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Phase III FIRST™ (MM-020/IFM 07-01) Trial of REVOLIMID® (lenalidomide) Plus Dexamethasone in Newly Diagnosed Multiple Myeloma Patients Who Are Not Candidates for Stem Cell Transplant Published in New England Journal of Medicine

Study met primary endpoint as significant progression-free survival benefit was seen for patients treated with continuous REVOLIMID plus dexamethasone compared with those treated with a standard of care

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that data from FIRST (MM-020/IFM 07-01)—an open-label phase III randomized study of continuous REVOLIMID (lenalidomide) in combination with dexamethasone in patients newly diagnosed with multiple myeloma (NDMM) who are not candidates for stem cell transplant—have been published in the Sept. 4 issue of the *New England Journal of Medicine*.

Initial findings, including that the trial had met its primary endpoint of progression free survival (PFS), were reported during the plenary session at the 55th American Society of Hematology annual meeting in December 2013.

The findings, as published in the *New England Journal of Medicine*, demonstrated that at a median follow-up of 37 months among surviving patients, the median progression-free survival was 25.5 months with continuous oral lenalidomide plus low-dose dexamethasone (Rd), 20.7 months with a fixed course of oral lenalidomide plus low-dose dexamethasone (Rd18) and 21.2 months with melphalan, prednisone and thalidomide (MPT). This resulted in a 28% reduction in risk of progression or death for patients treated with continuous Rd compared with those treated with MPT (HR 0.72; 95% CI, 0.61 to 0.85; P < 0.001) and a 30% reduction compared with Rd18 (HR 0.70; 95% CI, 0.60 to 0.82; P < 0.001) in the study.

The pre-planned interim analysis of overall survival demonstrated a 22% reduction in risk of death for continuous Rd vs. MPT (HR 0.78; 95% CI, 0.64 to 0.96; P=0.02), although the difference did not cross the pre-specified superiority boundary (P < 0.0096). As of the time of the analysis (May 24, 2013), 121 of 535 (23%) patients in the continuous Rd arm were still on therapy.

Additional secondary endpoints showed response rates were also significantly better with continuous Rd (75%) and with Rd18 (73%) than with MPT (62%; P < 0.001 for both comparisons). More patients achieved a very good partial response or better in the continuous Rd (44%) or Rd18 arms (43%) compared with MPT (28%). Complete response rates were 15%, 14% and 9% for continuous Rd, Rd18 and MPT, respectively. Median duration of response was 35.0 months with continuous Rd compared with 22.3 months for MPT (HR 0.63; P < 0.001) and 22.1 months for Rd18 (HR 0.60; P < 0.001). Median time to disease progression was 32.5 months for patients receiving continuous Rd compared with 23.9 months (HR 0.68; P < 0.001) for MPT and 21.9 months (HR 0.62; P < 0.001) for Rd18.

Safety results showed that grade 3/4 adverse events that occurred in at least 8% of patients in the continuous Rd arm, Rd18 arm or MPT arm included neutropenia (28%, 26%, 45%, respectively), anemia (18%, 16%, 19%), thrombocytopenia (8%, 8%, 11%), febrile neutropenia (1%, 3%, 3%), leukopenia (5%, 6%, 10%), infection (29%, 22%, 17%), pneumonia (8%, 8%, 6%), deep-vein thrombosis and/or pulmonary embolism (8%, 6%, 5%), asthenia (8%, 6%, 6%), fatigue (7%, 9%, 6%), and peripheral sensory neuropathy (1%, < 1%, 9%). Rates of grade 3/4 cardiac disorders for patients in the continuous Rd, Rd18 and MPT arms were 12%, 7% and 9%, respectively. The incidence of invasive second primary malignancies was 3% in patients taking continuous Rd, 6% in patients taking Rd18 and 5% in those taking MPT; the overall incidence of solid tumors was identical in the continuous Rd and MPT arms (3%) and 5% in the Rd18 arm.

