Press Release

PharmaEngine Announces Taiwan FDA Approval of ONIVYDE™ (irinotecan liposome injection) for the Treatment of Metastatic Pancreatic Cancer

ONIVYDE in combination with fluorouracil and leucovorin is the only regulatory approved treatment for the patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy

Taipei, Taiwan, October 22, 2015 -- PharmaEngine, Inc. (TWO: 4162) announced that the Taiwan Food and Drug Administration (TFDA) has approved ONIVYDE™ (irinotecan liposome injection) in combination with fluorouracil (5-FU) and leucovorin (LV) for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy. ONIVYDE is not indicated for use as a single agent. The TFDA is the first regulatory authority in the world granting the approval of ONIVYDE.

"We are very grateful that the TFDA granted the regulatory approval in such a rapid pace, especially the accelerated efforts made by the Center of Drug Evaluation (CDE) and the TFDA," said C. Grace Yeh, Ph.D., President and CEO of PharmaEngine. "We are highly appreciative to our license partner, Merrimack Pharmaceuticals, Inc. (NASDAQ: MACK), for their valuable collaboration, as well as their timely and full support during the review period. Also, we sincerely thank all the patients, the investigators and their caregivers for their participation and significant contribution to advance the management of pancreatic cancer patients. Lastly, PharmaEngine is proud of this remarkable achievement in our company's history, and we are indebted to many people who encouraged us to persevere for more than a decade in developing ONIVYDE."

ONIVYDE (formerly known as MM-398, PEP02, or nal-IRI) is a proprietary liposome encapsulation of irinotecan, a topoisomerase I inhibitor. The new drug application (NDA) to the TFDA was based on the NDA data package submitted by Merrimack to the U.S. FDA and the positive data from a global Phase 3 study (NAPOLI-1) conducted in patients with metastatic pancreatic cancer who previously received gemcitabine-based therapy. A total of 417 patients were recruited at 76 sites in 14 countries; 95 patients (22.8%) were from Taiwan which ranked the top enrollment rate. The study results of NAPOLI-1 showed ONIVYDE in combination with 5-FU/LV

achieved the primary and secondary endpoints by demonstrating a clinically and statistically significant improvement in overall survival, progression free survival and overall response rate compared to the control group of patients who received 5-FU/LV. The ONIVYDE monotherapy arm in this study did not achieve the primary endpoint. The most common adverse reactions (≥20%) with ONIVYDE were diarrhea, fatigue/asthenia, vomiting, nausea, decreased appetite, stomatitis and pyrexia and the most common severe laboratory abnormalities (≥10% Grade 3 or 4) were lymphopenia and neutropenia. This was the first global Phase 3 study in a post-gemcitabine setting to demonstrate a survival benefit in this aggressive disease.

Merrimack submitted an NDA to the U.S. FDA in April 2015 and was granted priority review in June with a Prescription Drug User Fee Act (PDUFA) date of October 24, 2015. The marketing authorization application (MAA) submitted to the European Medicines Agency (EMA) by Baxalta Incorporated in May 2015, was accepted for review in June 2015, and there are plans for submissions to other countries. ONIVYDE has orphan drug designation in the US, EU and elsewhere.

About Pancreatic Cancer

According to the 2013 statistical data from the Department of Health of Taiwan (DOH), pancreatic cancer is the eighth leading cause of cancer deaths in Taiwan and about 1,700 people die of pancreatic cancer every year. Metastatic pancreatic cancer is almost uniformly fatal, with an overall survival rate of approximately 6 percent at 5 years worldwide. The drug used for the first-line therapy of the pancreatic cancer is gemcitabine. Currently, the patients with metastatic pancreatic cancer who progressed following gemcitabine treatment have no set standard of care.

About ONIVYDE (MM-398, PEP02, or nal-IRI)

PharmaEngine licensed the Asian (2003) European (2005) development, manufacturing and commercialization rights of ONIVYDE from Hermes BioSciences, Inc., South San Francisco, CA. Hermes was acquired by Merrimack Pharmaceuticals, Inc., Cambridge, MA in 2009. After completed preclinical, Phase 1 and 2 clinical studies, PharmaEngine licensed its Asian and European rights except Taiwan, back to Merrimack in 2011. During 2011 and 2014, Merrimack sponsored the global phase 3 NAPOLI-1 study in metastatic pancreatic cancer patients. In September 2014, Merrimack licensed ONIVYDE outside of the U.S. and Taiwan to

Baxalta Incorporated (NYSE: BXLT), formerly Baxter International's BioScience business.

