Results from Phase IIb Study of POMALYST®/IMNOVID® (pomalidomide) Plus Low-Dose dexamethasone in Patients with Relapsed and Refractory Multiple Myeloma Presented at ASH

SAN FRANCISCO--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that results from the STRATUS™ trial (MM-010), a single-arm phase IIIb study of pomalidomide plus low-dose dexamethasone in patients with relapsed and refractory multiple myeloma were presented at the 56th American Society of Hematology annual meeting. Pomalidomide is marketed as POMALYST® in the United States and IMNOVID® in the European Union.

In the study, 599 patients with refractory, or relapsed and refractory, disease who had previously failed lenalidomide and bortezomib had been enrolled at the time of the data cutoff. The primary endpoint was safety, and key secondary endpoints included pomalidomide exposure, overall response rate (ORR; ≥ partial response), duration of response (DOR), progression-free survival (PFS), overall survival (OS), and cytogenetic analyses. Patients had a median five prior therapies. All patients received thromboprophylaxis with low-dose aspirin, low-molecular-weight heparin, or equivalent.

The most frequent grade 3-4 adverse events (AEs) were hematologic, including neutropenia (42%), neutropenic fever (5%), anemia (29%), and thrombocytopenia (22%); grade 3-4 non-hematological toxicities included pneumonia (11%), fatigue (5%), and hypercalcemia (4%). Grade 3/4 deep vein thrombosis was low (1%) with prophylaxis, and peripheral neuropathy was 1%. Dose reductions of either pomalidomide or low dose dexamethasone due to AEs were required in 18% of patients; 9% of discontinuations were due to AEs 9%.

At a median follow-up of 6.8 months with a median four cycles received, the median PFS and OS were 4.2 months and 11.9 months, respectively. The ORR was 35%, with 8% of patients achieving at least a very good partial response (VGPR). The median DOR was 6.8 months. In patients refractory to prior lenalidomide (n=572) or lenalidomide and bortezomib (n=473), similar PFS (4.2 months and 4.1 months), OS (12 months for each), and ORR (34% and 35%) were achieved.

In addition, a sub-group analysis was conducted to determine the impact of the therapy on patients with moderate renal impairment (RI). Of the 604 patients enrolled in the study, 215 had moderate RI (Creatinine clearance [CrCl] greater than 45 mL/min but less than 60 mL/min).

ORR was generally similar between patient groups receiving pomalidomide plus low-dose dexamethasone (37% with moderate renal impairment vs. 33% without moderate renal impairment) despite differences in renal function. The median DOR was 6 months vs. 7.9 months, respectively. PFS was slightly extended in patients without moderate renal impairment, but did not meet statistical significance (3.7 vs. 4.6 months, p=0.1142).

The most common grade 3-4 nonhematologic AEs were infections (29% vs. 30%) and pneumonia (12% vs. 11%). Twelve percent of patients with moderate RI and 7% of patients without moderate RI discontinued pomalidomide due to AEs.

Pomalidomide starting dose was 4 mg daily for days 1-21 of 28-day cycle. Dexamethasone was given at 40mg/day (20 mg for > 75 years) on days 1, 8, 15, 22. Dose intensity was comparable in both groups (94% and 93%). No dose adjustment was required for renal impairment.

About POMALYST®

In the U.S., pomalidomide is marketed as POMALYST and 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. Clinical benefit, such as improvement in survival or symptoms, has not been verified.

U.S. Regulatory Information for Pomalyst

Important Safety Information
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 REMS™.

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 POMALYST therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.

POMALYST REMS Program

Because of the embryo-fetal risk, POMALYST is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called “POMALYST REMS.” Prescribers and pharmacies 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 www.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 reaction, 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 confusional state may be a problem and not to take other medications that may cause dizziness or confusional state 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.

**Tumor Lysis Syndrome:** Tumor lysis syndrome (TLS) may occur in patients treated with pomalidomide. Patients at risk for TLS are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

**ADVERSE REACTIONS**

In the clinical trial 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 dex arms, the most common adverse reactions (≥30%), respectively, 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 dex arms, the most common Grade 3/4 adverse reactions (≥15%), respectively, 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 dex arms, the most common serious adverse reactions (≥5%), respectively, 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**

Pomalidomide is primarily metabolized by CYP1A2 and CYP3A. Pomalidomide is also a substrate for P-glycoprotein (P-gp). Avoid the use of strong CYP1A2 inhibitors. If medically necessary to co-administer strong inhibitors of CYP1A2 in the presence of strong inhibitors of CYP3A4 and P-gp, reduce POMALYST dose by 50%. 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 Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.

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. For more information, please visit www.celgene.com. Follow Celgene on Twitter @Celgene, and on Pinterest and LinkedIn.

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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