Celgene Announces Presentations of Investigational Studies in Solid Tumor and Blood Cancers at ASCO 2015

Total of eight approved therapies and investigational agents being evaluated in 15 diseases

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced more than 55 presentations reporting on investigational studies in blood and solid tumor cancers will be presented during the 51st American Society of Clinical Oncology meeting in Chicago, Ill. from May 30 to June 2, 2015.

Investigational data include:

- #1032 Efficacy of 12 weeks neoadjuvant nab-paclitaxel combined with carboplatinum vs. gemcitabine in triple-negative breast cancer: WSG-ADAPT TN randomized phase II trial - Poster - 8 a.m., Saturday, May 30, S Hall A
- #8523 Updated analysis of CALGB/ECOG/BMT CTN 100104: Lenalidomide (Len) vs. placebo (PBO) maintenance therapy after single autologous stem cell transplant (ASCT) for multiple myeloma (MM).- Poster - 8 a.m., Sunday, May 31, S Hall A
- #8524 FIRST study: Updated overall survival (OS) in stem cell transplant (SCT)-ineligible newly diagnosed multiple myeloma (NDMM) patients (pts) treated with continuous lenalidomide plus low-dose dexamethasone (Rd) vs melphalan, prednisone, and thalidomide (MPT)- Poster- 8 a.m., Sunday, May 31, S Hall A
- #8525 Effect of carfilzomib, lenalidomide, and dexamethasone (KRd) vs lenalidomide and dexamethasone (Rd) in patients with relapsed multiple myeloma (RMM) by line of therapy: Secondary analysis from an interim analysis of the phase III study ASPIRE (NCT01080391) - Poster - 8 a.m., Sunday, May 31, S Hall A
- #8030 Safety and efficacy of MPDL 3280A (anti-PD-L1) in combination with platinum-based doublet chemotherapy in patients with advanced non-small cell lung cancer (NSCLC) - Poster - 8 a.m., Monday, June 1, S Hall A
- #4118 A phase 1b study of the anti-cancer stem cell agent demcizumab (DEM) & gemcitabine (GEM) +/- paclitaxel protein-bound particles (nab-paclitaxel) in patients with pancreatic cancer - Poster - 8 a.m., Monday, June 1 S Hall A
- #8504 Evaluation of complete response rate at 30 months (CR30) as a surrogate for progression-free survival (PFS) in first-line follicular lymphoma (FL) studies: Results from the prospectively specified Follicular Lymphoma Analysis of Surrogacy Hypothesis (FLASH) analysis with individual patient data (IPD) of 3,837 patients (pts) - Oral - 10:30 a.m., Monday, June 1, Room E450
- #8508 ELOQUENT-2: A phase III, randomized, open-label study of lenalidomide (Len)/dexamethasone (dex) with/without elotuzumab (Elo) in patients (pts) with relapsed/refractory multiple myeloma (RRMM)- Oral - 10:30 a.m., Tuesday, June 2, Room E345b
- #8510 Phase II MMRC trial of extended treatment with carfilzomib (CFZ), lenalidomide (LEN), and dexamethasone (DEX) plus autologous stem cell transplantation (ASCT) in newly diagnosed multiple myeloma (NDMM) - Oral - 10:30 a.m., Tuesday, June 2, Room E354b

Other presentations will report on data from investigational uses of Celgene approved therapies and pipeline candidates in solid tumor cancers (breast, head and neck, lung, melanoma and pancreas) and blood cancers (multiple myeloma, lymphomas, chronic lymphocytic leukemia, acute myeloid leukemia and myelodysplastic syndromes).

For a complete listing of abstracts, visit the ASCO Web site at http://abstracts.asco.org/

About ABRAXANE®

ABRAXANE® is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy should have included an anthracycline unless clinically contraindicated.
ABRAXANE is indicated for the first-line treatment of locally advanced or metastatic non-small cell lung cancer, in combination with carboplatin, in patients who are not candidates for curative surgery or radiation therapy.

ABRAXANE is indicated for the first-line treatment of patients with metastatic adenocarcinoma of the pancreas, in combination with gemcitabine.