For additional results from the publication, visit <http://www.nejm.org/>

Based on the results of the FIRST study, Celgene submitted REVOLIMID in combination with dexamethasone for the treatment of newly diagnosed multiple myeloma patients with the European Medicines Agency (EMA) in February 2014 and with the U.S. Food and Drug Administration (FDA) in April 2014.

These results are from an investigational study. REVOLIMID is not indicated for use in newly diagnosed multiple myeloma patients in any country.

About FIRST™

In the FIRST (Frontline Investigation of REVLIMID + Dexamethasone Versus Standard Thalidomide) trial, 1,623 patients from 18 countries either ≥65 or < 65 years of age and ineligible for stem cell transplant were randomized 1:1:1 into three arms: REVLIMID plus low-dose dexamethasone in 28-day cycles until disease progression (continuous Rd); REVLIMID plus low-dose dexamethasone for 72 weeks (18 cycles, Rd18); or melphalan, prednisone and thalidomide in 42-day cycles for 72 weeks (12 cycles, MPT). The primary endpoint was a comparison of progression-free survival for continuous Rd versus MPT.

About REVLIMID®

REVLIMID is approved in combination with dexamethasone for the treatment of patients with multiple myeloma who have received at least one prior therapy in nearly 70 countries, encompassing Europe, the Americas, the Middle-East and Asia, and in combination with dexamethasone for the treatment of patients whose disease has progressed after one therapy in Australia and New Zealand.

REVLIMID is also approved in the United States, Canada, Switzerland, Australia, New Zealand and several Latin American countries, as well as Malaysia and Israel, for transfusion-dependent anaemia due to low- or intermediate-1-risk MDS associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities and in Europe for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate.

In addition, REVLIMID is approved in the United States for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib.

U.S. Regulatory Information for REVLIMID®

REVLIMID (lenalidomide) in combination with dexamethasone is indicated for the treatment of patients with multiple myeloma (MM) who have received at least one prior therapy

REVLIMID (lenalidomide) is indicated for the treatment of patients with transfusion-dependent anemia due to low- or intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities

REVLIMID (lenalidomide) is indicated for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib

REVLIMID is not indicated and not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS THROMBOEMBOLISM

Embryo-Fetal Toxicity

Do not use REVLIMID during pregnancy. Lenalidomide, a thalidomide analogue, caused limb abnormalities in a developmental monkey study. Thalidomide is a known human teratogen that causes severe life-threatening human birth defects. If lenalidomide is used during pregnancy, it may cause birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting REVLIMID treatment. Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment. To avoid embryo-fetal exposure to lenalidomide, REVLIMID is only available through a restricted distribution program, the REVLIMID REMS™ program (formerly known as the "RevAssist®" program).

Information about the REVLIMID REMS™ Program is available at www.celgeneriskmanagement.com or by calling the manufacturer's toll-free number 1-888-423-5436.

Hematologic Toxicity (Neutropenia and Thrombocytopenia)

REVLIMID can cause significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q MDS had to have a dose delay/reduction during the major study. Thirty-four percent of patients had to have a second dose

delay/reduction. Grade 3 or 4 hematologic toxicity was seen in 80% of patients enrolled in the study. Patients on therapy for del 5q MDS should have their complete blood counts monitored weekly for the first 8 weeks of therapy and at least monthly thereafter. Patients may require dose interruption and/or reduction. Patients may require use of blood product support and/or growth factors.

Venous Thromboembolism

REVLIMID has demonstrated a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients with MM who were treated with REVIMID and dexamethasone therapy. Patients and physicians are advised to be observant for the signs and symptoms of thromboembolism. Patients should be instructed to seek medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. It is not known whether prophylactic anticoagulation or antiplatelet therapy prescribed in conjunction with REVIMID may lessen the potential for venous thromboembolism. The decision to take prophylactic measures should be done carefully after an assessment of an individual patient's underlying risk factors.

