Updated Results of Phase III Study Evaluating Continuous REVLIMID® Therapy in Newly Diagnosed Multiple Myeloma

BOUDRY, Switzerland, Jun 12, 2010 (BUSINESS WIRE) -- Celgene International Sàrl (NASDAQ: CELG) announced that data from the planned second interim analysis (median follow-up of 21 months) of a phase III, randomized, double-blind study of continuous REVLIMID (lenalidomide) for the treatment of elderly patients with newly diagnosed multiple myeloma show improvement in progression-free survival (PFS), the primary endpoint of the study. The data were presented during the European Haematology Association's annual congress in Barcelona, Spain.

The study of 459 patients 65 years or older evaluated patients receiving lenalidomide in combination with melphalan and prednisone, followed by lenalidomide alone (MPR-R) (n=152); patients receiving lenalidomide in combination with melphalan and prednisone, followed by placebo (MPR) (n=153); and patients receiving placebo, melphalan and prednisone, followed by placebo (MP) (n=154).

Median PFS of the MPR-R arm has yet to be reached, while the MP arm had a median PFS of 13 months (p<0.001). Patients treated with MPR-R had a 58% reduction in the risk of disease progression compared to MP, an improvement over the reduction in risk of disease progression reported at the first interim analysis in December 2009. At the time of the second analysis, it was estimated that 55% of all patients receiving MPR-R would remain progression free after two years compared to only 16% of patients receiving MP.

In the safety population (the patients who received at least one dose of therapy on study), the most common grade 3 or 4 hematological adverse events included neutropenia (71%, MPR-R vs. 30%, MP), thrombocytopenia (39%, MPR-R vs. 14%, MP) and febrile neutropenia (7%, vs. 0%, MP). Grade 3 or 4 non-hematological adverse events included fatigue (6%, MPR-R vs. 3%, MP), deep-vein thrombosis/pulmonary embolism (4%, MPR-R vs. 1%, MP), and rash (5%, MPR-R vs. 1%, MP). No grade 3 or 4 peripheral neuropathy was experienced by patients in this study.

These data are from an investigational study. REVLIMID is not approved as an initial treatment for patients with multiple myeloma.

About REVLIMID®

REVLIMID is an IMiD® compound. REVLIMID and other IMiDs continue to be evaluated in over 100 clinical trials. The IMiDs pipeline is covered by a comprehensive intellectual property estate of issued and pending patent applications in the US, EU and other regions, including composition-of- matter and use patents.

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 50 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 and several Latin American countries, as well as Malaysia and Israel, for transfusion-dependent anemia 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.

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

REVLIMID (lenalidomide) is indicated for 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.
About Multiple Myeloma

Multiple myeloma (also known as myeloma or plasma cell myeloma) is a cancer of the blood in which malignant plasma cells are overproduced in the bone marrow. Plasma cells are white blood cells that help produce antibodies called immunoglobulins that fight infection and disease. However, most patients with multiple myeloma have cells that produce a form of immunoglobulin called paraprotein (or M protein) that does not benefit the body. In addition, the malignant plasma cells replace normal plasma cells and other white blood cells important to the immune system. Multiple myeloma cells can also attach to other tissues of the body, such as bone, and produce tumors. The cause of the disease remains unknown.

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.

This release contains certain forward-looking statements which involve known and unknown risks, delays, uncertainties and other factors not under the Company's control. The Company's actual results, performance, or achievements could be materially different from those projected by these forward-looking statements. The factors that could cause actual results, performance, or achievements to differ from the forward-looking statements are discussed in the Company's filings with the Securities and Exchange Commission, such as the Company's Form 10-K, 10-Q and 8-K reports. Given these risks and uncertainties, you are cautioned not to place undue reliance on the forward-looking statements.

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

REVLIMID® (lenalidomide) is indicated for 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.

Important Safety Information

WARNINGS:

1. POTENTIAL FOR HUMAN BIRTH DEFECTS.

Lenalidomide is an analogue of thalidomide. Thalidomide is a known human teratogen that causes severe life-threatening human birth defects. If lenalidomide is taken during pregnancy, it may cause birth defects or death to an unborn baby. Females should be advised to avoid pregnancy while taking REVLIMID® (lenalidomide).

Male Patients: It is not known whether lenalidomide is present in the semen of patients receiving the drug. Therefore, males receiving REVLIMID® (lenalidomide) must always use a latex condom during any sexual contact with females of childbearing potential even if they have undergone a successful vasectomy.

Special Prescribing Requirements

Because of this potential toxicity and to avoid fetal exposure to REVLIMID® (lenalidomide), REVLIMID® (lenalidomide) is only available under a special restricted distribution program. In the U.S., this program is called "RevAssist®". Under this program, only prescribers and pharmacists registered with the program can prescribe and dispense the product. In addition, REVLIMID® (lenalidomide) must only be dispensed to patients who are registered and meet all the conditions of the RevAssist® program.

