OTEZLA® (Apremilast) Showed Meaningful Improvements in Clinical and Quality-of-Life Measures of Psoriasis Beyond Those Captured by Assessing Skin Alone

Patients with moderate to severe plaque psoriasis showed meaningful improvements in skin, itch and quality-of-life measures among PASI 75 non-responders treated with OTEZLA, according to a post hoc sub-analysis of data from the phase 3 ESTEEM 1 trial.

Findings suggest a broad assessment of skin lesions, itching and quality of life may offer meaningful benefit with OTEZLA therapy in patients with moderate to severe plaque psoriasis.

A separate post hoc sub-analysis of data from the phase 3 ESTEEM 1 and 2 and phase 4 UNVEIL trials showed improvement in areas such as the scalp and nails with OTEZLA versus placebo.

SUMMIT N.J. -- 12 September 2018 -- Celgene Corporation (NASDAQ: CELG) today announced the results of two post hoc sub-analyses of clinical trials for OTEZLA® (apremilast) at the 27th European Academy of Dermatology and Venereology (EADV) Congress in Paris, France. Findings suggest OTEZLA offered meaningful improvements in outcomes important to patients with moderate to severe plaque psoriasis, which may not be captured by common measures of treatment efficacy that focus only on skin clearance, such as Psoriasis Area Severity Index (PASI) 75.

Plaque psoriasis is a multi-faceted disease that can manifest in numerous ways. Each patient has a different experience, and many are concerned about effects that go beyond the skin. This need for patient-centric care has been recognized by the World Health Organization -- a shift in the focus from treating the skin lesions of psoriasis to addressing the needs of the whole patient.

“Only considering skin clearance may not fully capture the effect a treatment may have on an individual’s disease burden and its impact on daily life,” said Dr. Denis Jullien, Department of Dermatology and Venereology, Edouard Herriot Hospital, Lyon, France and an author of the study. “For example, itching, which is not accounted for by PASI, is cited by over a third of patients as their overriding quality-of-life issue. These new analyses of OTEZLA studies can help inform both prescribers and patients when evaluating treatment decisions.”

The findings include a new post hoc sub-analysis of the phase 3 ESTEEM 1 trial assessing clinical and quality-of-life outcomes for patients with moderate to severe plaque psoriasis who did not achieve PASI 75 (a 75 percent reduction in PASI) at either weeks 32 or 52, but continued OTEZLA treatment in this time period (n=203/844).

For patients who did not achieve a PASI 75 at weeks 32 or 52, more than half achieved a 50 percent reduction in PASI score (PASI 50) at weeks 32 and 52 following treatment with OTEZLA. This
improvement, when taken together in disease-specific quality-of-life measures, may more reliably indicate clinically meaningful benefit. For example, itching, as measured by Visual Analogue Scale (VAS), was reduced from baseline by approximately 30 percent during weeks 4 to 52 in those patients (n=134) who were treated with OTEZLA from baseline and weeks 20 to 52 in patients (n=69) who were switched from placebo to OTEZLA at week 16. Quality of life, as measured by the Dermatology Life Quality Index (DLQI), was improved by at least 5 points in the two groups during the same time period.

Manifestations that are highly visible, such as scalp and nail psoriasis, can have a substantial effect on quality of life. A separate post hoc sub-analysis of the ESTEEM 1, 2 and UNVEIL studies examined changes in scalp and nail psoriasis, along with quality of life, following treatment with OTEZLA. The sub-analysis included patients who had nail psoriasis (n=768 in ESTEEM 1 and 2 and 73 in UNVEIL) or moderate to very severe scalp psoriasis (n=1,049 in ESTEEM 1 and 2 and 129 in UNVEIL) at baseline.

At week 32 in ESTEEM and UNVEIL, clearance of nail psoriasis [Nail Psoriasis Severity Index (NAPSI)=0] among patients receiving OTEZLA from baseline was achieved by 31.3 percent (n=146/466) and 36.2 percent (n=17/47) of patients, respectively. Among patients who were switched from placebo to OTEZLA at week 16, NAPSI clearance at week 32 was achieved by 15.5 percent (n=37/239) and 26.1 percent (n=6/23) of patients, respectively.

