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Phase II Study Evaluates Clinical Benefit of REVLIMID® in Combination Therapy for Patients with Metastatic Castration-Resistant Prostate Cancer (MCRPC)

Study reports 86.4% of patients achieved 50% reduction of PSA or better

BOUDRY, Switzerland, Jun 05, 2011 (BUSINESS WIRE) --

Celgene International Sàrl (NASDAQ: CELG) today announced results from a phase II investigator initiated study of REVLIMID (lenalidomide) in combination with Avastin (bevacizumab), docetaxel and prednisone in patients with metastatic castration-resistant prostate cancer were presented at the 2011 American Society of Clinical Oncology Annual Meeting in Chicago, Ill.

In the study, patients with chemotherapy naïve, progressive mCRPC were treated with docetaxel (75 mg/m2) and bevacizumab (15 mg/kg) on day one, plus lenalidomide (25 mg) on days 1-14, with daily prednisone (10 mg) and enoxaparin during each 21-day cycle.

At the time of presentation, 46 of the planned 51 patients were enrolled. The overall PSA response rate was 86.4% (38/44). More than 70 percent (31/44) of the patients on the trial had a reduction in PSA of at least 75%. Of 24 patients with measurable disease, the overall RECIST response rate was 87.5%, with one complete response, 20 partial responses and 3 patients with stable disease.

Grade 3 or higher toxicities in the study included neutropenia (39% 18/46), anemia (13% 6/46), infection (13% 6/46) and thrombocytopenia (9% 4/46). One patient had hypertension and two had febrile neutropenia. Two patients had perianal fistula. Osteonecrosis of the jaw occurred in 30% (14/46). Of these patients, nine had concomitant and four had a history of bisphosphonate use.

These results are from an investigational study. REVLIMID is not approved as a treatment for prostate cancer.

The combination of REVLIMID and docetaxel/prednisone for the initial treatment of patients with metastatic castration resistant prostate cancer is currently being evaluated in a pivotal Phase III trial (MAINSAIL).

About REVLIMID®

REVLIMID® is an IMiDs® compound. REVLIMID and other IMiDs continue to be evaluated in over 300 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 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, Japan 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.

Important Safety Information

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® (lenalidomide) 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, in the United States, 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.

Haematologic 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 haematologic 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 greater-than or equal to 15% of MM patients (REVLIMID/dexamethasone vs. dexamethasone/placebo): fatigue (44% vs. 42%), neutropenia (42% vs. 6%), constipation (41% vs. 21%), diarrhoea (39% vs. 27%), muscle cramp (33% vs. 21%), anaemia (31% vs. 24%), pyrexia (28% vs. 23%), peripheral enema (26% vs. 21%), nausea (26% vs. 21%), back pain (26% vs. 19%), upper respiratory tract infection (25% vs. 16%), dyspnœa (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 greater-than or equal to 15% of del 5q MDS patients (REVLIMID): diarrhoea (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%), dyspnœa (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 less-than or equal to Grade 2.

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

About Celgene Risk-Management

Celgene continues to be a pioneer in creating environments in which patients who can benefit from our disease-altering therapies are able to do so, and do so safely. We are fully committed to drug lifecycle safety, from clinical development to post-marketing surveillance. As a result, patients worldwide continue to benefit from our risk-management programs such as, S.T.E.P.S®, RevAssist®, RevMate®, and PRMP, which form the global foundation of our commitment to patient safety.

About Prostate Cancer

Prostate cancer is a form of cancer that develops in the prostate, a gland in the male reproductive system. Most prostate cancers are slow growing; however, there are cases of aggressive prostate cancers. The cancer cells may metastasize...
(spread) from the prostate to other parts of the body, particularly the bones and lymph nodes. Prostate cancer may cause pain, difficulty in urinating, problems during sexual intercourse, or erectile dysfunction. Other symptoms can potentially develop during later stages of the disease.

Rates of detection of prostate cancers vary widely across the world, with South and East Asia detecting less frequently than in Europe, and especially the United States. Prostate cancer tends to develop in men over the age of fifty and although it is one of the most prevalent types of cancer in men, many never have symptoms, undergo no therapy, and eventually die of other causes. This is because cancer of the prostate is, in most cases, slow-growing, symptom-free, and since men with the condition are older they often die of causes unrelated to the prostate cancer, such as heart/circulatory disease, pneumonia, other unconnected cancers, or old age. About 2/3 of cases are slow growing, the other third more aggressive and fast developing.

**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](http://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.***

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