Important Safety Information

WARNING - NEUTROPENIA

- Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1500 cells/mm³. In order to monitor the occurrence of bone marrow suppression, primarily neutropenia, which may be severe and result in infection, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving ABRAXANE.
- Note: An albumin form of paclitaxel may substantially affect a drug's functional properties relative to those of drug in solution. DO NOT SUBSTITUTE FOR OR WITH OTHER PACLITAXEL FORMULATIONS

CONTRAINDICATIONS

Neutrophil Counts

- ABRAXANE should not be used in patients who have baseline neutrophil counts of < 1500 cells/mm³

Hypersensitivity

- Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with the drug

WARNINGS AND PRECAUTIONS

Hematologic Effects

- Bone marrow suppression (primarily neutropenia) is dose-dependent and a dose-limiting toxicity of ABRAXANE. In clinical studies, Grade 3-4 neutropenia occurred in 34% of patients with metastatic breast cancer (MBC), 47% of patients with non-small cell lung cancer (NSCLC), and 38% of patients with pancreatic cancer.
- Monitor for myelotoxicity by performing complete blood cell counts frequently, including prior to dosing on Day 1 (for MBC) and Days 1, 8, and 15 (for NSCLC and for pancreatic cancer).
- Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1500 cells/mm³.
- In the case of severe neutropenia (< 500 cells/mm³ for 7 days or more) during a course of ABRAXANE therapy, reduce the dose of ABRAXANE in subsequent courses in patients with either MBC or NSCLC.
- In patients with MBC, resume treatment with every-3-week cycles of ABRAXANE after ANC recovers to a level > 1500 cells/mm³ and platelets recover to a level > 100,000 cells/mm³.
- In patients with NSCLC, resume treatment if recommended at permanently reduced doses for both weekly ABRAXANE and every-3-week carboplatin after ANC recovers to at least 1500 cells/mm³ and platelet count of at least 100,000 cells/mm³ on Day 1 or to an ANC of at least 500 cells/mm³ and platelet count of at least 50,000 cells/mm³ on Days 8 or 15 of the cycle.
- In patients with adenocarcinoma of the pancreas, withhold ABRAXANE and gemcitabine if the ANC is less than 500 cells/mm³ or platelets are less than 50,000 cells/mm³ and delay initiation of the next cycle if the ANC is less than 1500 cells/mm³ or platelet count is less than 100,000 cells/mm³ on Day 1 of the cycle. Resume treatment with appropriate dose reduction if recommended.

Nervous System

- Sensory neuropathy is dose- and schedule-dependent.
- The occurrence of Grade 1 or 2 sensory neuropathy does not generally require dose modification.
If ≥ Grade 3 sensory neuropathy develops, withhold ABRAXANE treatment until resolution to Grade 1 or 2 for MBC or until resolution to ≤ Grade 1 for NSCLC and pancreatic cancer followed by a dose reduction for all subsequent courses of ABRAXANE

**Sepsis**
- Sepsis occurred in 5% of patients with or without neutropenia who received ABRAXANE in combination with gemcitabine
- Biliary obstruction or presence of biliary stent were risk factors for severe or fatal sepsis
- If a patient becomes febrile (regardless of ANC), initiate treatment with broad-spectrum antibiotics
- For febrile neutropenia, interrupt ABRAXANE and gemcitabine until fever resolves and ANC ≥1500 cells/mm³, then resume treatment at reduced dose levels

**Pneumonitis**
- Pneumonitis, including some cases that were fatal, occurred in 4% of patients receiving ABRAXANE in combination with gemcitabine
- Monitor patients for signs and symptoms and interrupt ABRAXANE and gemcitabine during evaluation of suspected pneumonitis
- Permanently discontinue treatment with ABRAXANE and gemcitabine upon making a diagnosis of pneumonitis

**Hypersensitivity**
- Severe and sometimes fatal hypersensitivity reactions, including anaphylactic reactions, have been reported
- Patients who experience a severe hypersensitivity reaction to ABRAXANE should not be rechallenged with this drug

**Hepatic Impairment**
- Because the exposure and toxicity of paclitaxel can be increased with hepatic impairment, administration of ABRAXANE in patients with hepatic impairment should be performed with caution
- Patients with hepatic impairment may be at an increased risk of toxicity, particularly from myelosuppression, and should be monitored for development of profound myelosuppression
- For MBC and NSCLC, the starting dose should be reduced for patients with moderate or severe hepatic impairment
- For pancreatic adenocarcinoma, ABRAXANE is not recommended for patients with moderate to severe hepatic impairment (total bilirubin > 1.5 x ULN and AST ≤10 x ULN)

