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Oral OTEZLA® (apremilast) Long-Term Safety and Efficacy Data in Patients with Moderate to Severe Plaque Psoriasis Presented at AAD

Improvements in the severity of preexisting nail, scalp and palmoplantar psoriasis achieved at week 16 were maintained in OTEZLA responders through week 52 in ESTEEM 2

OTEZLA improved the severity of palmoplantar psoriasis at week 16 in a subset of patients across three trials

Long-term safety profile for up to 104 weeks in ESTEEM 1 was consistent with previously reported data from OTEZLA clinical trial programs, with no new safety signals and no clinically meaningful changes in laboratory values

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ: CELG) today announced that results from long-term efficacy and safety analyses of the ESTEEM phase III clinical trial program of Otezla® (apremilast) were presented at the 73rd Annual Meeting of the American Academy of Dermatology (AAD) in San Francisco, California. OTEZLA is the Company's oral, selective inhibitor of phosphodiesterase 4 (PDE4) approved for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy and for the treatment of adults with active psoriatic arthritis.

In ESTEEM 1 and 2, patients were randomized to treatment with OTEZLA 30 mg twice daily or placebo for the first 16 weeks. At week 16, patients either continued on OTEZLA or were switched from placebo to OTEZLA 30 mg twice daily through week 32. Patients initially randomized to OTEZLA who achieved a Psoriasis Area and Severity Index (PASI)-75 response (ESTEEM 1) or PASI-50 response (ESTEEM 2) at week 32 were then re-randomized to either OTEZLA 30 mg twice daily or placebo.

"Long-term data are critical in psoriasis, since patients may deal with this disease throughout their lives," said Jeffrey Crowley, M.D., Bakersfield Dermatology, Bakersfield, CA. "Having two-year safety results along with data showing that OTEZLA can provide long-term improvements in difficult-to-treat symptoms can be helpful for dermatologists and patients who are looking for different treatment options."

ESTEEM 2: 52-Week Data Observed in Patients with Nail, Scalp and Palmoplantar Involvement

An analysis of data from ESTEEM 2 presented at AAD showed sustained improvements at week 52 among PASI-50 responders (patients who achieved a 50 percent reduction in PASI at week 32) in difficult-to-treat areas such as nails, scalp and the palms of the hands and soles of the feet (known as palmoplantar psoriasis).

Among patients who had nail psoriasis at baseline with a Nail Psoriasis Severity Index (NAPSI) greater than or equal to one, 45 percent (78/175) of those treated with OTEZLA 30 mg twice daily had at least a 50 percent improvement in NAPSI (NAPSI-50) at week 16, compared with 19 percent (17/91) of those treated with placebo ($P < 0.0001$). NAPSI-50 achievement was generally maintained for up to 52 weeks in patients (69 percent, $n=35$) who received OTEZLA at baseline who were PASI-50 responders.

Of those patients who had moderate to very severe scalp psoriasis at baseline, 41 percent (72/176) of those treated with OTEZLA 30 mg twice daily had a Scalp Physician Global Assessment (ScPGA) score of clear (zero) or minimal (one) at week 16, compared with 17 percent (16/93) of those treated with placebo ($P < 0.0001$). ScPGA score of zero or one achievement was generally maintained for up to 52 weeks in patients (63 percent, $n=32$) who received OTEZLA at baseline who were PASI-50 responders.

Among patients who had moderate to severe psoriasis on their palms and feet at baseline, 65 percent (17/26) of those treated with OTEZLA 30 mg twice daily had a Palmoplantar Psoriasis Physician Global Assessment (PPPGA) score of clear (zero) or almost clear (one) at week 16, compared with 31 percent (5/16) of those treated with placebo ($P=0.0315$). PPPGA score of zero or one achievement was sustained up to week 52 ($n=4$ of 4 patients) in patients randomized to OTEZLA who were PASI-50 responders at week 32.

PSOR-005, ESTEEM 1 and ESTEEM 2: 16-Week Palmoplantar Data

An analysis of PSOR-005, ESTEEM 1 and ESTEEM 2 found that OTEZLA improved palmoplantar psoriasis in a subset of

patients with moderate to severe chronic plaque psoriasis who had palmoplantar involvement.

