Phase III Study with REVLIMID® Continuous Therapy Demonstrates Statistically Significant Improvement in Progression-Free Survival for Patients Newly Diagnosed with Multiple Myeloma

Study Showed a Median Progression-Free Survival of 31 Months for Patients ≤75 Years Old Receiving Lenalidomide Continuous Therapy Compared with 12 Months for Patients not Receiving Lenalidomide Continuous Therapy

Trend Reported for Extended Overall Survival in favor of Patients Receiving Lenalidomide Continuous Therapy

BOUDRY, Switzerland--(BUSINESS WIRE)--Dec. 12, 2011-- Celgene International Sàrl, a subsidiary of Celgene Corporation (NASDAQ: CELG), announced that data from the planned interim analysis of MM-015, a phase III, randomized, double-blind study of continuous REVLIMID (lenalidomide) therapy for the treatment of patients with newly diagnosed multiple myeloma who were ineligible for stem cell transplant, reported a clinically significant improvement in progression-free survival (PFS), the primary endpoint of the study. The data, presented at the 53rd Annual Meeting of the American Society of Hematology, focused on a pre-specified sub-analysis of patients who were 75 years or younger.

The study of 459 patients evaluated patients receiving one of the following treatment regimens: lenalidomide in combination with melphalan and prednisone, followed by continuous lenalidomide alone (MPR-R) (n=152); lenalidomide in combination with melphalan and prednisone, followed by placebo (MPR) (n=153); and placebo, melphalan and prednisone, followed by placebo (MP) (n=154).

In patients ≤75 years old, continuous lenalidomide therapy with MPR-R resulted in a median PFS of 31 months, while patients in the MP arm had a median PFS of 12 months (p<0.001). Patients in this age group treated with MPR-R had a 70% reduction in risk of disease progression compared with MP (HR 0.30). Additionally, a trend for extended overall survival was observed with MPR-R compared with MP (4-year 69% vs. 58%, p=0.133).

MPR induction alone provided a significant PFS benefit of 15 months compared with 12 months for MP (p=0.006). MPR induction also resulted in superior response rates vs. MP (73% vs. 47%) and ≥VGPR rates of 35% vs. 11%, respectively. Median time to response was 2 months for MPR vs. 3 months for MP.

The preplanned landmark analysis calculated PFS from maintenance entry for MPR-R and MPR and demonstrated that lenalidomide maintenance reduced the risk of progression by 65% for all patients irrespective of age (HR 0.34).

Induction with MPR in patients ≤75 years old had an acceptable safety profile, allowing the majority of patients to reach maintenance therapy with lenalidomide. During the induction phase, discontinuation resulted due to adverse events in 12% of MPR and 4% of MP patients. The most common grade 4 hematological adverse events during induction for MPR and MP included neutropenia (31% and 7%), thrombocytopenia (7% and 4%), and anemia (2% and 2%). The most frequent grade 3 or 4 non-hematological adverse events were infections (8% and 6%) and bone pain (3% and 4%).

Maintenance therapy with lenalidomide was well tolerated, with no evidence of cumulative toxicities. The most frequent grade 4 hematological adverse events during maintenance for MPR-R and MPR were thrombocytopenia (4% and 3%), anemia (3% and 1%), and neutropenia (1% and 0%). The most frequent grade 3 or 4 non-hematological adverse events included infections (5% and 3%), bone pain (5% and 1%) and fatigue (3% and 1%).

The study reported hematological and solid tumor second primary malignancies (SPMs) during induction and maintenance that were below the expected corresponding incidence rates in this disease setting including 12/150 in the MPR-R arm (3%), 10/152 in the MPR arm (2.6%) and 4/153 in the MP arm (1%).

These data are from an investigational study. REVLIMID is not approved as an initial treatment for patients with multiple myeloma.
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. Marketing Authorization Applications are currently being evaluated in a number of other countries.

Since 1998, Celgene continues to be a pioneer in creating environments in which patients can benefit from our disease-altering therapies safely. As a result, hundreds of thousands of patients worldwide have accessed the clinical benefits of our therapies through our performance-based risk management programs including, S.T.E.P.S.®, RevAssist® and RevMate®, which form the foundation of our commitment to patient safety.

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

REVLIMID is indicated for patients with transfusion-dependent anaemia due to Low- or Intermediate-1-risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

Important Safety Information

WARNING: FETAL RISK, HEMATOLOGIC TOXICITY, and DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

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 death to a developing baby. In women of childbearing potential, obtain 2 negative pregnancy tests before starting REVLIMID treatment. Women of childbearing potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment. To avoid fetal exposure to lenalidomide, REVLIMID is only available in the United States under a restricted distribution program called “RevAssist®.”