**Albumin (Human)**
- ABRAXANE contains albumin (human), a derivative of human blood

**Use in Pregnancy: Pregnancy Category D**
- ABRAXANE can cause fetal harm when administered to a pregnant woman
- If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus
- Women of childbearing potential should be advised to avoid becoming pregnant while receiving ABRAXANE

**Use in Men**
- Men should be advised not to father a child while receiving ABRAXANE

**ADVERSE REACTIONS**

**Randomized Metastatic Breast Cancer (MBC) Study**
- The most common adverse reactions (≥20%) with single-agent use of ABRAXANE vs paclitaxel injection in the MBC study
are alopecia (90%, 94%), neutropenia (all cases 80%, 82%; severe 9%, 22%), sensory neuropathy (any symptoms 71%, 56%; severe 10%, 2%), abnormal ECG (all patients 60%, 52%; patients with normal baseline 35%, 30%), fatigue/asthenia (any 47%, 39%; severe 8%, 3%), myalgia/arthritis (any 44%, 49%; severe 8%, 4%), AST elevation (any 39%, 32%), alkaline phosphatase elevation (any 36%, 31%), anemia (any 33%, 25%; severe 1%, < 1%), nausea (any 30%, 22%; severe 3%, < 1%), diarrhea (any 27%, 15%; severe < 1%, 1%) and infections (24%, 20%), respectively

- Sensory neuropathy was the cause of ABRAXANE discontinuation in 7/229 (3%) patients

- Other adverse reactions of note with the use of ABRAXANE vs paclitaxel injection included vomiting (any 18%, 10%; severe 4%, 1%), fluid retention (any 10%, 8%; severe 0%, < 1%), mucositis (any 7%, 6%; severe < 1%, 0%), hepatic dysfunction (elevations in bilirubin 7%, 7%), hypersensitivity reactions (any 4%, 12%; severe 0%, 2%), thrombocytopenia (any 2%, 3%; severe < 1%, < 1%), neutropenic sepsis (< 1%, < 1%), and injection site reactions (< 1%, 1%), respectively. Dehydration and pyrexia were also reported

- Renal dysfunction (any 11%, severe 1%) was reported in patients treated with ABRAXANE (n=229)

- In all ABRAXANE-treated patients (n=366), ocular/visual disturbances were reported (any 13%; severe 1%)

- Severe cardiovascular events possibly related to single-agent ABRAXANE occurred in approximately 3% of patients and included cardiac ischemia/infarction, chest pain, cardiac arrest, supraventricular tachycardia, edema, thrombosis, pulmonary thromboembolism, pulmonary emboli, and hypertension

- Cases of cerebrovascular attacks (strokes) and transient ischemic attacks have been reported

### Non-Small Cell Lung Cancer (NSCLC) Study

- The most common adverse reactions (≥20%) of ABRAXANE in combination with carboplatin are anemia, neutropenia, thrombocytopenia, alopecia, peripheral neuropathy, nausea, and fatigue

- The most common serious adverse reactions of ABRAXANE in combination with carboplatin for NSCLC are anemia (4%) and pneumonia (3%)

- The most common adverse reactions resulting in permanent discontinuation of ABRAXANE are neutropenia (3%), thrombocytopenia (3%), and peripheral neuropathy (1%)

- The most common adverse reactions resulting in dose reduction of ABRAXANE are neutropenia (24%), thrombocytopenia (13%), and anemia (6%)

- The most common adverse reactions leading to withholding or delay in ABRAXANE dosing are neutropenia (41%), thrombocytopenia (30%), and anemia (16%)

- The following common (≥10% incidence) adverse reactions were observed at a similar incidence in ABRAXANE plus carboplatin-treated and paclitaxel injection plus carboplatin-treated patients: alopecia (56%), nausea (27%), fatigue (25%), decreased appetite (17%), asthenia (16%), constipation (16%), diarrhea (15%), vomiting (12%), dyspnea (12%), and rash (10%); incidence rates are for the ABRAXANE plus carboplatin treatment group

- Adverse reactions with a difference of ≥2%, Grade 3 or higher, with combination use of ABRAXANE and carboplatin vs combination use of paclitaxel injection and carboplatin in NSCLC are anemia (28%, 7%), neutropenia (47%, 58%), thrombocytopenia (18%, 9%), and peripheral neuropathy (3%, 12%), respectively

