New Analyses of Oral OTEZLA® (Apremilast) Presented at EADV Show Efficacy in Difficult-to-Treat Areas of Moderate to Severe Plaque Psoriasis

Apremilast significantly improved preexisting scalp, nail, and palmoplantar psoriasis at week 16 in ESTEEM 2

Improvements in pruritus (itching) seen as early as week 2 in analyses of ESTEEM 1 and 2 and maintained through week 32

Improvement in mean PASI scores achieved with apremilast at week 32 remained stable through week 52 in ESTEEM 2

Long-term safety and tolerability profile in ESTEEM 2 was consistent with previously-reported long-term data from apremilast clinical trial program

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene International Sàrl, a wholly-owned subsidiary of Celgene Corporation (NASDAQ:CELG), today announced that results from additional efficacy and safety analyses of OTEZLA® (apremilast) from the ESTEEM phase III clinical trial program were released at the 23rd European Academy of Dermatology and Venereology (EADV) Congress in Amsterdam. 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.

ESTEEM 2: 32-Week Data in Patients with Nail, Scalp, and Palmoplantar Involvement

An analysis of ESTEEM 2 demonstrated that apremilast significantly improved psoriasis in difficult-to-treat areas such as: the palms of the hands and feet (known as palmoplantar psoriasis), nails and scalp. Among patients who had nail psoriasis at baseline (n=266), 45 percent treated with apremilast 30 mg twice daily had at least a 50 percent improvement in this symptom at week 16, compared with 19 percent of those treated with placebo (P < 0.0001). After 32 weeks of treatment with apremilast 30 mg twice daily, 55 percent of patients achieved at least a 50 percent improvement.

Of those patients who had moderate to severe psoriasis on their palms and feet at baseline (n=42), 65 percent had these symptoms reduced to clear or almost clear at week 16. Improvements over baseline in nail, scalp and palmoplantar psoriasis were seen for up to 32 weeks.

ESTEEM 1 and ESTEEM 2: 32-Week Pruritus Data

An analysis of ESTEEM 1 and 2 found that apremilast improved skin discomfort/pain. Patients report that pruritus (itching) is one of the most common and bothersome symptoms of psoriasis. Significantly greater improvements in itching scores at week 16 were seen for patients treated with apremilast 30 mg twice daily (decreases of 31.5 in ESTEEM 1 and 33.5 in ESTEEM 2) compared with placebo (decreases of 7.3 in ESTEEM 1 and 12.2 in ESTEEM 2; P < 0.0001 for both trials). A post-hoc analysis found that improvements in itching and in skin discomfort/pain with apremilast 30 mg twice daily were observed as early as week 2 and were maintained through week 32.

"Plaque psoriasis can be a very itchy condition. Psoriasis patients report that itching is a significant problem that can affect all aspects of their life from sleeping to concentrating," said Gil Yosipovitch, MD, Chair of Dermatology at Temple University School of Medicine, and Director of the Temple Itch Center. "These results suggest that apremilast may provide patients with durable relief from itching in as early as two weeks."

ESTEEM 2: 52-Week Efficacy Data

Long-term (52-week) results from 411 patients in the ESTEEM 2 trial demonstrated durability of clinical responses achieved with apremilast. For those patients who were treated with apremilast 30 mg twice daily for 52 weeks and who achieved a 50 percent improvement in Psoriasis Area and Severity Index (PASI) at week 32, mean improvements in PASI remained stable between weeks 32 and 52 (74 percent to 77 percent).

Analysis of data from ESTEEM 2 did not identify new or unexpected adverse events (AEs) for patients treated with apremilast,
and the rate of AEs did not increase in frequency over time. AEs reported in at least five percent of patients in any treatment group during the long-term 52-week apremilast-exposure period include nausea, diarrhea, nasopharyngitis, tension headache, headache, vomiting, psoriasis, upper-respiratory tract infection, and back pain. The discontinuation rate due to AEs for those treated with apremilast 30 mg twice daily for 52 weeks was approximately seven percent. No clinically meaningful changes in laboratory measurements were identified over the apremilast 52-week exposure period.

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 patients with 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, in the Canton of Neuchâtel, 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 the Company’s website at [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.

For inquiries, please contact:

Celgene

Investors:
Patrick E. Flanigan III, 908-673-9969
Vice President, Investor Relations

or
Media:
Catherine Cantone, 732-564-3592
Director, Corporate Communications

Source: Celgene International Sàrl

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