Celgene Announces New Data for OTEZLA® (Apremilast) Will Be Presented at European Academy of Dermatology and Venereology Congress

New analyses of LIBERATE trial assess effect of OTEZLA or etanercept versus placebo on patient-reported itching (pruritus) and health-related quality of life

Physician’s Global Assessment and Body Surface Area (PGAxBSA) composite tool evaluated for the assessment of disease severity and response to OTEZLA in ESTEEM 1

Pre-clinical study assesses the early potential of OTEZLA as a treatment for atopic dermatitis

BOUDRY, Switzerland--(BUSINESS WIRE)-- Celgene International Sàrl, a wholly-owned subsidiary of Celgene Corporation (NASDAQ:CELG), today announced that the latest research on Otezla® (apremilast), the Company's oral, selective inhibitor of phosphodiesterase 4 (PDE4), will be presented at the 24th European Academy of Dermatology and Venereology (EADV) Congress in Copenhagen, Denmark, October 7-11, 2015. Nine abstracts (one oral presentation and eight e-posters) evaluating the use of OTEZLA in plaque psoriasis and pre-clinical data in atopic dermatitis will be presented at the meeting.

Data to be presented include pre-specified analyses of the LIBERATE study assessing the impact of either oral OTEZLA 30 mg twice daily or weekly subcutaneous (SC) etanercept 50 mg, each compared with placebo, on changes in patient-reported pruritus (itching) and health-related quality of life through 32 weeks of treatment in patients with moderate to severe plaque psoriasis. Efficacy and safety results from the LIBERATE study were previously presented at this year's Annual Meeting of the American Academy of Dermatology in San Francisco, California. LIBERATE was not designed or powered to directly compare OTEZLA to etanercept.

A retrospective analysis of results from the ESTEEM 1 trial will examine the potential of an alternate tool to measure psoriasis disease severity, particularly in patients with moderate psoriasis. This composite tool, called Physician’s Global Assessment and Body Surface Area (PGAxBSA), will be compared with the Psoriasis Area and Severity Index (PASI) in its ability to measure the effect of treatment with OTEZLA in patients with plaque psoriasis. Improvement in PASI scores is a measurement typically used in registrational trials to examine the effectiveness of plaque psoriasis treatments.

Results from pre-clinical studies assessing the potential of apremilast, the active ingredient in OTEZLA, as a treatment for atopic dermatitis will also be presented. The data will evaluate the effect of apremilast on gene expression in human epidermal keratinocytes (skin cells) that have been stimulated by T helper 2 (Th2) and Th17 cytokines - proteins thought to be associated with skin inflammation. The impact of apremilast treatment on gene expression and skin symptoms in two mouse models of dermatitis will also be investigated. A phase II trial of apremilast in moderate to severe atopic dermatitis is ongoing.

"New data to be presented at EADV will not only further evaluate OTEZLA’s clinical benefit in plaque psoriasis, but also highlight our ongoing commitment to uncovering the potential of OTEZLA in other immune-related dermatologic diseases, such as atopic dermatitis," said Scott Smith, President, Celgene Inflammation & Immunology. "Furthermore, we are eager to assess the use of alternative endpoints in patients with moderate plaque psoriasis, for which PASI may be a less sensitive measure."

The following abstracts will be presented at EADV as an exchange of scientific and clinical information (all times, CEST):

Abstracts at a Glance
Oral Presentation FC08.05; Saturday October 10, 2015, 3:36 - 3:45 PM
Apremilast Regulates Human Keratinocyte Gene Expression in Vitro and Reduces Antigen-driven Dermatitis in Vivo; Mary Adams
Location: B3M1-4

Poster Number 1652
Metabolic and Weight Changes with Apremilast in Patients with Psoriasis: Pooled Laboratory Analysis of the Phase 3 ESTEEM 1 and 2 Trials; April Armstrong, MD
Location: e-Poster area
Poster Number P1653
Efficacy of Apremilast or Etanercept Compared with Placebo in Patients with Moderate to Severe Psoriasis: Results From the LIBERATE Study; Jennifer Soung, MD
Location: e-Poster area

Poster Number P1655
Evaluation of the Physician's Global Assessment and Body Surface Area Composite Tool for Assessing Psoriasis Response to Apremilast Therapy: Results from the ESTEEM 1 Study; Kristina Callis Duffin, MD
Location: e-Poster area

Poster Number 1656
Analysis of Psoriasis Area and Severity Index and Weight Change During Long-term Treatment with Apremilast in Patients with Moderate to Severe Plaque Psoriasis (ESTEEM 1); Kristian Reich, MD
Location: e-Poster area

Poster Number P1658
Safety of Apremilast and Etanercept Compared with Placebo in Patients with Moderate to Severe Psoriasis: Results From the LIBERATE Study; Melinda Gooderham, MD
Location: e-Poster area

Poster Number P1668
Impact of Apremilast or Etanercept on Pruritus and Health-Related Quality of Life in Patients with Moderate to Severe Psoriasis: Results From the LIBERATE Study; Kim Papp, MD
Location: e-Poster area

Poster Number P1706
Cost per Responder of Apremilast Versus Etanercept in Patients with Moderate to Severe Psoriasis Using Results From LIBERATE; Tom Tencer, MD
Location: e-Poster area

Poster Number P1771
Effect of Apremilast and Etanercept on Patient-Reported Outcomes in Patients with Moderate to Severe Plaque Psoriasis in the LIBERATE Study; Melinda Gooderham, MD
Location: e-Poster area

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 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 LIBERATE™

LIBERATE (PSOR-010; EvaLuation 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 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).

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**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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