CONTRAINDICATIONS

Pregnancy:

- REVIMID can cause fetal harm when administered to a pregnant female. Lenalidomide is contraindicated in females who are pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus

Allergic Reactions:

- REVIMID is contraindicated in patients who have demonstrated hypersensitivity (e.g., angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis) to lenalidomide

WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity:

- REVIMID is an analogue of thalidomide, a known human teratogen that causes life-threatening human birth defects or embryo-fetal death. An embryo-fetal development study in monkeys indicates that lenalidomide produced malformations in the offspring of female monkeys who received the drug during pregnancy, similar to birth defects observed in humans following exposure to thalidomide during pregnancy
- **Females of Reproductive Potential:** Must avoid pregnancy for at least 4 weeks before beginning REVIMID therapy, during therapy, during dose interruptions and for at least 4 weeks after completing therapy. Must commit either to abstain continuously from heterosexual sexual intercourse or to use two methods of reliable birth control beginning 4 weeks prior to initiating treatment with REVIMID, during therapy, during dose interruptions and continuing for 4 weeks following discontinuation of REVIMID therapy. Must obtain 2 negative pregnancy tests prior to initiating therapy
- **Males:** Lenalidomide 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 REVIMID and for up to 28 days after discontinuing REVIMID, even if they have undergone a successful vasectomy. Male patients taking REVIMID must not donate sperm
- **Blood Donation:** Patients must not donate blood during treatment with REVIMID 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 REVIMID

REVIMID REMS® Program

Because of embryo-fetal risk, REVIMID is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) the **REVIMID REMS Program (formerly known as the "RevAssist" Program)**. Prescribers and pharmacies must be certified with the program and patients must sign an agreement form and comply with the requirements. Further information about the **REVIMID REMS** program is available at www.celgeneriskmanagement.com or by telephone at 1-888-423-5436

Hematologic Toxicity: REVIMID can cause significant neutropenia and thrombocytopenia. **MM:** Patients taking REVIMID for MM should have their complete blood counts monitored every 2 weeks for the first 12 weeks and then monthly thereafter. In the pooled MM trials Grade 3 and 4 hematologic toxicities were more frequent in patients treated with the combination of REVIMID and dexamethasone than in patients treated with dexamethasone alone. **MCL:** Patients taking REVIMID for MCL should have their complete blood counts monitored weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, and then monthly

thereafter. In the MCL trial, Grade 3 or 4 neutropenia was reported in 43% of the patients. Grade 3 or 4 thrombocytopenia was reported in 28% of the patients. Patients may require dose interruption and/or dose reduction

Venous Thromboembolism: Venous thromboembolic events (predominantly deep venous thrombosis and pulmonary embolism) have occurred in patients with MM treated with lenalidomide combination therapy and patients with MDS or MCL treated with lenalidomide monotherapy. It is not known whether prophylactic anticoagulation or antiplatelet therapy prescribed in conjunction with REVLIMID may lessen the potential for venous thromboembolism

Increased Mortality in Patients With CLL: In a clinical trial in the first line treatment of patients with CLL, single agent REVLIMID therapy increased the risk of death as compared to single agent chlorambucil. In an interim analysis, there were 34 deaths among 210 patients on the REVLIMID treatment arm compared to 18 deaths among 211 patients in the chlorambucil treatment arm, and hazard ratio for overall survival was 1.92 [95% CI: 1.08-3.41] consistent with a 92% increase in risk of death. Serious adverse cardiovascular reactions, including atrial fibrillation, myocardial infarction, and cardiac failure occurred more frequently in the REVLIMID treatment arm. REVLIMID is not indicated and not recommended for use in CLL outside of controlled clinical trials

Second Primary Malignancies: Patients with MM treated with lenalidomide in studies including melphalan and stem cell transplantation had a higher incidence of second primary malignancies, particularly acute myelogenous leukemia (AML) and Hodgkin lymphoma, compared to patients in the control arms who received similar therapy but did not receive lenalidomide. Monitor patients for the development of second malignancies. Take into account both the potential benefit of lenalidomide and the risk of second primary malignancies when considering treatment with lenalidomide

