REVLIMID® and VIDAZA® Combination Therapy Achieves Nearly 30 Percent Complete Response in Untreated Elderly Patients with Acute Myeloid Leukemia

BOUDRY, Switzerland--(BUSINESS WIRE)--Dec. 10, 2012-- Celgene International Sàrl (NASDAQ: CELG) today announced that results from a study evaluating the combination of REVLIMID (lenalidomide) plus VIDAZA (azacitidine) in patients 60 years or older with untreated acute myeloid leukemia (AML) were presented at the American Society of Hematology annual meeting in Atlanta, GA.

In the phase II investigator-initiated study, patients received azacitidine 75 mg/m²/day, days 1-7 followed by lenalidomide 50 mg/day, days 8-28 of 42-day cycles. Treatment was continued until disease progression, unacceptable adverse event or completion of 12 cycles.

With 42 patients enrolled in the study, the overall response rate was 41%, with 28% of patients achieving a complete response (CR/CRi). The median time to CR and CRi was 12 and 6 weeks, respectively; the median duration of response (CR/CRi/PR) was 28 weeks (range 6 to >104 weeks). Median overall survival for all patients in the study was 20 weeks (range 1 to >121 weeks) and 69 weeks (range 10 to >121 weeks) for patients who responded to therapy. Additionally, median overall survival for responders was superior to non-responders (69 vs. 15 weeks p<0.01).

Most common adverse events were grade 1-2 and gastrointestinal in nature. There was one case each of grade 3 fever, sepsis, hyponatremia, pneumonitis and SIRS syndrome.

A three-arm phase II study in elderly AML patients is currently underway evaluating azacitidine monotherapy, azacitidine followed by lenalidomide (50 mg), and lenalidomide monotherapy.

These data are from an investigational study. REVLIMID® plus VIDAZA® is not approved for the treatment of acute myeloid 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.

U.S. Regulatory Information for Revlimid

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

REVLIMID® (lenalidomide) is indicated for the treatment of 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

**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](http://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:**

- REV may cause fetal harm when administered to a pregnant woman
- 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 must be used by female patients of childbearing potential for at least 4 weeks before beginning REVLIMID therapy, during therapy, during dose interruptions and for 4 weeks following discontinuation of REVLIMID therapy
- Male Patients: Clinical data has demonstrated the presence of lenalidomide in human semen. Male patients taking REVLIMID should not donate sperm. 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 and Pulmonary Embolism:

- 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
- REVLIMID capsules contain lactose. Risk-benefit of REVLIMID treatment should be evaluated in patients with lactose intolerance

Tumor Lysis Syndrome:

- Fatal instances of tumor lysis syndrome have been reported during treatment with lenalidomide. 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

Tumor Flare Reaction:

- Tumor flare reaction has occurred during investigational use of lenalidomide for chronic lymphocytic leukemia (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

Hepatotoxicity:

- Cases of transient liver laboratory abnormalities (predominantly transaminases) were reported in patients treated with lenalidomide. Treatment with lenalidomide should be interrupted and restarted once the levels return to baseline. Successful re-challenge without recurrence of liver laboratory elevation was reported in some patients

Second Primary Malignancies

- Patients with MM treated with lenalidomide in studies including melphalan and stem cell transplantation had a higher incidence of second primary malignancies, particularly acute myelogenous leukemia (AML) and Hodgkin lymphoma, compared to patients in the control arms who received similar therapy but did not receive lenalidomide. Monitor patients for the development of second malignancies. Take into account both the potential benefit of lenalidomide and the risk of second primary malignancies when considering treatment with lenalidomide

DRUG INTERACTIONS:

- Periodic monitoring of digoxin plasma levels, in accordance with clinical judgment and based on standard clinical practice
in patients receiving this medication, is recommended during administration of REVLIMID.

- It is not known whether there is an interaction between dexamethasone and warfarin. Close monitoring of PT and INR is recommended in MM patients taking concomitant warfarin.
- Erythropoietic agents, or other agents, that may increase the risk of thrombosis, such as estrogen containing therapies, should be used with caution in MM patients receiving lenalidomide with dexamethasone.

**USE IN SPECIFIC 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 (CLcr 30-60 mL/min) or severe renal impairment (CLcr < 30 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, 76% (269/353) vs 57% (199/350), 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.
- Grade 3/4 neutropenia occurred in 33.4% vs 3.4%; 2.3% experienced Grade 3/4 febrile neutropenia vs 0%.
- Deep vein thrombosis (DVT) was reported as a serious adverse drug reaction (7.4%) or Grade 3/4 (8.2%) compared to 3.1% and 3.4%. Discontinuations due to DVT were reported at comparable rates between groups.
- Pulmonary embolism (PE) was reported as a serious adverse drug reaction (3.7%) or Grade 3/4 (4.0%) compared to 0.9% and 0.9%. Discontinuations due to PE were reported at comparable rates between groups.
- 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 edema (26% vs 21%), nausea (26% vs 21%), back pain (26% vs 19%), upper respiratory tract infection (25% vs 16%), dyspnea (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.
- Grade 3 and 4 adverse events reported in ≥5% of patients with del 5q MDS were neutropenia (53%), thrombocytopenia (50%), pneumonia (7%), rash (7%), anemia (6%), leukopenia (5%), fatigue (5%), and back pain (5%).
- 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 edema (20%), cough (20%), dizziness (20%), headache (20%), muscle cramp (18%), dyspnea (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, WARNINGS AND PRECAUTIONS, and ADVERSE REACTIONS.

