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Long-Term Efficacy Data from the Phase III GeparSepto Study in High Risk Early Breast Cancer Patients Treated with ABRAXANE® Vs. Solvent-Based Paclitaxel to Be Reported

-- Phase III Secondary Endpoint Results Demonstrate A Significantly Higher Disease-free Survival Rate following ABRAXANE as Investigational Therapy in Neoadjuvant Breast Cancer --

NEU-ISENBURG, Germany & SUMMIT, N.J.--(BUSINESS WIRE)-- The German Breast Group (GBG) and Celgene Corporation (NASDAQ:CELG) today announced long-term invasive disease-free survival results from the GeparSepto clinical trial comparing the investigational use of ABRAXANE® (paclitaxel albumin-bound particles for injectable suspension) to paclitaxel in early high-risk breast cancer patients at the 2017 San Antonio Breast Cancer Symposium (SABCS). The results from the 1,206 patient study found that ABRAXANE demonstrated a significantly higher disease-free survival rate, a secondary efficacy endpoint, in high risk early breast cancer patients when compared to conventional solvent-based paclitaxel.

In this large Phase III study, of which disease-free survival was a secondary endpoint, the investigational use of ABRAXANE (N=600) was compared to conventional solvent-based paclitaxel (N=606) followed by epirubicin/cyclophosphamide in both arms given all before surgery. The study found a significantly higher disease-free survival (DFS) rate in patients receiving ABRAXANE compared to those receiving paclitaxel as part of a neoadjuvant treatment regimen [HR=0.69, 95% CI (0.54-0.89); p=0.0044]). The rates of DFS were 87.1% vs. 80.7% at 3 years and 83.5% vs. 76.2% at 4 years, respectively. A treatment effect was observed in the predefined subset of patients with triple negative tumors and hormone receptor-positive (HR+), human epidermal growth factor receptor 2 negative (HER2-) tumors. Patients with triple negative breast cancer (n=276) had DFS rates of 83.1% vs. 73.4% at 3 years, and 78.7% vs. 68.6% at 4 years. DFS was not significantly different in the TNBC subgroup [HR=0.66, 95% CI (0.42-1.04), p=0.0694]. HR+/HER2- patients had DFS rates of 86.3% vs. 78.6% at 3 years and 80.8% vs. 72.8% at 4 years [HR=0.71, 95% CI (0.49-1.02); p=0.0660]. Another secondary endpoint measure evaluated in the study was overall survival (OS). No difference in OS was observed, however the OS findings are not yet mature.

"These long-term findings show that weekly nab-paclitaxel followed by epirubicin/cyclophosphamide helped to significantly delay the progression of disease compared to solvent-based paclitaxel followed by epirubicin/cyclophosphamide in early high-risk breast cancer patients," stated Sibylle Loibl, Chair of GBG. "These findings are consistent with our previous findings and are very exciting, as they help us evaluate another potential treatment option for this high-risk patient group."

The primary endpoint of GeparSepto was pCR (pathological complete response) which has been reported previously and found a statistically significant and clinically meaningful 9% absolute improvement from 29% to 38% (p= < 0.001) when neoadjuvant (preoperative) chemotherapy was started with ABRAXANE instead of conventional solvent-based paclitaxel followed by epirubicin/cyclophosphamide given prior to surgery.

The most common adverse events (> 30%) that were previously reported included anemia, alopecia, peripheral sensory neuropathy neutropenia, leukopenia, fatigue, lymphopenia, increased alanine aminotransferase, increased aspartate aminotransferase, headache, nausea, mucositis/stomatitis/ esophagitis, diarrhea, infection, arthralgia, epistaxis, skin rash maculopapular, and myalgia.

Follow-up data regarding long-term neurotoxicity and quality of life will be collected during the study follow-up period. These results will be forthcoming in future analyses.

"These latest results are very encouraging, illustrating that an ABRAXANE-containing investigational regimen may have activity in high-risk breast cancer patients in the neoadjuvant setting," said Nadim Ahmed, President, Hematology and Oncology for Celgene. "The long-term outcomes from this study offer researchers additional insight into how to potentially treat patients more effectively at an earlier stage of the disease."