Information about the RevAssist program is available at www.REVLIMID.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. (see DOSAGE and ADMINISTRATION)

DEEP VEIN THROMBOSIS AND PULMONARY EMBOLISM

REVLIMID has demonstrated a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients with MM who were treated with REVLIMID 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 REVLIMID may lessen the potential for venous thromboembolic events. The decision to take prophylactic measures should be done carefully after an assessment of an individual patient’s underlying risk factors.

CONTRAINDICATIONS:

Pregnancy Category X:
Lenalidomide is contraindicated in pregnant women and women capable of becoming pregnant. Females of childbearing potential may be treated with lenalidomide provided adequate precautions are taken to avoid pregnancy.

**Allergic Reactions:**

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

**WARNINGS AND PRECAUTIONS:**

**Fetal Risk:**

- REVLIMID is an analogue of thalidomide, a known human teratogen that causes life-threatening human birth defects. An embryofetal development study in non-human primates 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. If REVLIMID is used during pregnancy, it may cause birth defects or death to a developing baby.
- Females of childbearing potential must be advised to avoid pregnancy while on REVLIMID. Two effective contraceptive methods should be used during therapy, during therapy interruptions, and for at least 4 weeks after completing therapy.
- Male Patients: It is not known whether lenalidomide is present in the semen of patients receiving the drug. Therefore, males receiving REVLIMID must always use a latex condom during any sexual contact with females of childbearing potential, even if they have undergone a successful vasectomy.

**Reproductive Risk and Special Prescribing Requirements (RevAssist Program):**

- Because of this potential toxicity and to avoid fetal exposure, REVLIMID is only available under a special restricted distribution program called "RevAssist." Prescribers and pharmacists registered with the program can prescribe and dispense the product to patients who are registered and meet all the conditions of the RevAssist program.

**Hematologic Toxicity—Multiple Myeloma:**

- REVLIMID can cause significant neutropenia and thrombocytopenia.
- Patients taking REVLIMID 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 studies Grade 3 and 4 hematologic toxicities were more frequent in patients treated with the combination of REVLIMID and dexamethasone than in patients treated with dexamethasone alone.
- Patients may require dose interruption and/or dose reduction.

**Deep Vein Thrombosis:**

- 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 treated with lenalidomide monotherapy.

**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.

**Tumour Lysis Syndrome:**

- Fatal instances of tumour lysis syndrome have been reported during treatment with lenalidomide. The patients at risk of tumour lysis syndrome are those with high tumour burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

**Tumour Flare Reaction:**

- Tumour flare reaction has occurred during investigational use of lenalidomide for chronic lymphocytic leukaemia (CLL).
and lymphoma, and is characterized by tender lymph node swelling, low grade fever, pain and rash. Treatment of CLL or lymphoma with lenalidomide outside of a well-monitored clinical trial is discouraged.

**DRUG INTERACTIONS:**
- Erythropoietic agents, or other agents, that may increase the risk of thrombosis, such as oestrogen containing therapies, should be used with caution in MM patients receiving lenalidomide with dexamethasone.

**USE IN SPECIAL POPULATIONS:**

**Nursing Mothers:**
- It is not known whether REVLIMID is excreted in human milk.
- 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.

**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 REVLIMID is primarily excreted unchanged by the kidney, adjustments to the starting dose of REVLIMID are recommended to provide appropriate drug exposure in patients with moderate or severe renal impairment (CLcr < 60 mL/min) and in patients on dialysis.

**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 with 199 patients (57%) in the placebo/dexamethasone treatment group.
- Of these patients who had one dose interruption with or without a dose reduction, 50% in the REVLIMID/dexamethasone treatment group underwent at least one additional dose interruption with or without a dose reduction compared with 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 with placebo/dexamethasone.
- 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%), anaemia (31% vs. 24%), pyrexia (28% vs. 23%), peripheral oedema (26% vs. 21%), nausea (26% vs. 21%), back pain (26% vs. 19%), upper respiratory tract infection (25% vs. 16%), dyspnoea (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.
- 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 oedema (20%), cough (20%), dizziness (20%), headache (20%), muscle cramp (18%), dyspnoea (17%), pharyngitis (16%), epistaxis (15%), asthenia (15%), upper respiratory tract infection (15%).

**DOSAGE AND ADMINISTRATION:**
- Treatment is continued or modified based upon clinical and laboratory findings. Dosing modifications are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicity judged to be related to REVLIMID.
- For other Grade 3 or 4 toxicities judged to be related to REVLIMID, hold treatment and restart at next lower dose level when toxicity has resolved to ≤Grade 2.

Please see full Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, WARNINGS AND
PRECAUTIONS, and ADVERSE REACTIONS.

About Celgene International Sàrl

Celgene International Sàrl, located in Boudry, in the Canton of Neuchâtel, Switzerland, is a wholly owned subsidiary and international headquarters of Celgene Corporation. 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 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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