Of those patients who had any palmoplantar psoriasis at baseline (PPPGA score of one or greater, n=427 across the three studies - 49 in PSOR-005, 254 in ESTEEM 1 and 124 in ESTEEM 2), a higher percentage of patients treated with OTEZLA 30 mg twice daily had PPPGA reduced to clear or almost clear compared with placebo at week 16 in all three trials [PSOR-005: 70 percent (19/27) vs. 32 percent (7/22), respectively, P=0.0072; ESTEEM 1: 63 percent (107/169) vs. 45 percent (38/85), respectively, P=0.0047; ESTEEM 2: 71 percent (55/78) vs. 37 percent (17/46), respectively, P=0.0003].

Among patients who had moderate to severe palmoplantar psoriasis at baseline (PPPGA score of three or greater) (n=144 across the three studies — 19 in PSOR-005, 83 in ESTEEM 1 and 42 in ESTEEM 2), a higher percentage of patients treated with OTEZLA 30 mg twice daily had PPPGA reduced to clear or almost clear compared with placebo at week 16 in PSOR-005 [67 percent (6/9) vs. 20 percent (2/10), respectively, P=0.0397] and ESTEEM 2 [65 percent (17/26) vs. 31 percent (5/16), respectively, P=0.0315]. There was no significant difference between the OTEZLA and placebo groups at week 16 in ESTEEM 1 [39 percent (22/57) vs. 31 percent (8/26), respectively, P=0.4912].

ESTEEM 1: Two-Year Safety Data

Long-term (104-week) results from the ESTEEM 1 trial showed that no new safety signals were identified in patients treated with OTEZLA 30 mg twice daily for up to two years (844 patients were randomized, 444 continued in the second year).

As with adverse events (AEs) reported during the first 52 weeks of exposure, most AEs reported during weeks 52 to 104 were mild or moderate in severity and did not lead to discontinuation. The most frequently reported AEs during the placebo-controlled period and the OTEZLA-exposure periods were diarrhea, upper respiratory tract infection, nausea, nasopharyngitis, tension headache and headache.

The exposure adjusted incidence rate (EAIR) for serious AEs did not increase with longer OTEZLA exposure, compared with the placebo-controlled period. There were no clinically meaningful changes in laboratory measurements identified over the OTEZLA 104-week exposure period. Incidence rates of major cardiac events, solid tumors, hematological malignancies and serious infections were comparable between the placebo and OTEZLA arms during the placebo-controlled period. No increase in incidence rates was noted with longer-term exposure to OTEZLA between weeks 52 to 104.

About ESTEEM

ESTEEM 1 and 2 are two large pivotal phase III 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 (ESTEEM2).

About PSOR-005

PSOR-005 is a phase IIb, multicenter, randomized, placebo-controlled, dose-ranging study evaluating OTEZLA in patients with a diagnosis of moderate to severe plaque psoriasis for at least six months prior to screening, and who are also candidates for phototherapy and/or systemic therapy. 352 patients were randomized 1:1:1:1 to receive oral placebo or OTEZLA 10, 20, or 30 mg twice daily after an initial five-day titration period, for the first 16 weeks, followed by a maintenance phase from weeks 16-24 in which placebo patients were randomly switched to OTEZLA 20 mg or 30 mg twice daily through week 24.

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 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. OTEZLA was also approved on January 16, 2015 by the European Commission (EC) in two therapeutic indications:

- 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

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, 1.3% (12/920) of patients treated with OTEZLA reported depression compared to 0.4% (2/506) on placebo; 0.1% (1/1308) of OTEZLA 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 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.

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% occurred in 12% (96/784) of patients treated with OTEZLA and in 5% (19/382) of patients treated with placebo. Body weight loss of $\geq 10\%$ occurred in 2% (16/784) of patients treated with OTEZLA 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 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 $\geq 5\%$ 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 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 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 Twitter @Celgene, and on [Pinterest](#) and [LinkedIn](#).

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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