Oral Anti-Cancer Therapy Pomalidomide Celgene Receives Positive CHMP Opinion as Treatment for Patients with Relapsed and Refractory Multiple Myeloma

BOUDRY, Switzerland--(BUSINESS WIRE)--May. 31, 2013-- Celgene International Sàrl, a wholly-owned subsidiary of Celgene Corporation (NASDAQ: CELG), today announced that the European Medicines Agency’s (EMA): Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for Pomalidomide Celgene in combination with dexamethasone for the treatment of relapsed and refractory multiple myeloma (rrMM) in patients who have received at least two prior therapies, including both lenalidomide and bortezomib, and have demonstrated disease progression while on their last therapy.

The CHMP reviews applications for all 27 member states in the European Union (EU), as well as Norway and Iceland. The European Commission, which generally follows the recommendation of the CHMP, is expected to make its final decision within two to three months.

Multiple Myeloma (MM) is a rare blood cancer in which plasma cells, important components of the immune system, replicate uncontrollably and accumulate in the bone marrow and interfere with the production of normal blood cells. Multiple myeloma remains incurable and nearly all MM patients who achieve an initial response to treatment will relapse and require additional treatment options.

“Celgene is the first company in more than 40 years to deliver two oral treatments for multiple myeloma,” said Alan Colowick, MD, President of Celgene Europe, the Middle East and Africa (EMEA). “These treatments continue to play an important role in increasing overall survival for patients living with this rare disease. Following the final decision by the European Commission within the next few months, we hope to bring oral pomalidomide, Celgene’s third and important treatment option for patients who have fully benefitted from other treatments including lenalidomide and need new options to help treat their disease. Our commitment to patients with this disease is a centerpiece of who we are as an organization and our focus on rare and debilitating diseases.”

The CHMP positive opinion was based on the results of the MM-003 study, a phase III, multi-centre, randomised (2:1), open-label study in 455 patients. The trial evaluated use of oral pomalidomide plus low-dose dexamethasone (n=302) compared with high-dose dexamethasone (n=153) in patients with relapsed and refractory multiple myeloma; according to the protocol, all patients were to have been treated with both bortezomib and lenalidomide prior to study entry. In the trial, progression-free survival (PFS), the primary endpoint, was significantly longer in patients who received pomalidomide plus low-dose dexamethasone (15.7 weeks) compared with those who received high-dose dexamethasone alone (8 weeks). Median overall survival, the secondary endpoint, was also significantly improved for pomalidomide plus low-dose dexamethasone arm, compared with high-dose dexamethasone only (due to patients still on therapy in the pomalidomide plus low-dose dexamethasone arm, the median has not yet been reached vs. 34 weeks in the high-dose dexamethasone arm).

The most commonly reported adverse reactions included anaemia, neutropenia, fatigue and thrombocytopenia. The most commonly reported Grade 3 or 4 adverse reactions included neutropenia, anaemia, thrombocytopenia and pneumonia.

About Pomalidomide

Pomalidomide is an oral immunomodulatory agent currently approved in the U.S. under the brand name Pomalyst and is under review in other countries. In the U.S., POMALYST® (pomalidomide) is indicated for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval in the U.S. is based on response rate in the MM-002 clinical trial. Clinical benefit, such as improvement in survival or symptoms, has not been verified in this study.

Important Safety Information based on approved U.S. Label
WARNING: EMBRYO-FETAL TOXICITY and VENOUS THROMBOEMBOLISM

Embryo-Fetal Toxicity
CONTRAINDICATIONS: Pregnancy

- POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.
- Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment

POMALYST is only available through a restricted distribution program called POMALYST REMSTM.

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity

- Females of Reproductive Potential: Must avoid pregnancy while taking POMALYST and for at least 4 weeks after completing therapy. Must commit either to abstain continuously from heterosexual sexual intercourse or to use 2 methods of reliable birth control, beginning 4 weeks prior to initiating treatment with POMALYST, during therapy, during dose interruptions and continuing for 4 weeks following discontinuation of POMALYST therapy. Must obtain 2 negative pregnancy tests prior to initiating therapy.
- Males: Pomalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking POMALYST and for up to 28 days after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
- Blood Donation: Patients must not donate blood during treatment with POMALYST and for 1 month following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.

Venous Thromboembolism

- Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE) occur in patients with multiple myeloma treated with POMALYST. Prophylactic anti-thrombotic measures were employed in the clinical trial. Consider prophylactic measures after assessing an individual patient’s underlying risk factors.

POMALYST REMS Program

Because of the embryo-fetal risk, POMALYST is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) called “POMALYST REMS.” Prescribers and pharmacists must be certified with the program; patients must sign an agreement form and comply with the requirements. Further information about the POMALYST REMS program is available at [celgeneriskmanagement.com] or by telephone at 1-888-423-5436.

Venous Thromboembolism: Patients receiving POMALYST have developed venous thromboembolic events reported as serious adverse reactions. In the trial, all patients were required to receive prophylaxis or antithrombotic treatment. The rate of DVT or PE was 3%. Consider anticoagulation prophylaxis after an assessment of each patient’s underlying risk factors.

