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Celgene Corporation Announces Positive Results from the Pivotal Phase III 'OPTIMISMM' Study of POMALYST/IMNOVID® for the Treatment of Relapsed or Refractory Multiple Myeloma

Study met its primary endpoint demonstrating significant improvement in progression-free survival (PFS) with POMALYST®/IMNOVID® in combination with bortezomib and dexamethasone (PVd) compared with bortezomib and low-dose dexamethasone

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that the Phase III, randomized, open-label, international clinical study, OPTIMISMM, achieved its primary endpoint, showing a statistically significant and clinically meaningful improvement in progression-free survival (PFS) for the pomalidomide arm versus the comparator arm.

OPTIMISMM evaluated the efficacy and safety of POMALYST/IMNOVID (pomalidomide) plus bortezomib and low-dose dexamethasone (PVd) versus bortezomib and low-dose dexamethasone in patients with relapsed/refractory multiple myeloma. It is the only phase III trial to investigate a triplet combination in patients who have all received prior lenalidomide (REVLIMID®), a population for which there is a growing unmet medical need.

"The OPTIMISMM results confirm the expanding role of pomalidomide in previously treated multiple myeloma patients," said Paul Richardson, M.D., Clinical Program Leader and Director of Clinical Research, Jerome Lipper Multiple Myeloma Center at the Dana Farber Cancer Institute, RJ Corman Professor of Medicine, Harvard Medical School and principal investigator of the study. "We see the PVd combination as an important step in improving care, and especially for patients previously treated with lenalidomide in this setting."

In the study, the safety profile was consistent with previously reported data. Detailed data from OPTIMISMM will be presented at future medical meetings.

The combination of POMALYST/IMNOVID, bortezomib and low-dose dexamethasone is not currently approved for use.

About POMALYST/IMNOVID

Indication

POMALYST® (pomalidomide) is a thalidomide analogue indicated, in combination with dexamethasone, for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- 1 **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.**
- 1 **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®.

Venous and Arterial Thromboembolism

- 1 **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**
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CONTRAINDICATIONS

- 1 **Pregnancy:** POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If POMALYST is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.

WARNINGS AND PRECAUTIONS

- 1 **Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS**
 - 1 **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 4 weeks after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
 - 1 **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.
- 1 **POMALYST REMS[®] Program: See Boxed WARNINGS**
 - 1 Prescribers and pharmacies must be certified with the **POMALYST REMS** program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive POMALYST. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.
 - 1 Further information about the **POMALYST REMS** program is available at www.CelgeneRiskManagement.com or by telephone at 1-888-423-5436.
- 1 **Venous and Arterial Thromboembolism: See Boxed WARNINGS.** Patients with known risk factors, including prior thrombosis, may be at greater risk, and actions should be taken to try to minimize all modifiable factors (e.g., hyperlipidemia, hypertension, smoking). Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.
- 1 **Increased Mortality with Pembrolizumab:** In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality. Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- 1 **Hematologic Toxicity:** Neutropenia (46%) was the most frequently reported Grade 3/4 adverse reaction in patients taking POMALYST in clinical trials, followed by anemia and thrombocytopenia. Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter. Patients may require dose interruption and/or modification.
- 1 **Hepatotoxicity:** Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST. Monitor liver function tests monthly. Stop POMALYST upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
- 1 **Hypersensitivity Reactions:** Angioedema and severe dermatologic reactions have been reported. Discontinue POMALYST for angioedema, skin exfoliation, bullae, or any other severe dermatologic reactions, and do not resume therapy.
- 1 **Dizziness and Confusional State:** In patients taking POMALYST in clinical trials, 14% experienced dizziness (1% Grade 3 or 4) and 7% a confusional state (3% Grade 3 or 4). 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.
- 1 **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.

- | **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 (TLS):** TLS may occur in patients treated with POMALYST. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

ADVERSE REACTIONS

Nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%). The most common adverse reactions ($\geq 15\%$) included neutropenia (51.3%), fatigue and asthenia (46.7%), upper respiratory tract infection (31%), thrombocytopenia (29.7%), pyrexia (26.7%), dyspnea (25.3%), diarrhea (22%), constipation (21.7%), back pain (19.7%), cough (20%), pneumonia (19.3%), bone pain (18%), edema peripheral (17.3%), peripheral neuropathy (17.3%), muscle spasms (15.3%), and nausea (15%). Grade 3 or 4 adverse reactions ($\geq 15\%$) included neutropenia (48.3%), thrombocytopenia (22%), and pneumonia (15.7%).

DRUG INTERACTIONS

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2. Consider alternative treatments. If a strong CYP1A2 inhibitor must be used, reduce POMALYST dose by 50%.

USE IN SPECIFIC POPULATIONS

- | **Pregnancy: See Boxed WARNINGS.** 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. There is a POMALYST pregnancy exposure registry that monitors pregnancy outcomes in females exposed to POMALYST during pregnancy as well as female partners of male patients who are exposed to POMALYST. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436.
- | **Lactation:** There is no information regarding the presence of pomalidomide in human milk, the effects of POMALYST on the breastfed infant, or the effects of POMALYST on milk production. 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 breastfed infants from POMALYST, advise a nursing woman to discontinue breastfeeding during treatment with POMALYST.
- | **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.
- | **Geriatric Use:** No dosage adjustment is required for POMALYST based on age. Patients > 65 years of age were more likely than patients ≤ 65 years of age to experience pneumonia.
- | **Renal Impairment:** Reduce POMALYST dose by 25% in patients with severe renal impairment requiring dialysis. Take dose of POMALYST following hemodialysis on hemodialysis days.
- | **Hepatic Impairment:** Reduce POMALYST dose by 25% in patients with mild to moderate hepatic impairment and 50% in patients with severe hepatic impairment.
- | **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces the AUC of pomalidomide by 32% by CYP1A2 induction.

Please see full [Prescribing Information](#), including **Boxed WARNINGS**.

About Celgene

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical 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 Securities and Exchange Commission.

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Celgene Corporation

Investors:

+1-908-673-9628

ir@celgene.com

or

Media:

+1-908-673-2275

media@celgene.com

Source: Celgene Corporation

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