

## **BeiGene Announces Acceptance of Supplemental Import Drug Application in China for ABRAXANE® in Metastatic Pancreatic Cancer**

CAMBRIDGE, Mass. and BEIJING, China; May 30, 2019 (GLOBE NEWSWIRE) -- BeiGene, Ltd. (NASDAQ: BGNE; HKEX: 06160), a commercial-stage biopharmaceutical company focused on developing and commercializing innovative molecularly-targeted and immuno-oncology drugs for the treatment of cancer, today announced that the China National Medical Products Administration (NMPA, formerly known as CFDA) has accepted the supplemental import drug application for ABRAXANE® (paclitaxel protein-bound particles for injectable suspension) (albumin-bound), in combination with gemcitabine, as a first-line treatment of patients with metastatic adenocarcinoma of the pancreas (mPC). ABRAXANE was first approved in China in 2008 for the treatment of patients with metastatic breast cancer. It is currently marketed in China by BeiGene under an exclusive license from Celgene Corporation.

“We’re delighted about the NMPA’s acceptance of the supplemental import drug submission of ABRAXANE as a treatment for Chinese patients with metastatic adenocarcinoma of the pancreas,” said Dr. Xiaobin Wu, General Manager of China and President of BeiGene. “ABRAXANE has been an important global treatment option for patients with metastatic adenocarcinoma of the pancreas outside of China, and we strive to provide access to ABRAXANE in China to those patients for whom there is great need for additional treatments to combat this deadly disease.”

### **About Pancreatic Cancer**

Pancreatic cancer is one of the deadliest cancers, with a nine percent five-year survival rate.<sup>i</sup> In 2018, there were an estimated 458,918 new cases globally, making it the 12<sup>th</sup> most common cancer in the world.<sup>ii</sup> Pancreatic cancer is difficult to detect in early stages, as the disease does not cause obvious symptoms. In addition, the pancreas is located deep in the abdomen, hindering the diagnosis of pancreatic cancer.

### **About ABRAXANE in Pancreatic Cancer**

In September 2013, the U.S. Food and Drug Administration (FDA) approved ABRAXANE in combination with gemcitabine as first-line treatment of patients with metastatic adenocarcinoma of the pancreas.

Clinical trials continue building on the foundation of ABRAXANE in combination with gemcitabine for a new wave of potential treatments, such as an ongoing Phase 2 cooperative group trial with SWOG S1505 (ClinicalTrials.gov, NCT02562716) investigating the safety and effectiveness of ABRAXANE in combination with gemcitabine as neoadjuvant treatment for localized pancreatic head adenocarcinoma.

### **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/mm<sup>3</sup>. 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<sup>3</sup>

### 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/mm<sup>3</sup>
- In the case of severe neutropenia (<500 cells/mm<sup>3</sup> 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<sup>3</sup> and platelets recover to a level >100,000 cells/mm<sup>3</sup>
- 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<sup>3</sup> and platelet count of at least 100,000 cells/mm<sup>3</sup> on Day 1 or to an ANC of at least 500 cells/mm<sup>3</sup> and platelet count of at least 50,000 cells/mm<sup>3</sup> 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/mm<sup>3</sup> or platelets are less than 50,000 cells/mm<sup>3</sup> and delay initiation of the next cycle if the ANC is less than 1500 cells/mm<sup>3</sup> or platelet count is less than 100,000 cells/mm<sup>3</sup> on Day 1 of the cycle. Resume treatment with appropriate dose reduction

if recommended

### **Nervous System**

- Sensory neuropathy is dose- and schedule-dependent
- The occurrence of Grade 1 or 2 sensory neuropathy does not generally require dose modification
- If  $\geq$  Grade 3 sensory neuropathy develops, withhold ABRAXANE treatment until resolution to Grade 1 or 2 for MBC or until resolution to  $\leq$  Grade 1 for NSCLC and pancreatic cancer followed by a dose reduction for all subsequent courses of ABRAXANE

### **Sepsis**

- Sepsis occurred in 5% of patients with or without neutropenia who received ABRAXANE in combination with gemcitabine
- Biliary obstruction or presence of biliary stent were risk factors for severe or fatal sepsis
- If a patient becomes febrile (regardless of ANC), initiate treatment with broad-spectrum antibiotics
- For febrile neutropenia, interrupt ABRAXANE and gemcitabine until fever resolves and ANC  $\geq 1500$  cells/mm<sup>3</sup>, 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/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 ( $\geq 10\%$  incidence) adverse reactions were observed at a similar incidence in ABRAXANE plus carboplatin–treated and paclitaxel injection plus carboplatin–treated patients: alopecia (56%), nausea (27%), fatigue (25%), decreased appetite (17%), asthenia (16%), constipation (16%), diarrhea (15%), vomiting (12%), dyspnea (12%), and rash (10%); incidence rates are for the ABRAXANE plus carboplatin treatment group
- Adverse reactions with a difference of  $\geq 2\%$ , Grade 3 or higher, with combination use of ABRAXANE and carboplatin vs combination use of paclitaxel injection and carboplatin in NSCLC are anemia (28%, 7%), neutropenia (47%, 58%), thrombocytopenia (18%, 9%), and peripheral neuropathy (3%, 12%), respectively
- Adverse reactions with a difference of  $\geq 5\%$ , Grades 1-4, with combination use of ABRAXANE and carboplatin vs combination use of paclitaxel injection and carboplatin in NSCLC are anemia (98%, 91%), thrombocytopenia (68%, 55%), peripheral neuropathy (48%, 64%), edema peripheral (10%, 4%), epistaxis (7%, 2%), arthralgia (13%, 25%), and myalgia (10%, 19%), respectively
- Neutropenia (all grades) was reported in 85% of patients who received ABRAXANE and carboplatin vs 83% of patients who received paclitaxel injection and carboplatin