Hepatotoxicity: Hepatic failure, including fatal cases, has occurred in patients treated with lenalidomide in combination with dexamethasone. The mechanism of drug-induced hepatotoxicity is unknown. Pre-existing viral liver disease, elevated baseline liver enzymes, and concomitant medications may be risk factors. Monitor liver enzymes periodically. Stop REVLIMID upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered

Allergic Reactions: Angioedema and serious dermatologic reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported. These events can be fatal. Patients with a prior history of Grade 4 rash associated with thalidomide treatment should not receive REVLIMID. REVLIMID interruption or discontinuation should be considered for Grade 2-3 skin rash. REVLIMID must be discontinued for angioedema, Grade 4 rash, exfoliative or bullous rash, or if SJS or TEN is suspected and should not be resumed following discontinuation for these reactions. REVLIMID capsules contain lactose. Risk-benefit of REVLIMID treatment should be evaluated in patients with lactose intolerance

Tumor Lysis Syndrome: Fatal instances of tumor lysis syndrome (TLS) have been reported during treatment with lenalidomide. The patients at risk of TLS are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken

Tumor Flare Reaction: Tumor flare reaction (TFR) has occurred during investigational use of lenalidomide for CLL and lymphoma, and is characterized by tender lymph node swelling, low grade fever, pain and rash. REVLIMID is not indicated and not recommended for use in CLL outside of controlled clinical trials

Monitoring and evaluation for TFR is recommended in patients with MCL. Tumor flare may mimic the progression of disease (PD). In patients with Grade 3 or 4 TFR, it is recommended to withhold treatment with lenalidomide until TFR resolves to ≤ Grade 1. In the MCL trial, approximately 10% of subjects experienced TFR; all reports were Grade 1 or 2 in severity. All of the events occurred in cycle 1 and one patient developed TFR again in cycle 11. Lenalidomide may be continued in patients with Grade 1 and 2 TFR without interruption or modification, at the physician's discretion. Patients with Grade 1 or 2 TFR may also be treated with corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) and/or narcotic analgesics for management of TFR symptoms. Patients with Grade 3 or 4 TFR may be treated for management of symptoms per the guidance for treatment of Grade 1 and 2 TFR

ADVERSE REACTIONS

Multiple Myeloma

- In the REVLIMID/dexamethasone treatment group, 269 patients (76%) underwent at least one dose interruption with or without a dose reduction of REVLIMID compared to 199 patients (57%) in the placebo/dexamethasone treatment group
- Of these patients who had one dose interruption with or without a dose reduction, 76% (269/353) vs 57% (199/350), 50% in the REVLIMID/dexamethasone treatment group underwent at least one additional dose interruption with or without a dose reduction compared to 21% in the placebo/dexamethasone treatment group
- Most adverse events and Grade 3/4 adverse events were more frequent in MM patients who received the combination of REVLIMID/dexamethasone compared to placebo/dexamethasone

- Grade 3/4 neutropenia occurred in 33.4% vs 3.4%; 2.3% experienced Grade 3/4 febrile neutropenia vs 0%
- Deep vein thrombosis (DVT) was reported as a serious adverse drug reaction (7.4%) or Grade 3/4 (8.2%) compared to 3.1% and 3.4%. Discontinuations due to DVT were reported at comparable rates between groups
- Pulmonary embolism (PE) was reported as a serious adverse drug reaction (3.7%) or Grade 3/4 (4.0%) compared to 0.9% and 0.9%. Discontinuations due to PE were reported at comparable rates between groups
- Adverse reactions reported in ≥15% of MM patients (REVLIMID/dexamethasone vs dexamethasone/placebo): fatigue (44% vs 42%), neutropenia (42% vs 6%), constipation (41% vs 21%), diarrhea (39% vs 27%), muscle cramp (33% vs 21%), anemia (31% vs 24%), pyrexia (28% vs 23%), peripheral edema (26% vs 21%), nausea (26% vs 21%), back pain (26% vs 19%), upper respiratory tract infection (25% vs 16%), dyspnea (24% vs 17%), dizziness (23% vs 17%), thrombocytopenia (22% vs 11%), rash (21% vs 9%), tremor (21% vs 7%), weight decreased (20% vs 15%), nasopharyngitis (18% vs 9%), blurred vision (17% vs 11%), anorexia (16% vs 10%), and dysgeusia (15% vs 10%)