- Adverse reactions with a difference of ≥5%, Grades 1-4, with combination use of ABRAXANE and carboplatin vs combination use of paclitaxel injection and carboplatin in NSCLC are anemia (98%, 91%), thrombocytopenia (68%, 55%), peripheral neuropathy (48%, 64%), edema peripheral (10%, 4%), epistaxis (7%, 2%), arthralgia (13%, 25%), and myalgia (10%, 19%), respectively

- Neutropenia (all grades) was reported in 85% of patients who received ABRAXANE and carboplatin vs 83% of patients who received paclitaxel injection and carboplatin

### Pancreatic Adenocarcinoma Study

- Among the most common (≥20%) adverse reactions in the phase III study, those with a ≥5% higher incidence in the ABRAXANE/gemcitabine group compared with the gemcitabine group are neutropenia (73%, 58%), fatigue (59%, 46%), peripheral neuropathy (54%, 13%), nausea (54%, 48%), alopecia (50%, 5%), peripheral edema (46%, 30%), diarrhea (44%, 24%), pyrexia (41%, 28%), vomiting (36%, 28%), decreased appetite (36%, 26%), rash (30%, 11%), and dehydration (21%, 11%)

- Of these most common adverse reactions, those with a ≥2% higher incidence of Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared with the gemcitabine group, respectively, are neutropenia (38%, 27%), fatigue (18%, 9%), peripheral neuropathy (17%, 1%), nausea (6%, 3%), diarrhea (6%, 1%), pyrexia (3%, 1%), vomiting (6%, 4%), decreased appetite (5%, 2%), and dehydration (7%, 2%)
- Thrombocytopenia (all grades) was reported in 74% of patients in the ABRAXANE/gemcitabine group vs 70% of patients in the gemcitabine group.

- The most common serious adverse reactions of ABRAXANE (with a ≥1% higher incidence) are pyrexia (6%), dehydration (5%), pneumonia (4%), and vomiting (4%).

- The most common adverse reactions resulting in permanent discontinuation of ABRAXANE were peripheral neuropathy (8%), fatigue (4%), and thrombocytopenia (2%).

- The most common adverse reactions resulting in dose reduction of ABRAXANE are neutropenia (10%) and peripheral neuropathy (6%).

- The most common adverse reactions leading to withholding or delay in ABRAXANE dosing are neutropenia (16%), thrombocytopenia (12%), fatigue (8%), peripheral neuropathy (15%), anemia (5%), and diarrhea (5%).

- Other selected adverse reactions with a ≥5% higher incidence for all-grade toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are asthenia (19%, 13%), mucositis (10%, 4%), dysgeusia (16%, 8%), headache (14%, 9%), hypokalemia (12%, 7%), cough (17%, 7%), epistaxis (15%, 3%), urinary tract infection (11%, 5%), pain in extremity (11%, 6%), arthralgia (11%, 3%), myalgia (10%, 4%), and depression (12%, 6%).

- Other selected adverse reactions with a ≥2% higher incidence for Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group are thrombocytopenia (13%, 9%), asthenia (7%, 4%), and hypokalemia (4%, 1%).

### Postmarketing Experience With ABRAXANE and Other Paclitaxel Formulations

- Severe and sometimes fatal hypersensitivity reactions have been reported with ABRAXANE. The use of ABRAXANE in patients previously exhibiting hypersensitivity to paclitaxel injection or human albumin has not been studied.

- There have been reports of congestive heart failure, left ventricular dysfunction, and atrioventricular block with ABRAXANE, primarily among individuals with underlying cardiac history or prior exposure to cardiotoxic drugs.

- There have been reports of extravasation of ABRAXANE. Given the possibility of extravasation, it is advisable to monitor closely the ABRAXANE infusion site for possible infiltration during drug administration.

### DRUG INTERACTIONS

- Caution should be exercised when administering ABRAXANE concomitantly with medicines known to inhibit or induce either CYP2C8 or CYP3A4.

### USE IN SPECIFIC POPULATIONS

#### Nursing Mothers

- It is not known whether paclitaxel is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

#### Pediatric

- The safety and effectiveness of ABRAXANE in pediatric patients have not been evaluated.

#### Geriatric

- No toxicities occurred notably more frequently among patients ≥65 years of age who received ABRAXANE for MBC.

