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Broad Range of Clinical Data Evaluating Celgene Therapies to Be Presented at American Society of Clinical Oncology (ASCO)

Presentations will include multiple solid tumor and blood cancers while highlighting the value of innovative research

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ: CELG) today announced that data from a broad range of company-sponsored and investigator-initiated studies evaluating Celgene investigational agents and investigational uses of marketed products will be presented at the American Society of Clinical Oncology Annual Meeting between June 2-6 in Chicago, Ill.

"We are part of an extremely exciting time in cancer research, where accelerating deep insights into the biology of disease and tumor microenvironment are leading to approaches that have the potential to make a major impact on patients' lives," said Michael Pehl, President, Hematology and Oncology for Celgene. "The studies being shared at ASCO this year reinforce our commitment to developing and delivering innovative treatment options to patients with cancer around the world."

In multiple myeloma, abstracts will continue to support the role of Celgene's IMiD[®] therapies as the foundation of multiple myeloma research, including in the maintenance setting. Additionally, data will be presented from the study evaluating the investigational R² regimen (REVLIMID[®] (lenalidomide) and rituximab combination), in previously-treated follicular lymphoma. Updated data from two studies in the ABOUND program evaluating ABRAXANE[®] (nab-paclitaxel) in non-small cell lung cancer will also be presented. Finally, results from multiple studies highlighting key Celgene research collaborations of investigational compounds will be presented, including updated data from a phase I dose escalation and expansion study of IDHIFA[®] (enasidenib) in patients with mutant-IDH2 relapsed/refractory acute myeloid leukemia, updated data from the first clinical study of anti-BCMA CAR-T therapy bb2121 in multiple myeloma, and results from a study of CAR-T therapy JCAR017 in previously-treated aggressive b-cell non-Hodgkin's lymphoma.

Selected abstracts include*:

Newly-diagnosed Multiple Myeloma

Abstract #8000; Oral; Sunday, June 4, 9:45 a.m., E354b, Daratumumab (DARA) in combination with carfilzomib, lenalidomide, and dexamethasone (KRd) in patients (pts) with newly diagnosed multiple myeloma (MMY1001): An open-label, phase Ib study (Jakubowiak)

Abstract #8001; Oral; Sunday, June 4, 9:57 a.m., E354b, Lenalidomide, adriamycin and dexamethasone versus bortezomib, lenalidomide and dexamethasone prior to scheduled stem cell transplant in newly diagnosed multiple myeloma (Knop)

Abstract #8002; Oral; Sunday, June 4, 10:09 a.m., E354b, An open-label, single arm, phase IIa study of bortezomib, lenalidomide, dexamethasone, and elotuzumab in newly diagnosed multiple myeloma (Laubach)

Abstract #8009; Poster Discussion; Monday, June 5, 3:00 p.m., E354b, Lenalidomide induction and maintenance therapy for myeloma: Results of the Myeloma XI Study (Jackson)

Abstract #8023; Poster; Monday, June 5, 8:00 a.m., Hall A, Impact of t(11;14) on outcomes in African American (AA) and non-AA (NAA) patients (Pts) with newly diagnosed multiple myeloma (NDMM): Connect[®] MM Registry (Gasparetto)

Relapsed/Refractory Multiple Myeloma

Abstract #8007; Oral; Sunday, June 4, 11:57 a.m., E354b, A phase Ib study of isatuximab in combination with pomalidomide (Pom) and dexamethasone (Dex) in relapsed/refractory multiple myeloma (RRMM) (Mikhael)

Abstract #8008; Oral; Sunday, June 4, 12:09 p.m., E354b, Phase I/II dose expansion of a trial investigating bendamustine and pomalidomide with dexamethasone (Ben-Pom-d) in patients with relapsed/refractory multiple myeloma (Sivaraj)

Abstract #8015; Poster Discussion; Monday, June 5, 3:00 p.m., E354b, Pembrolizumab (Pembro) plus lenalidomide (Len) and low-dose dexamethasone (Dex) for relapsed/refractory multiple myeloma (RRMM): Efficacy and biomarker analyses (Ocio)