IMPORTANT SAFETY INFORMATION

INDICATION

ONIVYDE™ (irinotecan liposome injection) is indicated, in combination with fluorouracil (5-FU) and leucovorin (LV), for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

Limitation of Use: ONIVYDE is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

WARNING: SEVERE NEUTROPENIA and SEVERE DIARRHEA

Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE. Severe or life-threatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE in combination with fluorouracil (5-FU) and leucovorin (LV). Withhold ONIVYDE for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment.

Severe diarrhea occurred in 13% of patients receiving ONIVYDE in combination with 5-FU/LV. Do not administer ONIVYDE to patients with bowel obstruction. Withhold ONIVYDE for diarrhea of Grade 2-4 severity. Administer loperamide for late diarrhea of any severity. Administer atropine, if not contraindicated, for early diarrhea of any severity.

CONTRAINDICATION

ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction to ONIVYDE or irinotecan HCl.

WARNING AND PRECAUTIONS

Severe Neutropenia

ONIVYDE can cause severe or life-threatening neutropenia and fatal neutropenic sepsis. In a clinical study, the incidence of fatal neutropenic sepsis was 0.8% among patients receiving ONIVYDE, occurring in one of 117 patients in the ONIVYDE plus

fluorouracil/leucovorin (ONIVYDE/5-FU/LV) arm and one of 147 patients receiving ONIVYDE as a single agent. Severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE/5-FU/LV vs 2% of patients receiving 5-FU/LV. Grade 3/4 neutropenic fever/neutropenic sepsis occurred in 3% of patients receiving ONIVYDE/5-FU/LV, and did not occur in patients receiving 5-FU/LV.

In patients receiving ONIVYDE/5-FU/LV, the incidence of Grade 3/4 neutropenia was higher among Asian [18/33 (55%)] vs White patients [13/73 (18%)]. Neutropenic fever/neutropenic sepsis was reported in 6% of Asian vs 1% of White patients.

Severe Diarrhea

ONIVYDE can cause severe and life-threatening diarrhea. Do not administer ONIVYDE to patients with bowel obstruction. Severe and life-threatening late-onset (onset >24 hours after chemotherapy) and early-onset diarrhea (onset ≤24 hours after chemotherapy, sometimes with other symptoms of cholinergic reaction) were observed. An individual patient may experience both early- and late-onset diarrhea. In a clinical study, Grade 3/4 diarrhea occurred in 13% of patients receiving ONIVYDE/5-FU/LV vs 4% receiving 5-FU/LV. Grade 3/4 late-onset diarrhea occurred in 9% of patients receiving ONIVYDE/5-FU/LV vs 4% in patients receiving 5-FU/LV; the incidences of early-onset diarrhea were 3% and no Grade 3/4 incidences, respectively. Of patients receiving ONIVYDE/5-FU/LV, 34% received loperamide for late-onset diarrhea and 26% received atropine for early-onset diarrhea.

Interstitial Lung Disease (ILD)

Irinotecan HCl can cause severe and fatal ILD. Withhold ONIVYDE in patients with new or progressive dyspnea, cough, and fever, pending diagnostic evaluation. Discontinue ONIVYDE in patients with a confirmed diagnosis of ILD.

Severe Hypersensitivity Reactions

Irinotecan HCl can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction.

Embryo-Fetal Toxicity

Based on animal data with irinotecan HCl and the mechanism of action of ONIVYDE, ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during and for one month after ONIVYDE treatment.

