REVLIMID® Approved for Treatment of Deletion 5q Myelodysplastic Syndromes in Japan

BOUDRY, Switzerland, Aug 20, 2010 (BUSINESS WIRE) --

Celgene International Sàrl (NASDAQ: CELG) announced that REVLIMID (lenalidomide) has been granted full marketing authorization by Japan's Ministry of Health, Labour and Welfare (MHLW) for the treatment of patients with myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenic abnormality. REVLIMID was also approved in June 2010 in combination with dexamethasone, for the treatment of patients with relapsed or refractory multiple myeloma who have received at least one prior standard therapy.

The approval of REVLIMID was based upon the safety and efficacy results of several international trials in patients with deletion 5q MDS, which have supported regulatory approval in 19 countries worldwide.

As a result of the approval, REVLIMID will be available through RevMate™, the company’s proprietary distribution program. Celgene is now registering physicians and medical centers throughout the country into RevMate as part of its strategic launch.

About REVLIMID

REVLIMID is an IMiDs® compound. REVLIMID and other IMiDs compounds continue to be evaluated in over 100 clinical trials. The IMiDs pipeline is covered by a comprehensive intellectual property estate of U.S. and foreign issued and pending patent applications 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 more than 50 countries, encompassing Europe, the Americas, the Middle-East and Asia, and in Australia and New Zealand it is approved in combination with dexamethasone for the treatment of patients whose disease has progressed after one therapy.

REVLIMID is also approved in the United States, Canada and several Latin American countries, as well as Malaysia and Israel, Australia and New Zealand for patients with 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.

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 ($CL_{cr} < 60$ 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...
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.

About Myelodysplastic Syndromes

Myelodysplastic syndromes (MDS) are a group of hematologic malignancies that affect approximately 300,000 people worldwide. Myelodysplastic syndromes occur when blood cells remain in an immature or "blast" stage within the bone marrow and never develop into mature cells capable of performing their necessary functions. Eventually, the bone marrow may be filled with blast cells suppressing normal cell development. MDS patients must often rely on blood transfusions to manage symptoms of anemia and fatigue and may develop life-threatening iron overload and/or toxicity from frequent transfusions, thus underscoring the critical need for new therapies targeting the cause of the condition rather than simply managing its symptoms.

About Deletion 5q Chromosomal Abnormality

Chromosomal (cytogenetic) abnormalities are detected in more than half of patients with myelodysplastic syndrome (MDS), and involve a deletion in all or part of one or more specific chromosomes. The most common cytogenetic abnormalities in MDS are deletions in the long arm of chromosomes 5, 7, and 20. Another common abnormality is an extra copy of chromosome 8. A deletion involving the 5q chromosome may be involved in 20 percent to 30 percent of all MDS patients. The World Health Organization has also recently identified a unique subset of MDS patients with a "5q- Syndrome" where the only chromosomal abnormality is a specific portion of the 5q chromosome.

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.

REVLIMID® is a registered trademark of Celgene Corporation.

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.

SOURCE: Celgene International Sàrl

Celgene International Sàrl
Kevin Loth, +41 32 729 86 21
Director of External Relations