Abstract #3010; Poster Discussion; Monday, June 5, 4:45 p.m., Hall D1, First-in-human multicenter study of bb2121 anti-BCMA CAR T-cell therapy for relapsed/refractory multiple myeloma: Updated results (Berdeja)

Abstract #8027; Poster; Monday, June 5, 8:00 a.m., Hall A, Phase II study of pomalidomide (POM) + low-dose dexamethasone (LoDEX) following second-line lenalidomide (LEN)-based treatment (Tx) in patients (Pts) with relapsed or refractory multiple myeloma (RRMM): An updated analysis of efficacy and safety (Siegel)

Maintenance in Multiple Myeloma

Abstract #8037; Poster; Monday, June 5, 8:00 a.m., Hall A, CALGB/ECOG 100104 (Alliance) study: Lenalidomide (LEN) vs placebo (PBO) maintenance (Maint) after stem cell transplant (SCT) for patients (Pts) with multiple myeloma: Overall survival (OS) and progression-free survival (PFS) adjusted for treatment (Tx) crossover (XO) (McCarthy)

Abstract #8040; Poster; Monday, June 5, 8:00 a.m., Hall A, Impact of post-autologous stem cell transplant (ASCT) maintenance therapy on outcomes in patients (Pts) with newly diagnosed multiple myeloma (NDMM) using the large prospective community-based Connect[®] MM Registry (Jagannath)

Acute Myeloid Leukemia

Abstract #7004; Oral; Tuesday, June 6, 10:57 a.m., E450ab, Enasidenib in mutant-IDH2 relapsed or refractory acute myeloid leukemia (R/R AML): Results of a phase I dose-escalation and expansion study (Stein)

Abstract #7015; Poster Discussion; Monday, June 5, 11:30 a.m., E354b, Differentiation syndrome associated with enasidenib, a selective inhibitor of mutant isocitrate dehydrogenase 2 (IDH2) (Fathi)

Abstract #7022; Poster; Monday, June 5, 8:00 a.m., Hall A, Molecular genetic testing patterns for patients with newly diagnosed acute myeloid leukemia (AML) enrolled in the CONNECT[®] MDS/AML Disease Registry (Pollyea)

Lymphoma/CLL

Abstract #7502; Oral; Saturday, June 3, 3:24 p.m., S100bc, Phase IIIb randomized study of lenalidomide plus rituximab (R2) followed by maintenance in relapsed/refractory NHL: Analysis of patients with double-refractory or early relapsed follicular lymphoma (FL) (Andorsky)

Abstract #7503; Oral; Saturday, June 3, 4:00 p.m., S100bc, A genetic risk-stratified, phase II study of fludarabine/antibody combinations in symptomatic, untreated chronic lymphocytic leukemia (CLL): Final results of Cancer and Leukemia Group B (CALGB) 10404 (Ruppert)

Abstract #7513; Poster Discussion; Monday, June 5, 1:15 p.m., E354b, CR rates in relapsed/refractory (R/R) aggressive B-NHL treated with the CD19-directed CAR T-cell product JCAR017 (TRANSCEND NHL 001) (Abramson)

Non-Small Cell Lung Cancer

Abstract #9058; Poster; Saturday, June 3, 8:00 a.m., Hall A, Safety and efficacy of nab-paclitaxel (nab-P)-based therapy in patients (pts) with non-small cell lung cancer (NSCLC) and performance status (PS) 2: Results from ABOUND.PS2 (Gajra)

Abstract #9059; Poster; Saturday, June 3, 8:00 a.m., Hall A, ABOUND.70+: Safety and efficacy of nab-paclitaxel/carboplatin (nab-P/C) in elderly patients (pts) with advanced non-small cell lung cancer (NSCLC) (Langer)