Hematologic Toxicity: Neutropenia of any grade was reported in 50% of patients and was the most frequently reported Grade 3/4 adverse event, followed by anemia and thrombocytopenia. Monitor patients for hematologic toxicities, especially neutropenia, with complete blood counts weekly for the first 8 weeks and monthly thereafter. Treatment is continued or modified for Grade 3 or 4 hematologic toxicities based upon clinical and laboratory findings. Dosing interruptions and/or modifications are recommended to manage neutropenia and thrombocytopenia.

Hypersensitivity Reactions: Patients with a prior history of serious hypersensitivity associated with thalidomide or lenalidomide were excluded from studies and may be at higher risk of hypersensitivity.
Dizziness and Confusional State: 18% of patients experienced dizziness and 12% of patients experienced a confusional state; 1% of patients experienced grade 3/4 dizziness, and 3% of patients experienced grade 3/4 confusional state. Instruct patients to avoid situations where dizziness or confusion may be a problem and not to take other medications that may cause dizziness or confusion without adequate medical advice.

Neuropathy: 18% of patients experienced neuropathy (approximately 9% peripheral neuropathy). There were no cases of grade 3 or higher neuropathy adverse reactions reported.

Risk of Second Primary Malignancies: Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.

ADVERSE REACTIONS

In the clinical trial MM-002 of 219 patients who received POMALYST alone (n=107) or POMALYST + low-dose dexamethasone (low-dose dex) (n=112), all patients had at least one treatment-emergent adverse reaction.

- In the POMALYST alone versus POMALYST + low dose dexamethasone arms, respectively, most common adverse reactions (≥30%) included fatigue and asthenia (55%, 63%), neutropenia (52%, 47%), anemia (38%, 39%), constipation (36%, 35%), nausea (36%, 22%), diarrhea (34%, 33%), dyspnea (34%, 45%), upper respiratory tract infection (32%, 25%), back pain (32%, 30%), and pyrexia (19%, 30%)
- 90% of patients treated with POMALYST alone and 88% of patients treated with POMALYST + low-dose dex had at least one treatment-emergent NCI CTC Grade 3 or 4 adverse reaction
- In the POMALYST alone versus POMALYST + low dose dexamethasone arms, respectively, most common Grade 3/4 adverse reactions (≥15%) included neutropenia (47%, 38%), anemia (22%, 21%), thrombocytopenia (22%, 19%), and pneumonia (16%, 23%). For other Grade 3 or 4 toxicities besides neutropenia and thrombocytopenia, hold treatment and restart treatment at 1 mg less than the previous dose when toxicity has resolved to less than or equal to Grade 2 at the physician’s discretion
- 67% of patients treated with POMALYST and 62% of patients treated with POMALYST + low-dose dex had at least one treatment-emergent serious adverse reaction
- In the POMALYST alone versus POMALYST + low dose dexamethasone arms, respectively, most common serious adverse reactions (≥5%) were pneumonia (14%, 19%), renal failure (8%, 6%), dyspnea (5%, 6%), sepsis (6%, 3%), pyrexia (3%, 5%), dehydration (5%, 3%), hypercalcemia (5%, 2%), urinary tract infection (0%, 5%), and febrile neutropenia (5%, 1%)

DRUG INTERACTIONS

No formal drug interaction studies have been conducted with POMALYST. Pomalidomide is primarily metabolized by CYP1A2 and CYP3A. Pomalidomide is also a substrate for P-glycoprotein (P-gp). Coadministration of POMALYST with drugs that are strong inhibitors or inducers of CYP1A2, CYP3A, or P-gp should be avoided. Cigarette smoking may reduce pomalidomide exposure due to CYP1A2 induction. Patients should be advised that smoking may reduce the efficacy of pomalidomide.

USE IN SPECIFIC POPULATIONS

Pregnancy: If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-332-1088 and also to Celgene Corporation at 1-888-423-5436.

Nursing Mothers: It is not known if pomalidomide is excreted in human milk. Pomalidomide was excreted in the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants from POMALYST, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of POMALYST in patients under the age of 18 have not been established.

Geriatric Use: No dosage adjustment is required for POMALYST based on age. Patients greater than or equal to 65 years of age were more likely than patients less than or equal to 65 years of age to experience pneumonia.

Renal and Hepatic Impairment: Pomalidomide is metabolized in the liver. Pomalidomide and its metabolites are primarily excreted by the kidneys. The influence of renal and hepatic impairment on the safety, efficacy, and pharmacokinetics of pomalidomide has not been evaluated. Avoid POMALYST in patients with a serum creatinine >3.0 mg/dL. Avoid POMALYST in patients with serum bilirubin >2.0 mg/dL and AST/ALT >3.0 x ULN.
Please see full U.S. Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.

POMALYST (pomalidomide) is indicated for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and bortezomib and have demonstrated disease progression on or within 60 days of completion of the last therapy. Approval is based on response rate in the MM-002 clinical trial. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

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. Celgene International Sàrl, located in Boudry, in the Canton of Neuchâtel, Switzerland, is a wholly owned subsidiary and international headquarters of Celgene Corporation. For more information, please visit the Company’s website at 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 our other reports filed with the Securities and Exchange Commission.

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