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OTEZLA® (Apremilast) Phase II Data Showed Clinically Meaningful Improvements in Patients with Active Ulcerative Colitis

Data shared at the 13th Congress of ECCO

Phase III program with OTEZLA (apremilast) in ulcerative colitis expected to begin in 2018

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) announced that data from a randomized, placebo-controlled, multi-center, phase II clinical trial of apremilast in patients with active ulcerative colitis who had failed at least one conventional therapy but were naïve to biologic therapy were presented in an oral session today at the 13th Congress of ECCO in Vienna (Abstract OP006, 3:30 p.m. CET). The results showed that a higher proportion of patients taking apremilast 30 mg twice daily (BID) achieved clinical remission versus placebo (nominally significant, $P < 0.05$). OTEZLA® (apremilast) is Celgene's oral selective inhibitor of phosphodiesterase 4 (PDE4).

In the study, a total of 170 patients were randomized to placebo, apremilast 40 mg BID or apremilast 30 mg BID. The primary endpoint of the study was Total Mayo Score (TMS) clinical remission at week 12 for the 40 mg BID arm. At week 12, TMS clinical remission was achieved by 21.8 percent of patients in the apremilast 40 mg BID arm (n=55) versus 13.8 percent in the placebo group (n=58; P=non-significant (NS)). In the apremilast 30 mg BID arm, 31.6 percent of patients (n=57) achieved clinical remission as measured by TMS at week 12 versus 13.8 percent in the placebo group (n=58; nominally significant, $P < 0.05$).

"The achievement of clinical remission, which requires endoscopic improvement of the mucosa, is a meaningful goal in the treatment of ulcerative colitis," said presenting author Silvio Danese, M.D., Ph.D., Head of the Inflammatory Bowel Disease Clinical and Research Center, Humanitas Research Hospital. "These findings suggest apremilast, which improved the likelihood of achieving remission in this 12-week study, merits further study in a larger trial."

Clinical remission as measured by Partial Mayo Score (PMS), a secondary endpoint, was achieved by 59.6 percent of patients in the apremilast 30 mg BID arm versus 36.2 percent in the placebo arm (nominally significant, P=0.0124) at week 12. PMS clinical remission was also achieved by 52.7 percent of patients in the apremilast 40 mg BID arm (P=NS versus placebo).

Additional secondary endpoints examined in the trial, including endoscopic remission (Mayo Endoscopic Score ≤1), TMS clinical response, serum biomarkers and mucosal healing (combined endoscopic and histologic remission), showed clinically meaningful improvements for apremilast 30 mg BID versus placebo.

"The strength of these data advances our plans to initiate a phase III program for OTEZLA® (apremilast) 30 mg in ulcerative colitis," said Terrie Curran, President, Celgene Inflammation and Immunology. "We remain committed to bringing forth innovative, oral, immunomodulatory treatment options for patients with inflammatory bowel disease."

Treatment-emergent adverse events reported in at least 5 percent of patients treated with apremilast included headache (23 percent with apremilast 30 mg BID, 26 percent with apremilast 40 mg BID and 7 percent with placebo); viral upper respiratory tract infection (9 percent, 4 percent and 2 percent, respectively); nausea (5 percent, 11 percent and 9 percent); abdominal pain (5 percent, 2 percent and 2 percent); back pain (0 percent, 6 percent and 2 percent); and asthenia (5 percent, 2 percent and 3 percent).

Apremilast is not approved for the treatment of ulcerative colitis in any country. In January 2018, the U.S. Food and Drug Administration designated apremilast an Orphan Drug for the potential treatment of pediatric patients with ulcerative colitis.

About Ulcerative Colitis

Ulcerative colitis is a chronic, relapsing condition triggered by an abnormal, prolonged immune response that creates long-

lasting inflammation and ulcers (sores) in the mucosa (lining) of the large intestine (colon). Symptoms usually develop over time, rather than suddenly. The disease can be debilitating and can sometimes lead to life-threatening complications. Ulcerative colitis is the most common form of inflammatory bowel disease worldwide. About one in every 198 people in Europe and one in every 402 people in North America have ulcerative colitis. In 2004, 2.1 million prescriptions were written to treat ulcerative colitis, and 716,000 ambulatory care visits were related to the disease. In 2010, there were 107,000 hospitalizations due to ulcerative colitis.

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 ≥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 ≥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.

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