- Myelosuppression, peripheral neuropathy, and arthralgia were more frequent in patients ≥65 years of age treated with ABRAXANE and carboplatin in NSCLC.

- Diarrhea, decreased appetite, dehydration, and epistaxis were more frequent in patients 65 years or older compared with patients younger than 65 years old who received ABRAXANE and gemcitabine in adenocarcinoma of the pancreas.

#### Renal Impairment

- There are insufficient data to permit dosage recommendations in patients with severe renal impairment or end stage renal disease (estimated creatinine clearance < 30 mL/min).
DOSE AND ADMINISTRATION

- Do not administer ABRAXANE to any patient with total bilirubin greater than 5 x ULN or AST greater than 10 x ULN
- For MBC and NSCLC, reduce starting dose in patients with moderate to severe hepatic impairment
- For adenocarcinoma of the pancreas, do not administer ABRAXANE to patients who have moderate to severe hepatic impairment
- Dose reductions or discontinuation may be needed based on severe hematologic, neurologic, cutaneous, or gastrointestinal toxicity
- Monitor patients closely

Please see full Prescribing Information, including Boxed WARNING.

About REVLIMID®

REVLIMID® (lenalidomide) in combination with dexamethasone (dex) is indicated for the treatment of patients with multiple myeloma (MM)

REVLIMID® 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

REVLIMID® is indicated for the treatment of patients with mantle cell lymphoma (MCL) whose disease has relapsed or progressed after two prior therapies, one of which included bortezomib

REVLIMID is not indicated and is not recommended for the treatment of patients with chronic lymphocytic leukemia (CLL) outside of controlled clinical trials

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY, HEMATOLOGIC TOXICITY, and VENOUS and ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

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 embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting REVLIMID treatment. Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after REVLIMID treatment. To avoid embryo-fetal exposure to lenalidomide, REVLIMID is only available through a restricted distribution program, the REVLIMID REMS® program (formerly known as the "RevAssist® program).

Information about the REVLIMID REMS® program is available at www.celgeneriskmanagement.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.

Venous and Arterial Thromboembolism

REVLIMID has demonstrated a significantly increased risk of deep vein thrombosis (DVT) and pulmonary embolism (PE), as well as risk of myocardial infarction and stroke in patients with MM who were treated with REVLIMID and...
dexamethasone therapy. Monitor for and advise patients about signs and symptoms of thromboembolism. Advise patients to seek immediate medical care if they develop symptoms such as shortness of breath, chest pain, or arm or leg swelling. Thromboprophylaxis is recommended and the choice of regimen should be based on an assessment of the patient's underlying risks.

CONTRAINDICATIONS

Pregnancy: REVLIMID can cause fetal harm when administered to a pregnant female and is contraindicated in females who are pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus

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

Embryo-Fetal Toxicity:

- REVLIMID is an analogue of thalidomide, a known human teratogen that causes life-threatening human birth defects or embryo-fetal death. An embryo-fetal development study in monkeys indicates that lenalidomide produced malformations in offspring of female monkeys who received drug during pregnancy, similar to birth defects observed in humans following exposure to thalidomide during pregnancy
- Females of Reproductive Potential: Must avoid pregnancy for at least 4 weeks before beginning REVLIMID therapy, during therapy, during dose interruptions and for at least 4 weeks after completing therapy. Must commit either to abstinence continuously from heterosexual sexual intercourse or to use two methods of reliable birth control beginning 4 weeks prior to initiating treatment with REVLIMID, during therapy, during dose interruptions and continuing for 4 weeks following discontinuation of REVLIMID. Must obtain 2 negative pregnancy tests prior to initiating therapy
- Males: Lenalidomide is present in the semen of patients receiving the drug. Males must always use a latex or synthetic condom during any sexual contact with females of reproductive potential while taking REVLIMID and for up to 28 days after discontinuing REVLIMID, even if they have undergone a successful vasectomy. Male patients taking REVLIMID must not donate sperm
- Blood Donation: Patients must not donate blood during treatment with REVLIMID and for 1 month following discontinuation of the drug because the blood might be given to a pregnant female patient whose fetus must not be exposed to REVLIMID

REVLIMID REMS® Program

Because of embryo-fetal risk, REVLIMID is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) the REVLIMID REMS® program (formerly known as the "RevAssist®" program). Prescribers and pharmacies must be certified with the program and patients must sign an agreement form and comply with the requirements.