ABRAXANE is not approved for neoadjuvant treatment of breast cancer, or for the treatment regimens studied in GeparSepto in any country. See label excerpts below for more information.

About GeparSepto

GeparSepto is a phase III clinical trial evaluating the safety and efficacy of the investigational use of a weekly treatment regimen of nab-paclitaxel compared to a solvent-based paclitaxel, both followed by epirubicin/cyclophosphamide given all before surgery to treat high-risk early breast cancer.

The trial evaluated 1,206 patients with high risk early breast cancer. Patients received either nab-paclitaxel 150 mg/m^2 or paclitaxel 80 mg/m^2 weekly for 12 weeks followed by epirubicin 90 mg/m^2 and cyclophosphamide 600 mg/m^2 every 3 weeks for 12 weeks. HER2 positive patients also received trastuzumab 8 (6) mg/kg and pertuzumab 840 (420) mg every 3 weeks during neoadjuvant treatment. The nab-paclitaxel dose was reduced to 125 mg/m^2 after recruitment of 464 patients because of the evaluation of an interim safety analysis. The median age in each treatment arm was 49 (nab-paclitaxel) and 48 (paclitaxel) years. The primary endpoint of the trial was pathological complete response (pCR). Secondary endpoints evaluated in the study included invasive disease-free survival (DFS), distant disease-free survival (DDFS) and overall survival (OS).

Grade 3 and 4 neutropenia occurred in 23% and 38% of patients, respectively, in the nab-paclitaxel arm compared to 25% and 36% in the solvent-based paclitaxel arm. Peripheral sensory neuropathy was more common with nab-paclitaxel (8% for the 125 mg/m^2 dose and 15% for the 150 mg/m^2 dose) compared with solvent-based paclitaxel 80 mg/m^2. Taxane discontinuation due to an adverse event occurred in 16% of patients on nab-paclitaxel and 6% on solvent-based paclitaxel.

Overall, 23% of patients were noted to have at least one serious adverse event based on the study drug received (26% in the nab-paclitaxel group and 21% in the solvent-based paclitaxel group [p=0.057]). There were three deaths (during epirubicin plus cyclophosphamide treatment) in the nab-paclitaxel group due to sepsis, diarrhea, and an accident unrelated to the trial, compared to one death in the solvent-based paclitaxel group (during paclitaxel treatment) due to cardiac failure.

GeparSepto is the largest randomized Phase III study ever completed with ABRAXANE and the first one completed in high risk early breast cancer. Celgene provided funding support for the GeparSepto trial.

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.

Important Safety Information

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**

CONTRADINDICATIONS

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 a clinical study, Grade 3-4 neutropenia occurred in 34% of patients with metastatic breast cancer (MBC)
- Monitor for myelotoxicity by performing complete blood cell counts frequently, including prior to dosing on Day 1
- Do not administer ABRAXANE to patients with baseline absolute neutrophil counts (ANC) of less than 1,500 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 MBC
- Resume treatment with every-3-week cycles of ABRAXANE after ANC recovers to a level > 1500 cells/mm^3 and platelets recover to > 100,000 cells/mm^3

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 until resolution to Grade 1 or 2 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, 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

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 to 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

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
- Reduce starting dose in MBC 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 the German Breast Group

GBG is a large independent academic network of over 500 study centers in Germany with the world- wide largest experience in conducting neoadjuvant breast cancer trials. Since 1998, with joined forces from AGO-B, over 10.000 patients participated in the neoadjuvant "Gepardo" trial series. GBG has recruited at totality of over 35.000 patients to trials in breast cancer of all indications. Reports on these trials were previously published in the New England Journal of Medicine, The Lancet Oncology, the Journal of Clinical Oncology and the Journal of the National Cancer Institute (for more information go to www.germanbreastgroup.de). The GBG Research Institute received unrestricted grants and the provision of medication from Celgene and Roche for the conduct of the GeparSepto study. ABRAXANE is approved in the US and Europe for patients with metastatic breast cancer.

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. 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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