Press Release

PharmaEngine Announces U.S. FDA Approves Merrimack's ONIVYDE™ (irinotecan liposome injection) in Combination with Fluorouracil and Leucovorin for the Treatment of Metastatic Adenocarcinoma of the Pancreas after Disease Progression Following Gemcitabine-Based Therapy

Taipei, Taiwan, October 23, 2015 -- PharmaEngine, Inc. (TWO: 4162) announced the U.S. FDA has approved Merrimack's (NASDAQ: MACK) 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 on October 22. Earlier on the same day, the Taiwan FDA approved ONIVYDE/5-FU/LV for the same indication. ONIVYDE is not indicated for use as a single agent.

"ONIVYDE is the first cancer drug to begin its clinical development in Taiwan and go on to receive regulatory approval by the US FDA," said C. Grace Yeh, Ph.D., President and CEO of PharmaEngine. "We applaud Merrimack for achieving this important milestone and we are pleased to have supported Merrimack in completing the final phase of the development for this new drug application (NDA). We believe that ONIVYDE will become an established therapeutic option for the management of metastatic pancreatic cancer in the foreseeable future."

ONIVYDE (formerly known as MM-398, PEP02, or nal-IRI) is a proprietary liposomal encapsulation of irinotecan, a topoisomerase inhibitor. The NDA for ONIVYDE was based on the results of the international Phase 3 study (NAPOLI-1). ONIVYDE plus 5-FU/LV achieved the study's primary endpoint by demonstrating a clinically and statistically significant improvement in overall survival, as well as demonstrating improvement in progression free survival compared to the control group of patients who received 5-FU/LV alone. The ONIVYDE monotherapy arm did not achieve the primary endpoint and, therefore, is not indicated as a single agent. 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. For additional safety information, please see the Important Safety Information below. This was the first global Phase 3 study in a post-gemcitabine setting to demonstrate a survival benefit in this aggressive disease.

The marketing authorization application (MAA) submitted to the European Medicines Agency by Baxalta Incorporated is under review 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 most recent information from World Health Organization (WHO), 330,000 people die of pancreatic cancer per year and pancreatic cancer is the seventh-leading cause of cancer-related death in the world. Metastatic pancreatic cancer is almost uniformly fatal, with an overall survival rate of approximately 6 percent at 5 years worldwide. Currently, patients with metastatic pancreatic cancer who progress after gemcitabine treatment have no set standard of care.

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

PharmaEngine licensed the Asian (2003) and European (2005) development, manufacturing and commercialization rights for 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. From 2012 to 2014, Merrimack sponsored the global Phase 3 study in metastatic pancreatic cancer patients who progressed after receiving a gemcitabine-containing regimen. 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.

Please see full US Prescribing Information for ONIVYDE.

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 US FDA and in the NDA review by the EMA and the TFDA, 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.

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