July 10, 2018

Anti-PD-L1 Immunotherapy Plus ABRAXANE® Significantly Reduced the Risk of Disease Worsening or Death in Patients with Metastatic or Locally Advanced Triple Negative Breast Cancer in Phase III IMpassion130 Study

- First Phase III study to demonstrate a statistically significant progression-free survival improvement in first-line metastatic triple negative breast cancer (TNBC) -

- IMpassion130 is the third positive Phase III study to demonstrate a clinical benefit with the investigational combination TECENTRIQ® plus ABRAXANE®; studies in triple negative breast cancer and in non-small cell lung cancer -

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ:CELG) today announced that the Phase III IMpassion130 study, which was sponsored by Roche, met its co-primary endpoint of progression-free survival (PFS). This is the first phase III study to demonstrate a statistically significant PFS improvement in first-line metastatic or unresectable locally advanced triple negative breast cancer (TNBC), a type of breast cancer with high unmet need.

Results demonstrated that the investigational combination of TECENTRIQ® (atezolizumab) plus ABRAXANE® (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) compared to ABRAXANE® monotherapy, as an initial (first-line) treatment, significantly reduced the risk of disease worsening or death (PFS) in patients with metastatic or unresectable locally advanced TNBC in the intention-to-treat (ITT) and PD-L1 positive populations. Overall survival is encouraging in the PD-L1 positive population at this interim analysis, and follow up will continue until the next planned analysis. Safety in the TECENTRIQ® plus ABRAXANE® arm appeared consistent with the known safety profiles of the individual medicines, and no new safety signals were identified with the combination.

"The IMpassion130 results are extremely encouraging for patients with this highly aggressive form of breast cancer for which there are limited options," said Jay Backstrom, M.D., Chief Medical Officer for Celgene. "This is the third positive Phase III study to demonstrate a clinical benefit with TECENTRIQ® plus ABRAXANE® as part of a treatment regimen; the other studies evaluated this investigational combination in non-small cell lung cancer patients. These data demonstrate the potential role of ABRAXANE® as a preferred chemotherapy partner for immunotherapy combinations."

Results will be presented at an upcoming medical meeting.

ABRAXANE® is not approved in combination with TECENTRIQ® for any indication in any geography.

About the IMpassion130 Study

IMpassion130 is a Phase III multicenter, randomized, double-blind study evaluating the efficacy, safety, and pharmacokinetics of TECENTRIQ® and ABRAXANE® compared with placebo in combination with ABRAXANE® in people with locally advanced or metastatic TNBC who have not received prior systemic therapy for metastatic breast cancer. The study enrolled 902 people who were randomized equally (1:1). The co-primary endpoints were progression-free survival (PFS) per investigator assessment (RECIST 1.1) and overall survival (OS). PFS and OS were assessed in all randomized participants [intention-to-treat (ITT)] and in those whose disease expressed the PD-L1 protein. Secondary endpoints included objective response rate, duration of response and time to deterioration in Global Health Status/Health-Related Quality of Life.

During the treatment duration, people in:

- **Arm A** received TECENTRIQ® at a fixed dose of 840 milligrams via intravenous (IV) infusion on Days 1 and 15 of each 28-day cycle and ABRAXANE® at a dose of 100 milligrams per square meter via IV infusion on Days 1, 8, and 15 of each 28-day cycle. ABRAXANE® was administered for a target of at least 6 cycles, with no maximum. Participants received both agents until unacceptable toxicity or disease progression.

- **Arm B** received ABRAXANE® at a dose of 100 milligrams per square meter via IV infusion on Days 1, 8, and 15 of each 28-day cycle. ABRAXANE® was administered for a target of at least 6 cycles, with no maximum, and placebo was administered via IV infusion on Days 1 and 15 of each 28-day cycle. Participants received both agents until unacceptable toxicity or disease progression.

About Triple Negative Breast Cancer

Breast cancer is the second most common cancer among women in the United States. According to the American Cancer Society, it is estimated that about 266,000 American women will be diagnosed with invasive breast cancer in 2018, and nearly 41,000 will die from the disease. Approximately 10-20 percent of breast cancers are triple negative breast cancer (TNBC). TNBC is an aggressive form of the disease with a high unmet need. It can be more difficult to treat because it is not sensitive to hormone therapy or medicines that target HER2.

TECENTRIQ® is a registered trademark of Genentech, a member of the Roche Group.

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.

Important Safety Information for ABRAXANE®

WARNING - NEUTROPENIA

- **Do not administer ABRAXANE therapy to patients who have baseline neutrophil counts of less than 1500 cells/mm^3. 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/mm^3

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) and 47% of patients with non-small cell lung cancer (NSCLC)
- 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

- Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1500 cells/mm^3
- In the case of severe neutropenia (< 500 cells/mm^3 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/mm^3 and platelets recover to a level > 100,000 cells/mm^3
- 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/mm^3 and platelet count of at least 100,000 cells/mm^3 on Day 1 or to an ANC of at least 500 cells/mm^3 and platelet count of at least 50,000 cells/mm^3 on Days 8 or 15 of the cycle

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 followed by a dose reduction for all subsequent courses of ABRAXANE

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

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 ≥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

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

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
- Dose reductions or discontinuation may be needed based on severe hematologic or neurologic 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.

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Forward-Looking Statements

This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a number of factors, many of which are discussed in more detail in our Annual Report on Form 10-K and our other reports filed with the Securities and Exchange Commission.

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