Further information about the REVLIMID REMS® program is available at www.celgeneriskmanagement.com or by telephone at 1-888-423-5436

Hematologic Toxicity: REVLIMID can cause significant neutropenia and thrombocytopenia. Monitor patients with neutropenia for signs of infection. Advise patients to observe for bleeding or bruising, especially with use of concomitant medications that may increase risk of bleeding. MM: Patients taking REVLIMID/dex should have their complete blood counts (CBC) assessed every 7 days for the first 2 cycles, on days 1 and 15 of cycle 3, and every 28 days thereafter. MCL: Patients taking REVLIMID for MCL should have their CBCs monitored weekly for the first cycle (28 days), every 2 weeks during cycles 2-4, and then monthly thereafter. Patients may require dose interruption and/or dose reduction. For MDS: See Boxed WARNINGS

Venous and Arterial Thromboembolism: Venous thromboembolic events (DVT and PE) and arterial thromboses are increased in patients treated with REVLIMID. A significantly increased risk of DVT (7.4%) and PE (3.7%) occurred in patients with MM after at least one prior therapy, treated with REVLIMID/dex compared to placebo/dex (3.1% and 0.9%) in clinical trials with varying use of anticoagulant therapies. In NDM study, in which nearly all patients received antithrombotic prophylaxis, DVT (3.6%) and PE (3.8%) were reported in the Rd continuous arm. Myocardial infarction (MI, 1.7%) and stroke (CVA, 2.3%) are increased in patients with MM after at least 1 prior therapy who were treated with REVLIMID/dex therapy compared with placebo/dex (0.6%, and 0.9%) in clinical trials. In NDM study, MI (including acute) was reported (2.3%) in the Rd Continuous arm. Frequency of serious adverse reactions of CVA was (0.8%) in the Rd Continuous arm. Patients with known risk factors, including prior thrombosis, may be at greater risk and actions should be taken to try to minimize all modifiable factors (e.g. hyperlipidemia, hypertension, smoking). In controlled clinical trials that did not use concomitant thromboprophylaxis, 21.5% overall thrombotic events occurred in patients with refractory and relapsed MM who were treated with REVLIMID/dex compared
In newly diagnosed patients the most frequently reported Grade 3 or 4 adverse reactions in Arm Rd Continuous

Increased Mortality in Patients With CLL: In a clinical trial in the first line treatment of patients with CLL, single agent

Second Primary Malignancies: In clinical trials in patients with MM receiving REVLIMID, an increase of invasive second primary malignancies (SPM) notably AML and MDS have been observed. The increase of AML and MDS occurred predominantly in NDMM patients receiving REVLIMID in combination with oral melphalan (5.3%) or immediately following high dose intravenous melphalan and ASCT (up to 5.2%). The frequency of AML and MDS cases in the REVLIMID/dex arms was observed to be 0.4%. Cases of B-cell malignancies (including Hodgkin's Lymphomas) were observed in clinical trials where patients received REVLIMID in the post-ASCT setting. Patients who received REVLIMID-containing therapy until disease progression did not show a higher incidence of invasive SPM than patients treated in the fixed duration REVLIMID-containing arms. Monitor patients for the development of second primary malignancies. Take into account both the potential benefit of REVLIMID and risk of second primary malignancies when considering treatment

Hepatotoxicity: Hepatic failure, including fatal cases, has occurred in patients treated with REVLIMID in combination with dex. The mechanism of drug-induced hepatotoxicity is unknown. Pre-existing viral liver disease, elevated baseline liver enzymes, and concomitant medications may be risk factors. Monitor liver enzymes periodically. Stop REVLIMID upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered

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 (TLS) have been reported during treatment with lenalidomide. The patients at risk of TLS 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 (TFR) has occurred during investigational use of lenalidomide for CLL and lymphoma, and is characterized by tender lymph node swelling, low grade fever, pain and rash