Abstract #9092; Poster; Saturday, June 3, 8:00 a.m., Hall A, Atezolizumab (atezo) plus platinum-based chemotherapy (chemo) in non-small cell lung cancer (NSCLC): Update from a phase Ib study (Liu)

Abstract #9095; Poster; Saturday, June 3, 8:00 a.m., Hall A, Nivolumab (nivo) + nab-paclitaxel (nab-P) + carboplatin (C) in patients (pts) with non-small cell lung cancer (NSCLC): Interim results from a multicenter phase I study (Waterhouse)

Biliary Tract Cancer

Abstract #9095; Poster; Saturday, June 3, 8:00 a.m., Hall A, A phase II trial of gemcitabine (G), cisplatin (C), and nab-paclitaxel (N) in advanced biliary tract cancers (aBTCs) (Shroff)

The safety and efficacy of the agents and/or uses under investigation have not been established. There is no guarantee that the agents will receive health authority approval or become commercially available in any country for the uses being investigated.

A complete listing of abstracts can be found on the ASCO website at <http://am.asco.org/program>

*All times Central Time

About ABRAXANE®

ABRAXANE® for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) 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 \geq Grade 3 sensory neuropathy develops, withhold ABRAXANE treatment until resolution to Grade 1 or 2 for MBC or until resolution to \leq 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/arthralgia (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 $\geq 2\%$, 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 $\geq 5\%$, 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 ($\geq 20\%$) adverse reactions in the phase III study, those with a $\geq 5\%$ 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 $\geq 2\%$ 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 $\geq 1\%$ 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 $\geq 5\%$ 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 $\geq 2\%$ 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

- A higher incidence of epistaxis, diarrhea, dehydration, fatigue, and peripheral edema was found in patients 65 years or older who received ABRAXANE for MBC in a pooled analysis of clinical studies
- 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)

DOSAGE 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 as maintenance therapy in patients with MM following autologous hematopoietic stem cell transplantation (auto-HSCT)

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).

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 risk 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: See Boxed WARNINGS

- 1 Females of Reproductive Potential: **See Boxed WARNINGS**
- 1 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 4 weeks after discontinuing REVLIMID, even if they have undergone a successful vasectomy. Male patients taking REVLIMID must not donate sperm
- 1 Blood Donation: Patients must not donate blood during treatment with REVLIMID and for 4 weeks 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: See Boxed WARNINGS: Prescribers and pharmacies must be certified with the REVLIMID REMS program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive REVLIMID. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements

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 or REVLIMID maintenance therapy 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. **MDS:** 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 dose reduction. Please see the **Black Box WARNINGS** for further information. **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

Venous and Arterial Thromboembolism: See Boxed WARNINGS: Venous thromboembolic events (DVT and PE) and arterial thromboses (MI and CVA) are increased in patients treated with REVLIMID. 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). Thromboprophylaxis is recommended and the regimen should be based on patient's underlying risks. ESAs and estrogens may further increase the risk of thrombosis and their use should be based on a benefit-risk decision

Increased Mortality in Patients with CLL: In a clinical trial in the first-line treatment of patients with CLL, single agent REVLIMID therapy increased the risk of death as compared to single agent chlorambucil. Serious adverse cardiovascular reactions, including atrial fibrillation, myocardial infarction, and cardiac failure, occurred more frequently in the REVLIMID arm. REVLIMID is not indicated and not recommended for use in CLL outside of controlled clinical trials

Second Primary Malignancies (SPM): In clinical trials in patients with MM receiving REVLIMID, an increase of hematologic plus solid tumor SPM, notably AML and MDS, have been observed. Monitor patients for the development of SPM. Take into account both the potential benefit of REVLIMID and risk of SPM when considering treatment

Hepatotoxicity: Hepatic failure, including fatal cases, has occurred in patients treated with REVLIMID/dex. 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 treatment should be evaluated in patients with lactose intolerance