IMPORTANT SAFETY INFORMATION

About VIDAZA®

In December 2008, VIDAZA became the first and only drug approved by the European Commission to demonstrate a significant extension of overall survival compared to conventional care regimens, for patients with intermediate-2 and high-risk MDS and AML (20-30% blasts). Earlier in 2008, the U.S. FDA also included this extension of overall survival in its approved VIDAZA indication for treatment of all five French, American, British (FAB) MDS subtypes, which includes both low-risk and high-risk patients. These subtypes include: refractory anemia (RA), refractory anemia with ringed sideroblasts (RARS) if accompanied by neutropenia, or thrombocytopenia or requiring transfusions, refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMML). The more recent WHO classification system incorporates RAEB-T patients within the AML category. VIDAZA has received orphan drug designation in several markets including the European Union, the U.S. and Japan.

VIDAZA® (azacitidine for injection) is indicated for treatment of patients with the following French-American-British (FAB) myelodysplastic syndrome subtypes: refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) (if accompanied by neutropenia or thrombocytopenia or requiring transfusions), refractory anemia with excess blasts (RAEB), refractory anemia with excess blasts in transformation (RAEB-T), and chronic myelomonocytic leukemia (CMML).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS:

- VIDAZA is contraindicated in patients with a known hypersensitivity to azacitidine or mannitol and in patients with advanced malignant hepatic tumors

WARNINGS AND PRECAUTIONS:

Anemia, Neutropenia and Thrombocytopenia:

- Because treatment with VIDAZA is associated with anemia, neutropenia, and thrombocytopenia, complete blood counts should be performed as needed to monitor response and toxicity, but at a minimum, prior to each dosing cycle

Severe Pre-existing Hepatic Impairment:

- Because azacitidine is potentially hepatotoxic in patients with severe preexisting hepatic impairment, caution is needed in patients with liver disease.

Renal Abnormalities:

- In addition, azacitidine and its metabolites are substantially excreted by the kidneys and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function

Use in Pregnancy:

- VIDAZA may cause fetal harm when administered to a pregnant woman. Women of childbearing potential should be apprised of the potential hazard to the fetus. Men should be advised not to father a child while receiving VIDAZA

USE IN SPECIFIC POPULATIONS:

Nursing Mothers:
Nursing mothers should be advised to discontinue nursing or the drug, taking into consideration the importance of the drug to the mother.

ADVERSE REACTIONS:

- In Studies 1 and 2, the most commonly occurring adverse reactions by SC route were nausea (70.5%), anemia (69.5%), thrombocytopenia (65.5%), vomiting (54.1%), pyrexia (51.8%), leukopenia (48.2%), diarrhea (36.4%), injection site erythema (35.0%), constipation (33.6%), neutropenia (32.3%), and ecchymosis (30.5%). Other adverse reactions included dizziness (18.6%), chest pain (16.4%), febrile neutropenia (16.4%), myalgia (15.9%), injection site reaction (13.8%), and malaise (10.9%). In Study 3, the most common adverse reactions by IV route also included petechiae (45.8%), weakness (35.4%), rigors (35.4%), and hypokalemia (31.3%)
- In Study 4, the most commonly occurring adverse reactions were thrombocytopenia (69.7%), neutropenia (65.7%), anemia (51.4%), constipation (50.3%), nausea (48.0%), injection site erythema (42.9%), and pyrexia (30.3%). The most commonly occurring Grade 3/4 adverse reactions were neutropenia (61.1%), thrombocytopenia (58.3%), leukopenia (14.9%), anemia (13.7%), and febrile neutropenia (12.6%)

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

About Acute Myeloid Leukemia

Acute myeloid leukemia (AML) is a cancer of myeloid blood cells that often transforms from MDS upon disease progression. AML is the proliferation of abnormal cells that accumulate in the bone marrow and interfere with the production of all types of normal blood cells (multi-lineage dysplasia). AML has traditionally been treated with high intensity chemotherapy, which is poorly tolerated by the majority of the patients who are afflicted – the elderly. Many of these patients may go untreated, and because they are ineligible for curative therapy, life expectancy is short and often measured in weeks to months.

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 Corporation

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