Among patients with moderate to severe scalp psoriasis at baseline, clear or minimal involvement of scalp psoriasis [Scalp Physician’s Global Assessment (ScPGA) response of 0 or 1] was achieved by greater proportions of patients receiving OTEZLA versus placebo at week 16 in both trials: 45.2 percent (n=351/694) versus 22.5 percent (n=80/355), respectively, in ESTEEM and 44.1 percent (n=30/68) versus 33.3 percent (n=23.3) in UNVEIL.

Of patients who had nail psoriasis or moderate to very severe scalp psoriasis at baseline, a DLQI of 0 or 1 was achieved by greater proportions of patients receiving OTEZLA versus placebo at week 16 [28.7 percent (n=206/719) versus 8.1 percent (n=29/358), respectively, in ESTEEM and 23.7 percent (n=23/97) versus 10.6 percent (n=5/47) in UNVEIL].

“The ESTEEM and UNVEIL clinical trials continue to provide important learnings about OTEZLA for the treatment of psoriasis as well as quality of life for people who live with this chronic condition,” said Volker Koscielny, Vice President Global Medical Affairs, Inflammation & Immunology at Celgene. “These sub-analyses of UNVEIL and ESTEEM suggest that appropriate patients with moderate to severe plaque psoriasis who experience manifestations beyond skin may benefit from treatment with OTEZLA.”

**About Psoriasis**

Psoriasis affects 125 million people worldwide, including around 14 million people in Europe and 7.5 million people in the United States. It is a chronic and systemic inflammatory disorder, and is immune-mediated, meaning it is caused by an immune reaction in the body.

Psoriasis lesions can often be found on areas close to the joints such as the elbows and knees but can also appear on the scalp. Nail psoriasis affects up to 50 percent of people with psoriasis. Up to 84 percent of people with psoriasis experience itching, and over a third of patients actually cite itch as the most important factor contributing to their disease.

Around 75 percent of people living with psoriasis believe it has a negative impact on their quality of life and 83 percent of patients with psoriasis actively conceal the visible signs of their disease.
About ESTEEM

ESTEEM 1 and 2 are two large pivotal phase 3 randomized, placebo-controlled studies evaluating OTEZLA 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 and/or systemic therapy. Approximately 1,250 patients were randomized 2:1 to receive either OTEZLA 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 OTEZLA 30 mg twice daily through week 32, and a randomized withdrawal phase for responders from week 32 to week 52 based on their initial OTEZLA randomization and Psoriasis Area and Severity Index (PASI) 75 response (ESTEEM 1) or (PASI) 50 (ESTEEM 2). A 5-year extension study of ESTEEM 1 and 2 is ongoing.

About UNVEIL

UNVEIL is the first prospective, randomized, controlled study to evaluate the clinical efficacy and safety of OTEZLA in patients with moderate plaque psoriasis (defined as a BSA involvement of 5-10 percent and sPGA of 3 based on a 0 to 5 scale) who were naïve to systemic and biologic therapies. Patients (n=221) were randomized 2:1 to receive either OTEZLA 30 mg twice daily or placebo for 16 weeks, followed by an open-label extension phase in which placebo patients were switched to OTEZLA through week 52. All doses were titrated over the first week of treatment. At baseline, more than 80 percent of patients had previously received topical therapy. The primary endpoint was the mean percentage change from baseline in the product of Physician's Global Assessment (PGA) and BSA (percent) at week 16.

About OTEZLA® (apremilast)

OTEZLA® (apremilast) 30 mg tablets 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 is not well defined.

U.S. PRESCRIBING INFORMATION

INDICATIONS

OTEZLA® (apremilast) is indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

IMPORTANT SAFETY INFORMATION

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

Diarrhea, Nausea and Vomiting: Cases of severe diarrhea, nausea, and vomiting were associated with the use of OTEZLA. Most events occurred within the first few weeks of treatment. In some cases, patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea,
or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting; advise patients to contact their healthcare provider. Consider OTEZLA dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting.

Depression: 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.

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

Weight Decrease: Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of OTEZLA.

Psoriasis: Body weight loss of 5-10% occurred in 12% (96/784) of patients treated with OTEZLA and in 5% (19/382) of patients treated with placebo. Body weight loss of ≥10% occurred in 2% (16/784) of patients treated with OTEZLA compared to 1% (3/382) of patients treated with placebo.

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

Psoriasis: Adverse reactions reported in ≥5% of patients were (OTEZLA%, 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: 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 Celgene
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 next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn, Facebook and YouTube.

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 our other reports filed with the U.S. Securities and Exchange Commission.

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