CELGENE TO HIGHLIGHT NEW AND UPDATED HEMATOLOGY AND ONCOLOGY CLINICAL DATA AT UPCOMING AMERICAN SOCIETY OF CLINICAL ONCOLOGY (ASCO) 2019 ANNUAL MEETING

Presentations include innovative cancer research, including novel CAR T technology, as well as key disease areas, including myelofibrosis and multiple myeloma

MAY 15, 2019 — SUMMIT, N.J. — Celgene Corporation (NASDAQ: CELG) today announced that data from more than 40 company-sponsored, global alliance and investigator-initiated clinical studies evaluating Celgene’s investigational and approved therapies will be presented at the American Society of Clinical Oncology (ASCO) 2019 Annual Meeting, May 31-June 4, in Chicago.

“We look forward to sharing important clinical data that underscore the progress we are making in advancing our mid-late-stage pipeline of investigational cancer therapies,” said Dr. Alise Reicin, President, Global Clinical Development for Celgene. “The studies highlighted this year reinforce the impact of our investigational and approved therapies, on patients with high unmet needs.”

Of note, Celgene will present new sub-group analyses from the multicenter, phase 1 TRANSCEND NHL 001 study evaluating the investigational therapy lisocabtagene maraleucel (liso-cel), a CD19-directed chimeric antigen receptor (CAR) T-cell product, in adult patients with relapsed/refractory non-Hodgkin’s lymphoma (NHL) who have secondary CNS lymphoma and new data from the multicenter, phase 1/2 TRANSCEND CLL 004 trial in adult patients with relapsed/refractory chronic lymphocytic leukemia. Abstracts will also highlight investigational therapies or new uses for approved therapies in the treatment of myelofibrosis, multiple myeloma (MM) and pancreatic cancer. These include an analysis of efficacy and safety using additional stringent criteria to define patients who are relapsed/refractory or intolerant to ruxolitinib in the multicenter, phase 2 JAKARTA2 clinical trial of fedratinib in previously-treated myelofibrosis patients; the first clinical data for the investigational CELMoD® compound iberdomide (CC-220) in combination with dexamethasone in patients with relapsed/refractory MM; and data from the apact study of ABRAXANE in combination with gemcitabine as adjuvant treatment for patients with surgically-resected pancreatic cancer.

REVLIMID in combination with rituximab, liso-cel, and fedratinib are not approved for any use in any country.

Selected abstracts include:

CAR T
Abstract #7501: TRANSCEND CLL 004: Minimal residual disease (MRD) negative responses after lisocabtagene maraleucel (liso-cel; JCAR017), a CD19-directed CAR T cell product, in patients (Pts) with relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL). (Oral presentation; Tuesday, June 4, 9:57 a.m. to 10:09 a.m., E451, lead author: Siddiqi)

Abstract #7515: Lisocabtagene maraleucel (liso-cel) treatment of patients (Pts) with
relapsed/refractory (R/R) B-cell non-Hodgkin lymphoma (NHL) and secondary CNS lymphoma: Initial results from TRANSCEND NHL 001. (Poster Discussion; Monday, June 3, 11:30 a.m. to 1 p.m., E450, lead author: Abramson)

Abstract #7516: Safety and preliminary efficacy in patients (pts) with relapsed/refractory (R/R) mantle cell lymphoma (MCL) receiving lisocabtagene maraleucel (liso-cel) in TRANSCEND NHL 001. (Poster Discussion; Monday, June 3, 11:30 a.m. to 1 p.m., E450, lead author: Wang)

Abstract #6637: Burden of cytokine release syndrome (CRS) and neurologic events (NE) in patients (pts) with relapsed/refractory non-Hodgkin lymphoma (NHL) receiving lisocabtagene maraleucel (liso-cel; JCAR017) in TRANSCEND NHL 001. (Poster Saturday, June 1, 1:15 p.m. to 4:15 p.m., Hall A, lead author: Abramson)

Abstract e19052: TRANSCEND NHL 001: Health-related quality of life (HRQL) and symptom (sx) impact in patients (pts) with relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL) receiving lisocabtagene maraleucel (liso-cel; JCAR017). (ePub only, lead author: Patrick)

**Lymphoma**

Abstract #7513: MAGNIFY: Phase IIIb interim analysis of induction R² followed by maintenance in relapsed/refractory indolent non-Hodgkin lymphoma (Poster Discussion; Monday, June 3, 11:30 a.m. to 1 p.m., E450, lead author: Andorsky)

Abstract #7514: Efficacy and time to next treatment following lenalidomide/rituximab (R²) or rituximab/placebo in patients with R/R indolent NHL (AUGMENT). (Poster Discussion; Monday, June 3, 11:30 a.m. to 1 p.m., E450, lead author: Gribben)