2. HEMATOLOGIC TOXICITY (NEUTROPENIA AND THROMBOCYTOPENIA).

This drug is associated with significant neutropenia and thrombocytopenia. Eighty percent of patients with del 5q myelodysplastic syndromes 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 myelodysplastic syndromes 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)

3. DEEP VENOUS THROMBOSIS AND PULMONARY EMBOLISM.

This drug has demonstrated a significantly increased risk of deep venous thrombosis (DVT) and pulmonary
embolism (PE) in patients with multiple myeloma who were treated with REVLIMID® (lenalidomide) combination
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® (lenalidomide) 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.

You can get the information about REVLIMID® (lenalidomide) and the RevAssist® program on the Internet at
www.REVLIMID.com or by calling the manufacturer’s toll-free number at 1-888-423-5436.

ADDITIONAL WARNINGS: HEMATOLOGIC TOXICITY

Multiple Myeloma

- In the pooled multiple myeloma studies, Grade 3 and 4 hematologic toxicities were more frequent in patients
treated with the combination of REVLIMID® (lenalidomide) and dexamethasone than in patients treated with
dexamethasone alone.
- Patients on therapy should have their complete blood counts monitored every 2 weeks for the first 12
weeks and then monthly thereafter.
- Patients may require dose interruption and/or dose reduction.

CONTRAINDICATIONS:

Pregnancy Category X:

- Lenalidomide is contraindicated in pregnant women and women capable of becoming pregnant. When there is no
alternative, females of childbearing potential may be treated with lenalidomide provided adequate precautions are taken
to avoid pregnancy.

Hypersensitivity:

- REVLIMID® (lenalidomide) is contraindicated in any patients who have demonstrated hypersensitivity to the drug or its
components.

PRECAUTIONS:

Angioedema, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis

- 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® (lenalidomide). REVLIMID® (lenalidomide) interruption or
discontinuation should be considered for Grade 2-3 skin rash. REVLIMID® (lenalidomide) 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.

Tumor Lysis Syndrome

- Lenalidomide has antineoplastic activity and therefore the complications of tumor lysis syndrome may occur. The
patients at risk of tumor lysis syndrome are those with high tumor burden prior to treatment. These patients should be
monitored closely and appropriate precautions taken.
Renal impairment:

- Since lenalidomide is primarily excreted unchanged by the kidney, adjustments to the starting dose of REVLIMID® (lenalidomide) are recommended to provide appropriate drug exposure in patients with moderate or severe (CL\textsubscript{cr} < 60 mL/min) renal impairment and in patients on dialysis.
- Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it would be prudent to monitor renal function.

Nursing mothers: It is not known whether REVLIMID® (lenalidomide) 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.

ADVERSE REACTIONS:

Multiple Myeloma

- In the REVLIMID® (lenalidomide)/dexamethasone treatment group, 151 patients (45%) underwent at least one dose interruption with or without a dose reduction of REVLIMID® (lenalidomide) compared to 21% in the placebo/dexamethasone treatment group.
- Of these patients who had one dose interruption with or without a dose reduction, 50% in the REVLIMID® (lenalidomide)/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® (lenalidomide)/dexamethasone compared to placebo/dexamethasone.

Other adverse events reported in multiple myeloma patients (REVLIMID® (lenalidomide)/dexamethasone vs dexamethasone/placebo): constipation (39% vs 19%), fatigue (38% vs 37%), insomnia (32% vs 37%), muscle cramp (30% vs 21%), diarrhea (29% vs 25%), neutropenia (28% vs 5%), anemia (24% vs 17%), asthenia (23% vs 25%), pyrexia (23% vs 19%), nausea (22% vs 19%), headache (21% vs 21%), peripheral edema (21% vs 19%), dizziness (21% vs 15%), dyspnea (20% vs 15%), tremor (20% vs 7%), decreased weight (18% vs 14%), thrombocytopenia (17% vs 10%), rash (16% vs 8%), back pain (15% vs 14%), hyperglycemia (15% vs 14%), and muscle weakness (15% vs 15%).

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 reactions reported in del 5q MDS patients (REVLIMID® (lenalidomide)): 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%), and pharyngitis (16%).

DOSAGE AND ADMINISTRATION:

- Dosing 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® (lenalidomide).
- For other Grade 3 or 4 toxicities judged to be related to REVLIMID® (lenalidomide), hold treatment and restart at next lower dose level when toxicity has resolved to less than or equal to Grade 2.

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

SOURCE: Celgene

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