. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn and YouTube.

OTEZLA® is a registered trademark and LIBERATE™ is a trademark of Celgene Corporation. All other trademarks are the property of their respective owners.

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. Celgene Corporation undertakes 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 Celgene’s 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 Celgene’s Annual Report on Form 10-K and other reports filed with the U.S. Securities and Exchange Commission.


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