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Investigational Data Presented at ASCO GI Evaluate ABRAXANE® Regimen for Patients with Locally Advanced Pancreatic Cancer

Phase II LAPACT trial results reported on the safety and efficacy of ABRAXANE + gemcitabine induction therapy on tumor burden, disease control, and symptoms

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ: CELG) today announced primary endpoint findings and updated results of secondary endpoints from the phase II international LAPACT trial of ABRAXANE® (paclitaxel protein-bound particles for injectable suspension) (albumin-bound) plus gemcitabine in patients with locally advanced pancreatic cancer. The results were presented today at the 2018 American Society of Clinical Oncology Gastrointestinal Cancers Symposium (ASCO GI) in San Francisco, California.

An analysis of patients with newly diagnosed, locally advanced pancreatic cancer treated with up to 6 cycles of ABRAXANE + gemcitabine as an investigational induction therapy (n=106) found that patients had a median time to treatment failure (TTF) of 8.8 months (90% CI: 6.67-9.82), which exceeded the protocol-specified target of 6.6 months (primary endpoint). Secondary endpoints included evaluation of the disease control rate (DCR), overall response rate (ORR), progression free survival (PFS) and overall survival (OS) in patients treated with an ABRAXANE + gemcitabine induction therapy. The updated analysis found a 77.6% DCR ≥ 16 wks (DCR ≥ 16 wks: stable disease (SD) ≥ 16 wks = 44.9%, CR = 0%, PR = 32%) and 65.4% DCR ≥ 24 wks (DCR ≥ 24 wks: SD ≥ 24 wks = 32.7%, CR = 0%, PR = 32%). The ORR was 32% (CR=0%, PR=32%), the median PFS was 10.8 months (9.26-11.63; 90% CI) and 12-month estimated OS was 72% (64.5% - 78.9%; 90% CI). One or more treatment emergent adverse event occurred in 99% of patients during induction. The most common Grade ≥ 3 adverse events (AE) (≥10%) were neutropenia (42%), anemia (11%), and fatigue (10%).

"Pancreatic cancer remains an extremely challenging disease to treat because it is often diagnosed at the metastatic stage, and even those diagnosed with locally advanced disease typically have a poor prognosis," said Dr. Pascal Hammel, Gastroenterologist/Oncologist, Hôpital Beaujon, Clichy France. "Disease control is key in our patients with locally advanced disease, as it may lead to opportunities for additional treatment interventions, including radiotherapy, or even, in some favorable cases, surgical resection. The results from this study are encouraging, as it shows that induction therapy has the potential to help us achieve disease control in these locally advanced patients."

In this prospective, phase II trial conducted in the US, Canada and Europe, patients with protocol-defined locally advanced, unresectable pancreatic cancer received an induction regimen of up to 6 cycles of ABRAXANE + gemcitabine, followed by the investigator's choice (IC) of either (a) continuation of the ABRAXANE + gemcitabine regimen, (b) treatment with chemoradiation, or (c) surgery. More than half of patients (57.5%, n = 61/106) completed the induction phase with ABRAXANE + gemcitabine treatment. Forty two percent (45/106) of patients did not complete induction treatment and the reasons for treatment discontinuation during induction included adverse events (n = 20), progressive disease (n = 8), protocol non-compliance (n = 5), physician decision (n = 6), death (n = 2), and other reasons (n = 4). At the time of data cut-off, 45 patients in the intent to treat cohort received IC therapy after induction: 11% (12/106) of patients continued ABRAXANE + gemcitabine per the protocol; 16% (17/106) received chemoradiation; and 15% of patients (16/106) with unresectable disease at the start of the study underwent tumor resection surgery following ABRAXANE + gemcitabine induction therapy. The LAPACT presentation also reported patient-reported quality of life findings across twenty-nine different symptom measures using the EORTC QLQ-C30 questionnaires.

Other relevant grade ≥3 TEAEs included thrombocytopenia (7.5%), peripheral sensory neuropathy (3.8%), diarrhea (3.8%), and febrile neutropenia (3.8%). AEs of any grade included: neutropenia (58.5%), fatigue (50%), anemia (47.2%), diarrhea (46.2%), thrombocytopenia (41.5%), peripheral sensory neuropathy (23.6%), and febrile neutropenia (3.8%).

"Since its approval to treat metastatic pancreatic cancer in 2013, the ABRAXANE + gemcitabine regimen has become a standard of care in first-line metastatic pancreatic cancer," said Nadim Ahmed, President, Hematology and Oncology for Celgene. "The findings from LAPACT offer insight into the potential of ABRAXANE-based treatment for locally advanced pancreatic cancer patients and it's encouraging to see a nearly 9-month time to treatment failure in these patients treated with an ABRAXANE regimen."

ABRAXANE is not indicated for the first-line treatment of locally advanced pancreatic cancer.

ABOUT LAPACT

LAPACT is an international, non-randomized, open-label, multi-center, phase II clinical trial conducted at 42 centers in 5 countries. The study evaluated the safety and efficacy of the investigational use of ABRAXANE in combination with gemcitabine as a first-line treatment of patients with locally advanced pancreatic cancer who were not eligible for resection surgery at trial initiation.

The trial evaluated 106 patients with locally advanced pancreatic cancer who had not received prior treatment for their pancreatic cancer and were classified as unresectable at the start of the trial. Patients were given ABRAXANE 125 mg/m² followed by gemcitabine 1000 mg/m² on days 1, 8 and 15 of a 28-day cycle for up to six cycles. Patients completing six cycles of treatment were given subsequent investigator-determined treatment of either: continuation of the ABRAXANE + gemcitabine regimen; chemoradiation therapy with capecitabine or gemcitabine + radiation; or surgical intervention. The median age of the patients was 65 years.

Currently, there are more than 130 studies evaluating the use of ABRAXANE in patients with pancreatic cancer in combination with more than 50 novel agents.

ABOUT ABRAXANE

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 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 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 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 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 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

- 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

- | 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
- | Do not administer ABRAXANE to patients with metastatic adenocarcinoma of the pancreas 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: [@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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For Celgene:

Investors:

908-673-9628

investors@celgene.com

Media:

908-673-2275

media@celgene.com

Source: Celgene Corporation

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