ADVERSE REACTIONS

- The most common (≥20%) adverse reactions in which patients receiving ONIVYDE/5-FU/LV experienced a ≥5% higher incidence of any Grade vs the 5-FU/LV arm, were diarrhea (any 59%, 26%, severe 13%, 4 %) [early diarrhea (any 30%, 15%; severe 3%, 0%), late diarrhea (any 43%, 17%; severe 9%, 4%)], fatigue/asthenia (any 56%, 43%; severe 21%, 10%), vomiting (any 52%, 26%; severe 11%, 3%), nausea (any 51%, 34%; severe 8%, 4%), decreased appetite (any 44%, 32%; severe 4%, 2%), stomatitis (any 32%, 12%; severe 4%, 1%), pyrexia (any 23%, 11%; severe 2%, 1%).
- Of less common (<20%) adverse reactions, patients receiving ONIVYDE/5-FU/LV who experienced Grade 3/4 adverse reactions at a ≥2% higher incidence of Grade 3/4 toxicity vs the 5-FU/LV arm, respectively, were sepsis (3%, 1%), neutropenic fever/neutropenic sepsis (3%, 0%), gastroenteritis (3%, 0%), intravenous catheter-related infection (3%, 0%), weight loss (2%, 0%), and dehydration (4%, 2%).
- The laboratory abnormalities in which patients receiving ONIVYDE/5-FU/LV experienced a ≥5% higher incidence vs the 5-FU/LV arm, were anemia (any 97%, 86%; severe 6%, 5%), lymphopenia (any 81%, 75%; severe 27%, 17%), neutropenia (any 52%, 6%; severe 20%, 2%), thrombocytopenia (any 41%, 33%; severe 2%, 0%), increased alanine aminotransferase (any 51%, 37%; severe 6%, 1%), hypoalbuminemia (any 43%, 30%; severe 2%, 0%), hypomagnesemia (any 35%, 21%; severe 0%, 0%), hypokalemia (any 32%, 19%; severe 2%, 2%), hypocalcemia (any 32%, 20%; severe 1%, 0%), hypophosphatemia (any 29%, 18%; severe 4%, 1%), hyponatremia (any 27%, 12%; severe 5%, 3%), increased creatinine (any 18%, 13%; severe 0%; 0%).
- ONIVYDE can cause cholinergic reactions manifesting as rhinitis, increased salivation, flushing, bradycardia, miosis, lacrimation, diaphoresis, and intestinal hyperperistalsis with abdominal cramping and early onset diarrhea. Grade 1 or 2 cholinergic symptoms other than early diarrhea occurred in 12 (4.5%) ONIVYDE-treated patients.

- Infusion reactions, consisting of rash, urticaria, periorbital edema, or pruritus, occurring on the day of ONIVYDE administration were reported in 3% of patients receiving ONIVYDE or ONIVYDE/5-FU/LV.
- The most common serious adverse reactions (≥2%) of ONIVYDE were diarrhea, vomiting, neutropenic fever or neutropenic sepsis, nausea, pyrexia, sepsis, dehydration, septic shock, pneumonia, acute renal failure, and thrombocytopenia.

DRUG INTERACTIONS

Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme inducing therapies ≥2 weeks prior to initiation of ONIVYDE. Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible, and discontinue strong CYP3A4 inhibitors ≥1 week prior to starting therapy.

USE IN SPECIFIC POPULATIONS

Pregnancy and Reproductive Potential

Advise pregnant women of the potential risk to a fetus. Advise males with female partners of reproductive potential to use effective contraception during and for 4 months after ONIVYDE treatment.

Lactation

Advise nursing women not to breastfeed during and for one month after ONIVYDE treatment.

Pediatric

Safety and effectiveness of ONIVYDE have not been established in pediatric patients.

DOSAGE AND ADMINISTRATION

The recommended dose of ONIVYDE is 70 mg/m^2 based on irinotecan free base (equivalent to 80 mg/m^2 of irinotecan as the hydrochloride trihydrate) intravenous infusion over 90 minutes every two weeks, administered prior to leucovorin and fluorouracil. The recommended starting dose of ONIVYDE in patients known to be homozygous for the UGT1A1*28 allele is 50 mg/m^2 based on irinotecan free base (equivalent to 60 mg/m^2 of irinotecan as the hydrochloride trihydrate) administered by intravenous infusion over 90 minutes. There is no recommended dose of ONIVYDE

for patients with serum bilirubin above the upper limit of normal. Pre-medicate with a corticosteroid and an anti-emetic 30 minutes prior to ONIVYDE. Withhold ONIVYDE for Grade 3 or 4 adverse reactions. Resume ONIVYDE with reduced dose once adverse reaction recovered to ≤Grade 1. Discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction and in patients with a confirmed diagnosis of interstitial lung disease.
Do not substitute ONIVYDE for other drugs containing irinotecan HCl.

About PharmaEngine (TWO: 4162)

PharmaEngine, Inc. is a biopharmaceutical company headquartered in Taipei, Taiwan. PharmaEngine focuses on the development of new medications for the treatment of cancer and Asian prevalent diseases. PharmaEngine has three ongoing projects: PEP02 (MM-398, ONIVYDE) approved by the TFDA and under NDA and MAA review by the US FDA and the EMA, respectively; PEP503 (NBTXR3) in a global pivotal trial of soft tissue sarcoma; and PEP06 in lead optimization. For further information, please visit PharmaEngine's website at http://www.pharmaengine.com.

Contact

Peter Wu, Director, Corporate Development
Telephone No.: (+886)-2-2515-8228, ext. 500
Mobile phone No.: (+886)-935-154-559
Email: peter.wu@pharmaengine.com