Dosing Study Evaluates REVLIMID® in Previously Treated Patients with Chronic Lymphocytic Leukemia

Study Reported Overall Response Rate of 38%, and REVLIMID® (Lenalidomide) Was Well Tolerated

BOUDRY, Switzerland--(BUSINESS WIRE)--Dec. 11, 2011-- Celgene International Sàrl, a subsidiary of Celgene Corporation (NASDAQ: CELG), announced interim results of CLL-009, a study evaluating three starting doses of REVLIMID® (lenalidomide), followed by step-wise dose escalation as tolerated in patients with chronic lymphocytic leukemia (CLL) who have received at least one prior therapy. The findings were presented during the 53rd Annual Meeting of the American Society of Hematology in San Diego, CA.

In this ongoing study, patients are being enrolled and randomized to receive a blinded starting dose of 5 mg, 10 mg or 15 mg of lenalidomide daily for each 28-day cycle. The objectives of the study are to determine the safety and efficacy of different lenalidomide dose regimens in subjects with relapsed or refractory CLL. Dose escalation may take place every 28 days, in 5 mg/day increments, as tolerated. Tumor lysis syndrome (TLS) prophylaxis, comprising oral hydration and allopurinol 300 mg/day, was initiated at least three days prior to initiating lenalidomide and for a minimum of the first three treatment cycles.

At the time of the analysis, 60 out of 90 patients had been enrolled, and 29/46 (63% of eligible patients) had successful dose escalation above their starting dose levels.

Twenty-nine patients have been assessed for response, resulting in one (3%) complete response, 10 (35%) partial responses, 14 (48%) patients with stable disease, two (7%) patients with progressive disease and two (7%) patients who were not evaluable, resulting in an overall response rate (CR + PR) of 38%.

The most common grade 3/4 adverse events observed in the study were neutropenia (52%, 31/60), thrombocytopenia (25%, 15/60), fatigue (13%, 8/60) and tumor flare (10%, 6/60). Two patients experienced TLS with another experiencing laboratory TLS. Lenalidomide was discontinued in 29/60 (48%) patients, most commonly due to AE (n=11) and progressive disease (n=9). Six patients died, 2 due to disease progression, 2 due to pneumonia (not suspected treatment related), 1 due to pneumonia (suspected treatment related), and one due to an unknown cause (suspected treatment related).

These data are from an investigational study. REVLIMID is not approved for chronic lymphocytic leukemia.

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 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 to 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 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.
- 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 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%), and 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, PRECAUTIONS, and ADVERSE REACTIONS.

About Chronic Lymphocytic Leukaemia

CLL is the most common type of leukaemia in adults, accounting for approximately 30-40% of all forms of leukaemia in Western countries. Overall incidence of CLL is around four per 100,000 and is 50% more common in men than in women. CLL is currently considered incurable; therefore the aim of treatment is to control the disease and extending the time patients live without their disease worsening.

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.

Source: Celgene International Sàrl

Celgene International Sàrl

Investors:
+41 32 729 8303
ir@celgene.com
or
Media:
+41 32 729 8304
media@celgene.com