Tumor Lysis Syndrome (TLS): Fatal instances of 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 (TFR): TFR has occurred during investigational use of lenalidomide for CLL and lymphoma. 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 REVLIMID until TFR resolves to \leq Grade 1. REVLIMID may be continued in patients with Grade 1 and 2 TFR without interruption or modification, at the physician's discretion

Impaired Stem Cell Mobilization: A decrease in the number of CD34+ cells collected after treatment (> 4 cycles) with REVLIMID has been reported. Consider early referral to transplant center to optimize timing of the stem cell collection

Thyroid Disorders: Both hypothyroidism and hyperthyroidism have been reported. Measure thyroid function before start of REVLIMID treatment and during therapy

ADVERSE REACTIONS

Multiple Myeloma

- 1 **In newly diagnosed:** The most frequently reported Grade 3 or 4 reactions included neutropenia, anemia, thrombocytopenia, pneumonia, asthenia, fatigue, back pain, hypokalemia, rash, cataract, lymphopenia, dyspnea, DVT, hyperglycemia, and leukopenia. The highest frequency of infections occurred in Arm Rd Continuous (75%) compared to Arm MPT (56%). There were more Grade 3 and 4 and serious adverse reactions of infection in Arm Rd Continuous than either Arm MPT or Rd18

- | The most common adverse reactions reported in $\geq 20\%$ (Arm Rd Continuous): diarrhea (46%), anemia (44%), neutropenia (35%), fatigue (33%), back pain (32%), asthenia (28%), insomnia (28%), rash (26%), decreased appetite (23%), cough (23%), dyspnea (22%), pyrexia (21%), abdominal pain (21%), muscle spasms (20%), and thrombocytopenia (20%)
- | **Maintenance Therapy Post Auto-HSCT:** The most frequently reported Grade 3 or 4 reactions in $\geq 20\%$ (REVLIMID arm) included neutropenia, thrombocytopenia, and leukopenia. The serious adverse reactions of lung infection and neutropenia (more than 4.5%) occurred in the REVLIMID arm
- | The most frequently reported adverse reactions in $\geq 20\%$ (REVLIMID arm) across both maintenance studies (Study 1, Study 2) were neutropenia (79%, 61%), thrombocytopenia (72%, 24%), leukopenia (23%, 32%), anemia (21%, 9%), upper respiratory tract infection (27%, 11%), bronchitis (5%, 47%), nasopharyngitis (2%, 35%), cough (10%, 27%), gastroenteritis (0%, 23%), diarrhea (55%, 39%), rash (32%, 8%), fatigue (23%, 11%), asthenia (0%, 30%), muscle spasm (0%, 33%), and pyrexia (8%, 21%)
- | **After at least one prior therapy:** The most common adverse reactions reported in $\geq 20\%$ (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%), and weight decreased (20% vs 15%)

Myelodysplastic Syndromes

- | Grade 3 and 4 adverse events reported in $\geq 5\%$ 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 $\geq 15\%$ 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 $\geq 5\%$ 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%)
- | Adverse events reported in $\geq 15\%$ 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 is recommended due to increased C_{max} and AUC with concomitant REVLIMID therapy. Patients taking concomitant therapies such as erythropoietin stimulating agents or estrogen containing therapies may have an increased risk of thrombosis. It is not known whether there is an interaction between dex and warfarin. Close monitoring of PT and INR is recommended in patients with MM taking concomitant warfarin

USE IN SPECIFIC POPULATIONS:

- | **PREGNANCY: See Boxed WARNINGS:** If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a REVLIMID pregnancy exposure registry that monitors pregnancy outcomes in females exposed to REVLIMID during pregnancy as well as female partners of male patients who are exposed to REVLIMID. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to REVLIMID to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436
- | **LACTATION:** There is no information regarding the presence of lenalidomide in human milk, the effects of REVLIMID on the breastfed infant, or the effects of REVLIMID on milk production. Because many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants from REVLIMID, advise female patients not to breastfeed during treatment with REVLIMID

- | **PEDIATRIC USE:** Safety and effectiveness have not been established in pediatric patients
- | **RENAL IMPAIRMENT:** Adjust the starting dose of REVLIMID based on the creatinine clearance value and for patients on dialysis

Please see full [Prescribing Information](#), including **Boxed WARNINGS**.