### **Pancreatic Adenocarcinoma Study**

- Among the most common ( $\geq 20\%$ ) adverse reactions in the phase III study, those with a  $\geq 5\%$  higher incidence in the ABRAXANE/gemcitabine group compared with the gemcitabine group are neutropenia (73%, 58%), fatigue (59%, 46%), peripheral neuropathy (54%, 13%), nausea (54%, 48%), alopecia (50%, 5%), peripheral edema (46%, 30%), diarrhea (44%, 24%), pyrexia (41%, 28%), vomiting (36%, 28%), decreased appetite (36%, 26%), rash (30%, 11%), and dehydration (21%, 11%)
- Of these most common adverse reactions, those with a  $\geq 2\%$  higher incidence of Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared with the gemcitabine group, respectively, are neutropenia (38%, 27%), fatigue (18%, 9%), peripheral neuropathy (17%, 1%), nausea (6%, 3%), diarrhea (6%, 1%), pyrexia (3%, 1%), vomiting (6%, 4%), decreased appetite (5%, 2%), and dehydration (7%, 2%)
- Thrombocytopenia (all grades) was reported in 74% of patients in the ABRAXANE/gemcitabine group vs 70% of patients in the gemcitabine group
- The most common serious adverse reactions of ABRAXANE (with a  $\geq 1\%$  higher incidence) are pyrexia (6%), dehydration (5%), pneumonia (4%), and vomiting (4%)
- The most common adverse reactions resulting in permanent discontinuation of ABRAXANE were peripheral neuropathy (8%), fatigue (4%), and thrombocytopenia (2%)
- The most common adverse reactions resulting in dose reduction of ABRAXANE are neutropenia (10%) and peripheral neuropathy (6%)
- The most common adverse reactions leading to withholding or delay in ABRAXANE dosing are neutropenia (16%), thrombocytopenia (12%), fatigue (8%), peripheral neuropathy (15%), anemia (5%), and diarrhea (5%)
- Other selected adverse reactions with a  $\geq 5\%$  higher incidence for all-grade toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group, respectively, are asthenia (19%, 13%), mucositis (10%, 4%), dysgeusia (16%, 8%), headache (14%, 9%), hypokalemia (12%, 7%), cough (17%, 7%), epistaxis (15%, 3%), urinary tract infection (11%, 5%), pain in extremity (11%, 6%), arthralgia (11%, 3%), myalgia (10%, 4%), and depression (12%, 6%)
- Other selected adverse reactions with a  $\geq 2\%$  higher incidence for Grade 3-4 toxicity in the ABRAXANE/gemcitabine group compared to the gemcitabine group are thrombocytopenia (13%, 9%), asthenia (7%, 4%), and hypokalemia (4%, 1%)

### **Postmarketing Experience With ABRAXANE and Other Paclitaxel Formulations**

- Severe and sometimes fatal hypersensitivity reactions have been reported with ABRAXANE. The use of ABRAXANE in patients previously exhibiting hypersensitivity to paclitaxel injection or human albumin has not been studied. 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 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 BeiGene**

BeiGene is a global, commercial-stage, research-based biotechnology company focused on molecularly-targeted and immuno-oncology cancer therapeutics. With a team of approximately 2,400 employees in China, the United States, Australia and Europe, BeiGene is advancing a pipeline consisting of novel oral small molecules and monoclonal antibodies for cancer. BeiGene is also working to create combination solutions aimed to have both a meaningful and lasting impact on cancer patients. BeiGene markets ABRAXANE<sup>®</sup> (nanoparticle albumin-bound paclitaxel), REVLIMID<sup>®</sup> (lenalidomide), and VIDAZA<sup>®</sup> (azacitidine) in China under a license from Celgene Corporation.<sup>iii</sup>

### **Forward-Looking Statements**

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and other federal securities laws, including statements regarding the advancement of, and anticipated development, regulatory milestones and commercialization of ABRAXANE. Actual results may differ materially from those indicated in the forward-looking statements as a result of various important factors, including BeiGene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; BeiGene's ability to achieve commercial success for its marketed products and drug candidates, if approved; BeiGene's ability to obtain and maintain protection of intellectual property for its technology and drugs; BeiGene's reliance on third parties to conduct drug development, manufacturing and other services; BeiGene's limited operating history and BeiGene's ability to obtain additional funding for operations and to complete the development and commercialization of its drug candidates, as well as those risks more fully discussed in the section entitled "Risk Factors" in BeiGene's most recent quarterly report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other

important factors in BeiGene's subsequent filings with the U.S. Securities and Exchange Commission. All information in this press release is as of the date of this press release, and BeiGene undertakes no duty to update such information unless required by law.

**Investor Contact**

Craig West  
+1 857-302-5189  
ir@beigene.com

**Media Contact**

Liza Heapes  
+ 1 857-302-5663  
media@beigene.com

---

<sup>i</sup> <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-facts-and-figures-2019.pdf>

<sup>ii</sup> <http://gco.iarc.fr/>

<sup>iii</sup> ABRAXANE®, REVLIMID®, and VIDAZA® are registered trademarks of Celgene Corporation