**Multiple Myeloma**

Abstract #8006: First clinical (phase 1b/2a) study of iberdomide (CC-220; IBER), a CELMoD, in combination with dexamethasone (DEX) in patients (pts) with relapsed/refractory multiple myeloma (RRMM). (Oral presentation; Sunday, June 2, 11:45 a.m. to 11:57 a.m., E451, lead author: Lonial)

**Myelofibrosis**

Abstract #7057: Fedratinib (FEDR) in myelofibrosis (MF) patients previously treated with ruxolitinib (RUX): A reanalysis of the JAKARTA-2 study. (Poster; Monday, June 3, 8 a.m. to 11 a.m., Hall A, lead author: Harrison)

**Pancreatic Cancer**

Abstract #4000: APACT: phase III, multicenter, international, open-label, randomized trial of adjuvant nab-paclitaxel plus gemcitabine (nab-P/G) vs gemcitabine (G) for surgically resected pancreatic adenocarcinoma. (Oral presentation; Sunday, June 2, 9:45 a.m. to 9:57 a.m., Arie Crown Theater, lead author: Tempero)

A complete listing of abstracts can be found on the ASCO abstracts website.

*All times Central Time*
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

Severe Hypersensitivity Reactions: REVLIMID is contraindicated in patients who have demonstrated severe hypersensitivity (e.g., angioedema, Stevens-Johnson syndrome, toxic epidermal necrolysis) to lenalidomide

WARNINGS AND PRECAUTIONS
Embryo-Fetal Toxicity: See Boxed WARNINGS
- Females of Reproductive Potential: See Boxed WARNINGS
- 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
- 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 as 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

Increased Mortality with Pembrolizumab: In clinical trials in patients with multiple myeloma, the addition of pembrolizumab to a thalidomide analogue plus dexamethasone resulted in increased mortality.
Treatment of patients with multiple myeloma with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.

**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.

**Severe Cutaneous Reactions Including Hypersensitivity Reactions:** Angioedema and severe cutaneous reactions including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported. DRESS may present with a cutaneous reaction (such as rash, or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. 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, TEN, or DRESS is suspected and should not be resumed following discontinuation for these reactions.

**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 ≤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.

**Early Mortality in Patients with MCL:** In another MCL study, there was an increase in early deaths (within 20 weeks), 12.9% in the REVLIMID arm versus 7.1% in the control arm. Risk factors for early deaths include high tumor burden, MIPI score at diagnosis, and high WBC at baseline (≥10 x 10^9/L).

**ADVERSE REACTIONS**

**Multiple Myeloma**

- **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 ≥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 ≥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 ≥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 ≥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 32%), peripheral edema (26% vs 22%), 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 ≥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%)
- 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 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 in patients on dialysis.

Please see full **Prescribing Information**, including Boxed WARNINGS.

About ABRAXANE

**Indications**

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
- Cross-hypersensitivity between ABRAXANE and other taxane products has been reported and may include severe reactions such as anaphylaxis. Patients with a previous history of hypersensitivity to other taxanes should be closely monitored during initiation of ABRAXANE therapy

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

Embryo Fetal Toxicity
• Based on mechanism of action and findings in animals, ABRAXANE can cause fetal harm when administered to a pregnant woman
• Advise females of reproductive potential of the potential risk to a fetus.
• Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with ABRAXANE and for at least six months after the last dose of ABRAXANE
• Advise male patients with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with ABRAXANE and for at least three months after the last dose of 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
• 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 $\geq 2\%$ 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. In postmarketing experience, cross-hypersensitivity between ABRAXANE and other taxanes has been reported

• 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**

**Pregnancy**

• Based on the mechanism of action and findings in animals, ABRAXANE can cause fetal harm when administered to a pregnant woman. Advise females of the potential risk to a fetus and to avoid becoming pregnant while receiving ABRAXANE

**Lactation**

• Paclitaxel and/or its metabolites were excreted into the milk of lactating rats. Nursing must be discontinued when receiving treatment with ABRAXANE and for two weeks after the last dose

**Females and Males of Reproductive Potential**

• Females of reproductive potential should have a pregnancy test prior to starting treatment with ABRAXANE

• Advise females of reproductive potential to use effective contraception and avoid becoming pregnant during treatment with ABRAXANE and for at least six months after the last dose of ABRAXANE [see Warnings and Precautions]

• Advise males with female partners of reproductive potential to use effective contraception and avoid fathering a child during treatment with ABRAXANE and for at least three months after the last dose of ABRAXANE [see Warnings and Precautions]

• Based on findings in animals, ABRAXANE may impair fertility in females and males of reproductive potential
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 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: Twitter, 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. 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 U.S. Securities and Exchange Commission, including factors related to the proposed transaction between Bristol-Myers Squibb and Celgene, such as, but not limited to, the risks that: management’s time and attention is diverted on transaction related issues; disruption from the transaction make it more difficult to maintain business, contractual and operational relationships; legal proceedings are instituted against Bristol-Myers Squibb, Celgene or the combined company could delay or prevent the proposed transaction; and Bristol-Myers Squibb, Celgene or the combined company is unable to retain key personnel.

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