



February 17, 2018

OTEZLA® (Apremilast) Phase III Data Showed Significant Improvements in Patients with Active Behçet's Disease with Oral Ulcers

RELIEF™ trial demonstrated statistically significant reductions in oral ulcers with apremilast 30 mg versus placebo through week 12

Significant improvements in key secondary endpoints, including oral ulcer pain, overall disease activity and quality of life

Data presented at the 2018 AAD Annual Meeting

Regulatory submissions in the U.S. and Japan planned for later this year

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that data from the phase III RELIEF™ clinical trial of OTEZLA® (apremilast) in patients with active Behçet's Disease with oral ulcers were presented in a late-breaking oral presentation at the 2018 American Academy of Dermatology (AAD) Annual Meeting. The results showed statistically significant reductions in oral ulcers with apremilast 30 mg twice daily (BID) versus placebo through week 12. OTEZLA (apremilast) is Celgene's oral selective inhibitor of phosphodiesterase 4 (PDE4).

Behçet's Disease is a rare, chronic, multi-system inflammatory syndrome. Oral ulcers, the most common manifestation of Behçet's Disease, can be disabling and have a substantial effect on quality of life. This study primarily evaluated the effect of apremilast on recurring oral ulcers in patients with active Behçet's Disease who were previously treated with at least one topical or systemic medication.

"Reducing oral ulcers, which are painful and can negatively impact quality of life, is an important goal in the treatment of people with Behçet's syndrome," said Gulen Hatemi, M.D., Associate Professor, Istanbul University Cerrahpassa Medical School. "These findings suggest that apremilast, which reduced oral ulcers and oral ulcer pain, and improved disease activity in this pivotal study, has the potential to be a treatment option for patients with active Behçet's syndrome with oral ulcers, for which few treatment alternatives exist."

In the study, a total of 207 patients were randomized to apremilast 30 mg BID or placebo. At week 12, the area under the curve (AUC) for the number of oral ulcers was statistically significantly reduced with apremilast 30 mg BID versus placebo (129.5 vs. 222.1; $P < 0.0001$), the trial's primary endpoint. The AUC assesses the change in the number of oral ulcers over time, accounting for the clinical characteristic that oral ulcers repeatedly remit and recur. Statistically significant improvements were also seen with apremilast in multiple secondary endpoints, including oral ulcer pain ($P < 0.0001$), overall disease activity (Behçet's Syndrome Activity Score: $P < 0.0001$; Behçet's Disease Current Activity Index: $P=0.0335$) and quality of life ($P=0.0003$).

The most common adverse events (AEs) observed in the trial were diarrhea (41.3 percent with apremilast, 19.4 percent for placebo), nausea (19.2 percent with apremilast, 10.7 percent for placebo), headache (14.4 percent for apremilast, 9.7 percent for placebo) and upper respiratory tract infection (11.5 percent for apremilast, 4.9 percent for placebo). The safety profile was consistent with the known safety profile of apremilast.

Celgene plans to submit supplemental New Drug Applications for apremilast 30 mg BID for the treatment of active Behçet's Disease with oral ulcers in the U.S. and Japan in the second half of this year. The Company also plans to submit a Type II Variation to the Marketing Authorization Application in the EU in 2019.

"The positive phase III findings in Behçet's Disease reflect the unique aspects of the profile of OTEZLA® (apremilast) 30 mg across inflammatory-related diseases," said Terrie Curran, President, Celgene Inflammation and Immunology. "OTEZLA® (apremilast) 30 mg has the potential to provide a clinically meaningful new treatment option for patients and doctors and to become the first product indicated specifically for the treatment of active Behçet's Disease with oral ulcers."

Apremilast is not approved for the treatment of Behçet's Disease in any country.

About the RELIEF™ Study

The RELIEF™ study is a phase III randomized, placebo-controlled, double-blind study evaluating apremilast 30 mg BID in 207 patients with active Behçet's Disease who were previously treated with at least one topical or systemic medication. This 52-week study was conducted at 63 sites across 10 countries. The primary endpoint was the area under the curve (AUC) for the number of oral ulcers at week 12. Secondary objectives of the study included change from baseline in pain of oral ulcers, Behçet's Syndrome Activity Score, Behçet's Disease Current Activity Index and Behçet's Disease quality of life score at week 12.

About Behçet's Disease

Although the root cause is unknown, Behçet's Disease is associated with abnormalities of the immune system and inflammation of the blood vessels. Behçet's Disease is characterized by recurrent oral and genital ulcers, skin lesions, uveitis, arthritis, vasculopathy, and central nervous system and gastrointestinal involvement.

Prevalence of Behçet's Disease is highest in the Middle East, Asia and Japan. Behçet's Disease has been classified in the U.S. as a rare or "orphan" disease by the National Institutes of Health. At this time, there are no approved therapies to treat Behçet's Disease in the U.S.

About OTEZLA®

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.

OTEZLA is indicated for the treatment of adult patients with active psoriatic arthritis.

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

Psoriatic Arthritis: Treatment with OTEZLA is associated with an increase in depression. During clinical trials, 1.0% (10/998) reported depression or depressed mood compared to 0.8% (4/495) treated with placebo. Suicidal ideation and behavior was observed in 0.2% (3/1441) of patients on OTEZLA, compared to none in placebo treated patients. Depression was reported as serious in 0.2% (3/1441) of patients exposed to OTEZLA, compared to none in placebo treated patients (0/495). Two patients who received placebo committed suicide compared to none on OTEZLA

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 \geq 10% occurred in 2% (16/784) of patients treated with OTEZLA compared to 1% (3/382) of patients treated with placebo

Psoriatic Arthritis: Body weight loss of 5-10% was reported in 10% of patients taking OTEZLA and in 3.3% of patients taking 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 \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)

Psoriatic Arthritis: 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 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.

Hyperlinks are provided as a convenience and for informational purposes only. Celgene bears no responsibility for the security or content of external websites.

View source version on [businesswire.com](http://www.businesswire.com): <http://www.businesswire.com/news/home/20180217005007/en/>

Celgene Corporation

Investors:

Patrick E. Flanigan III, 908-673-9969

Corporate Vice President, Investor Relations

or

Media:

Catherine Cantone, 908-897-4256

Senior Director, Corporate Communications

Source: Celgene Corporation

News Provided by Acquire Media