Monitoring and evaluation for TFR is recommended in patients with MCL. Tumor flare may mimic the progression of disease (PD). In patients with Grade 3 or 4 TFR, it is recommended to withhold treatment with lenalidomide until TFR resolves to Grade 1. In the MCL trial, approximately 10% of subjects experienced TFR; all reports were Grade 1 or 2 in severity. All of the events occurred in cycle 1 and one patient developed TFR again in cycle 11. Lenalidomide may be continued in patients with Grade 1 and 2 TFR without interruption or modification, at the physician's discretion. Patients with Grade 1 or 2 TFR may also be treated with corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs) and/or narcotic analgesics for management of TFR symptoms. Patients with Grade 3 or 4 TFR may be treated for management of symptoms per the guidance for treatment of Grade 1 and 2 TFR

Impaired Stem Cell Mobilization: A decrease in the number of CD34+ cells collected after treatment (> 4 cycles) with

ADVERSE REACTIONS

Multiple Myeloma

- In newly diagnosed patients the most frequently reported Grade 3 or 4 adverse reactions in Arm Rd Continuous included neutropenia (27.8%), anemia (18.2%), thrombocytopenia (8.3%), pneumonia (11.3%), asthenia (7.7%), fatigue (7.3%), back pain (7%), hypokalemia (6.6%), rash (7.3%), cataract (5.8%), dyspnea (5.6%), DVT (5.6%), hyperglycemia (5.3%), lymphopenia and leukopenia. The frequency of infections in Arm Rd Continuous was 75%
Adverse reactions reported in ≥20% of NDMM patients in Arm Rd Continuous: diarrhea (45.5%), anemia (43.8%), neutropenia (35%), fatigue (32.5%), back pain (32%), insomnia (27.6%), asthenia (28.2%), rash (26.1%), decreased appetite (23.1%), cough (22.7%), pyrexia (21.4%), muscle spasms (20.5%), and abdominal pain (20.5%). The frequency of onset of cataracts increased over time with 0.7% during the first 6 months and up to 9.6% by the second year of treatment with Arm Rd Continuous.

**After at least one prior therapy** most adverse reactions and Grade 3 or 4 adverse reactions were more frequent in MM patients who received the combination of REVLIMID/dex compared to placebo/dex. Grade 3 or 4 adverse reactions included neutropenia 33.4% vs 3.4%, febrile neutropenia 2.3% vs 0%, DVT 8.2% vs 3.4% and PE 4% vs 0.9% respectively.

Adverse reactions reported in ≥15% of MM patients (REVLIMID/dex vs dex/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**

- 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%), dyspnea (5%), and back pain (5%)
- Adverse events reported in ≥15% of del 5q MDS patients (REVLIMID): thrombocytopenia (61.5%), neutropenia (58.8%), 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%), upper respiratory tract infection (15%)

**Mantle Cell Lymphoma**

- Grade 3 and 4 adverse events reported in ≥5% of patients treated with REVLIMID in the MCL trial (N=134) included neutropenia (43%), thrombocytopenia (28%), anemia (11%), pneumonia (9%), leukopenia (7%), fatigue (7%), diarrhea (6%), dyspnea (6%), and febrile neutropenia (6%)
- Serious adverse events reported in ≥2 patients treated with REVLIMID monotherapy for MCL included chronic obstructive pulmonary disease, clostridium difficile colitis, sepsis, basal cell carcinoma, and supraventricular tachycardia
- Adverse events reported in ≥15% of patients treated with REVLIMID in the MCL trial included neutropenia (49%), thrombocytopenia (36%), fatigue (34%), anemia (31%), diarrhea (31%), nausea (30%), cough (28%), pyrexia (23%), rash (22%), dyspnea (18%), pruritus (17%), peripheral edema (16%), constipation (16%), and leukopenia (15%)

**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 dex 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 after making a benefit-risk assessment in patients receiving REVLIMID.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy:** If pregnancy does occur during treatment, immediately discontinue the drug. Under these conditions, refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. Any suspected fetal exposure to REVLIMID must be reported to the FDA via the MedWatch program at 1-800-332-1088 and also to Celgene Corporation at 1-888-423-5436

**Nursing Mothers:** It is not known whether REVLIMID is excreted in human milk. Because many drugs are excreted in human milk and 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.

**Pediatric Use:** Safety and effectiveness in patients below the age of 18 have not been established.
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.

Please see [accompanying or enclosed, etc] full Prescribing Information, including Boxed WARNINGS.

About Celgene

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 www.celgene.com. Follow Celgene on Social Media: @Celgene, Pinterest, LinkedIn and YouTube.

Forward-Looking Statements

This press release may contain 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 other reports filed with the Securities and Exchange Commission.

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