About POMALYST®

POMALYST® (pomalidomide) is a thalidomide analogue indicated, in combination with dexamethasone, for patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on or within 60 days of completion of the last therapy.

Important Safety Information

WARNING: EMBRYO-FETAL TOXICITY and VENOUS AND ARTERIAL THROMBOEMBOLISM

Embryo-Fetal Toxicity

- | **POMALYST is contraindicated in pregnancy. POMALYST is a thalidomide analogue. Thalidomide is a known human teratogen that causes severe birth defects or embryo-fetal death. In females of reproductive potential, obtain 2 negative pregnancy tests before starting POMALYST treatment.**
- | **Females of reproductive potential must use 2 forms of contraception or continuously abstain from heterosexual sex during and for 4 weeks after stopping POMALYST treatment.**

POMALYST is only available through a restricted distribution program called **POMALYST REMS®**.

Venous and Arterial Thromboembolism

- | **Deep venous thrombosis (DVT), pulmonary embolism (PE), myocardial infarction, and stroke occur in patients with multiple myeloma treated with POMALYST. Prophylactic antithrombotic measures were employed in clinical trials. Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.**

CONTRAINDICATIONS

- | **Pregnancy:** POMALYST can cause fetal harm and is contraindicated in females who are pregnant. If POMALYST is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential risk to a fetus.

WARNINGS AND PRECAUTIONS

- | **Embryo-Fetal Toxicity & Females of Reproductive Potential: See Boxed WARNINGS**
 - | **Males:** Pomalidomide 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 POMALYST and for up to 4 weeks after discontinuing POMALYST, even if they have undergone a successful vasectomy. Males must not donate sperm.
 - | **Blood Donation:** Patients must not donate blood during treatment with POMALYST and for 1 month following discontinuation of POMALYST therapy because the blood might be given to a pregnant female patient whose fetus must not be exposed to POMALYST.
- | **POMALYST REMS® Program: See Boxed WARNINGS**
 - | Prescribers and pharmacies must be certified with the **POMALYST REMS** program by enrolling and complying with the REMS requirements; pharmacies must only dispense to patients who are authorized to receive POMALYST. Patients must sign a Patient-Physician Agreement Form and comply with REMS requirements; female patients of reproductive potential who are not pregnant must comply with the pregnancy testing and contraception requirements and males must comply with contraception requirements.
 - | Further information about the **POMALYST REMS** program is available at www.CelgeneRiskManagement.com or by telephone at 1-888-423-5436.

- | **Venous and Arterial Thromboembolism: See Boxed WARNINGS.** 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). Thromboprophylaxis is recommended, and the choice of regimen should be based on assessment of the patient's underlying risk factors.
- | **Hematologic Toxicity:** Neutropenia (46%) was the most frequently reported Grade 3/4 adverse reaction in patients taking POMALYST in clinical trials, followed by anemia and thrombocytopenia. Monitor complete blood counts weekly for the first 8 weeks and monthly thereafter. Patients may require dose interruption and/or modification.
- | **Hepatotoxicity:** Hepatic failure, including fatal cases, has occurred in patients treated with POMALYST. Elevated levels of alanine aminotransferase and bilirubin have also been observed in patients treated with POMALYST. Monitor liver function tests monthly. Stop POMALYST upon elevation of liver enzymes. After return to baseline values, treatment at a lower dose may be considered.
- | **Hypersensitivity Reactions:** Angioedema and severe dermatologic reactions have been reported. Discontinue POMALYST for angioedema, skin exfoliation, bullae, or any other severe dermatologic reactions, and do not resume therapy.
- | **Dizziness and Confusional State:** In patients taking POMALYST in clinical trials, 14% experienced dizziness (1% Grade 3 or 4) and 7% a confusional state (3% Grade 3 or 4). Instruct patients to avoid situations where dizziness or confusional state may be a problem and not to take other medications that may cause dizziness or confusional state without adequate medical advice.
- | **Neuropathy:** In patients taking POMALYST in clinical trials, 18% experienced neuropathy (2% Grade 3 in one trial) and 12% peripheral neuropathy.
- | **Second Primary Malignancies:** Cases of acute myelogenous leukemia have been reported in patients receiving POMALYST as an investigational therapy outside of multiple myeloma.
- | **Tumor Lysis Syndrome (TLS):** TLS may occur in patients treated with POMALYST. Patients at risk are those with high tumor burden prior to treatment. These patients should be monitored closely and appropriate precautions taken.