Myelodysplastic Syndromes

- Thrombocytopenia (61.5%; 91/148) and neutropenia (58.8%; 87/148) were the most frequently reported adverse events observed in the del 5q MDS population
- Grade 3 and 4 adverse events reported in ≥ 5% of patients with del 5q MDS were neutropenia (53%), thrombocytopenia (50%), pneumonia (7%), rash (7%), anemia (6%), leukopenia (5%), fatigue (5%), dyspnea (5%), and back pain (5%)
- Other adverse events reported in ≥15% of del 5q MDS patients (REVLIMID): diarrhea (49%), pruritus (42%), rash (36%), fatigue (31%), constipation (24%), nausea (24%), nasopharyngitis (23%), arthralgia (22%), pyrexia (21%), back pain (21%), peripheral edema (20%), cough (20%), dizziness (20%), headache (20%), muscle cramp (18%), dyspnea (17%), pharyngitis (16%), epistaxis (15%), asthenia (15%), upper respiratory tract infection (15%)

Mantle Cell Lymphoma

- Grade 3 and 4 adverse events reported in ≥5% of patients treated with REVIMID in the MCL trial (N=134) included neutropenia (43%), thrombocytopenia (28%), anemia (11%), pneumonia (9%), leukopenia (7%), fatigue (7%), diarrhea (6%), dyspnea (6%), and febrile neutropenia (6%)
- Serious adverse events reported in ≥2 patients treated with REVIMID monotherapy for MCL included chronic obstructive pulmonary disease, clostridium difficile colitis, sepsis, basal cell carcinoma, and supraventricular tachycardia
- Adverse events reported in ≥15% of patients treated with REVIMID in the MCL trial included neutropenia (49%), thrombocytopenia (36%), fatigue (34%), anemia (31%), diarrhea (31%), nausea (30%), cough (28%), pyrexia (23%), rash (22%), dyspnea (18%), pruritus (17%), peripheral edema (16%), constipation (16%), and leukopenia (15%)
- Adverse events occurring in patients treated with REVIMID in the MCL trial resulted in at least one dose interruption in 76 (57%) patients, at least one dose reduction in 51 (38%) patients, and discontinuation of treatment in 26 (19%) patients

DRUG INTERACTIONS

Periodic monitoring of digoxin plasma levels, in accordance with clinical judgment and based on standard clinical practice in patients receiving this medication, is recommended during administration of REVIMID. It is not known whether there is an interaction between dexamethasone and warfarin. Close monitoring of PT and INR is recommended in MM patients taking concomitant warfarin. Erythropoietic agents, or other agents, that may increase the risk of thrombosis, such as estrogen containing therapies, should be used with caution in MM patients receiving lenalidomide with dexamethasone

USE IN SPECIFIC POPULATIONS

Pregnancy: If pregnancy does occur during treatment, immediately discontinue the drug. Under these conditions, refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. Any suspected fetal exposure to REVIMID must be reported 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 whether REVIMID is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 18 have not been established

Geriatric Use: Since elderly patients are more likely to have decreased renal function, care should be taken in dose selection. Monitor renal function

Renal Impairment: Since REVOLIMID is primarily excreted unchanged by the kidney, adjustments to the starting dose of REVOLIMID are recommended to provide appropriate drug exposure in patients with moderate (CLcr 30-60 mL/min) or severe renal impairment (CLcr < 30 mL/min) and in patients on dialysis

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 us on Twitter @Celgene as well.

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 Celgene Corporation's Annual Report on Form 10-K and other reports filed with the Securities and Exchange Commission.

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