ADVERSE REACTIONS

Nearly all patients treated with POMALYST + low-dose dex experienced at least one adverse reaction (99%). The most common adverse reactions included neutropenia (51.3%), fatigue and asthenia (46.7%), upper respiratory tract infection (31%), thrombocytopenia (29.7%), pyrexia (26.7%), dyspnea (25.3%), diarrhea (22%), constipation (21.7%), back pain (19.7%), cough (20%), pneumonia (19.3%), bone pain (18%), edema peripheral (17.3%), peripheral neuropathy (17.3%), muscle spasms (15.3%), and nausea (15%). Grade 3 or 4 adverse reactions included neutropenia (48.3%), thrombocytopenia (22%), and pneumonia (15.7%).

DRUG INTERACTIONS

Avoid concomitant use of POMALYST with strong inhibitors of CYP1A2. Consider alternative treatments. If a strong CYP1A2 inhibitor must be used, reduce POMALYST dose by 50%.

USE IN SPECIFIC POPULATIONS

- | **Pregnancy: See Boxed WARNINGS.** If pregnancy does occur during treatment, immediately discontinue the drug and refer patient to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. There is a POMALYST pregnancy exposure registry that monitors pregnancy outcomes in females exposed to POMALYST during pregnancy as well as female partners of male patients who are exposed to POMALYST. This registry is also used to understand the root cause for the pregnancy. Report any suspected fetal exposure to POMALYST to the FDA via the MedWatch program at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436.
- | **Lactation:** There is no information regarding the presence of pomalidomide in human milk, the effects of POMALYST on the breastfed infant, or the effects of POMALYST on milk production. Pomalidomide was excreted in the milk of lactating rats. Because many drugs are excreted in human milk and because of the potential for adverse reactions in breastfed infants from POMALYST, advise a nursing woman to discontinue breastfeeding during treatment with POMALYST.
- | **Pediatric Use:** Safety and effectiveness have not been established in pediatric patients.
- | **Geriatric Use:** No dosage adjustment is required for POMALYST based on age. Patients > 65 years of age were more likely than patients ≤65 years of age to experience pneumonia.
- | **Renal Impairment:** Reduce POMALYST dose by 25% in patients with severe renal impairment requiring dialysis.

Take dose of POMALYST following hemodialysis on hemodialysis days.

- | **Hepatic Impairment:** Reduce POMALYST dose by 25% in patients with mild to moderate hepatic impairment and 50% in patients with severe hepatic impairment.
- | **Smoking Tobacco:** Advise patients that smoking may reduce the efficacy of POMALYST. Cigarette smoking reduces the AUC of pomalidomide by 32% by CYP1A2 induction.

Please see full [Prescribing Information](#), including **Boxed WARNINGS**.

About Celgene

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global biopharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through next-generation solutions in protein homeostasis, immuno-oncology, epigenetics, immunology and neuro-inflammation. For more information, please visit www.celgene.com. Follow Celgene on Social Media: [@Celgene](#), [Pinterest](#), [LinkedIn](#), [Facebook](#) and [YouTube](#).

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. Celgene undertakes 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 Celgene's Annual Report on Form 10-K and other reports filed with the Securities and Exchange Commission.

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