



MERRIMACK

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Merrimack Announces U.S. FDA Approval of ONIVYDE™ (irinotecan liposome injection) for the Treatment of Patients with Metastatic Pancreatic Cancer

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

Merrimack will host an investor conference call and webcast at 4:30 p.m., Eastern Time, today

CAMBRIDGE, Mass., Oct. 22, 2015 /PRNewswire/ -- Merrimack (Nasdaq: MACK) today announced that ONIVYDE™ (irinotecan liposome injection) has been approved by the U.S. Food and Drug Administration (FDA) in combination with fluorouracil (5-FU) and leucovorin 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. With this approval, ONIVYDE in combination with 5-FU and leucovorin becomes the first and only FDA-approved treatment option for patients in this setting.

Experience the interactive Multimedia News Release here: <http://www.multivu.com/players/English/7657251-merrimack-onivyde-fda-approval>

"This is an important day for patients facing pancreatic cancer," said Andrea Wang-Gillam, M.D., Ph.D., Associate Professor of Medicine, Clinical Director of GI Oncology Program, Division of Oncology, at Washington University School of Medicine, St. Louis, and a key investigator on the ONIVYDE Phase 3 NAPOLI-1 study. "With a long history of failed clinical studies in the post-gemcitabine setting, this approval is a significant achievement in the oncology community. It brings a new therapy to the many patients who are facing this aggressive disease and are in need of treatment options."

"We are thrilled to be able to deliver this groundbreaking therapy to patients battling metastatic pancreatic cancer," said Robert Mulroy, President and CEO of Merrimack. "Pancreatic cancer is an aggressive and devastating disease, with very few patients surviving beyond one year. ONIVYDE provides a clinically significant treatment option to a patient population where there is currently no standard of care. We are grateful to the many patients, clinicians, researchers and partners that worked with us to make ONIVYDE available. Today's approval by the FDA is a pivotal milestone in our company's history, representing years of hard work and commitment to our mission of engineering new treatment options for cancer patients in need."

The FDA approval is based on the results of an international Phase 3 randomized, controlled study (NAPOLI-1). In this study, ONIVYDE in combination with 5-FU and leucovorin achieved its primary endpoint of a significant improvement in overall survival ($p=0.014$, unstratified HR=0.68, 95% CI: [0.50-0.93]) with a 45% improvement in median overall survival of 6.1 months for patients receiving the ONIVYDE combination regimen compared to 4.2 months for patients who received 5-FU and leucovorin alone. The ONIVYDE combination also demonstrated improvement in progression free survival (3.1 months vs. 1.5 months, HR=0.55, 95% CI: [0.41-0.75]). The monotherapy regimen in this study did not achieve its primary endpoint and, therefore, ONIVYDE is not indicated as a single agent. The most common adverse reactions ($\geq 20\%$) of ONIVYDE were diarrhea, fatigue/asthenia, vomiting, nausea, decreased appetite, stomatitis and pyrexia, and the most common severe laboratory abnormalities ($\geq 10\%$ Grade 3 or 4) were lymphopenia and neutropenia. For additional safety information, please see Important Safety Information including Boxed Warning below.

"This is a pivotal achievement for the pancreatic cancer community because it provides a new treatment option for some patients facing this difficult disease," said Julie Fleshman, President and CEO of the Pancreatic Cancer Action Network. "We applaud the dedication of those involved in this advancement, knowing it will impact our goal to double pancreatic cancer survival by 2020."

There are approximately 49,000 patients diagnosed with pancreatic cancer each year in the United States¹, the overwhelming majority of whom have adenocarcinoma². Most patients receive gemcitabine-based therapy during either

adjuvant/neoadjuvant treatment for locally advanced disease or during first- or second-line therapy for metastatic disease, but are left with no standard of care therapy upon progression³. ONIVYDE in combination with 5-FU and leucovorin is now approved for these patients whose disease has progressed following gemcitabine-based therapy.

Merrimack expects ONIVYDE to be available in the United States next week and is committed to supporting rapid physician and patient access to this therapy. PROVYDE™ (ONIVYDE Access Center) offers a variety of reimbursement support services for healthcare providers and financial assistance services for patients. For more information, please call 1-844-ONIVYDE or visit www.ONIVYDE.com.

Baxalta Incorporated (NYSE: BXL) is responsible for the development and commercialization of ONIVYDE outside of the United States and Taiwan under the exclusive licensing agreement that Merrimack and Baxalta entered into in September 2014. In May 2015, the European Medicines Agency (EMA) accepted for review Baxalta's marketing authorization application (MAA) for ONIVYDE based on the same clinical results.

"We are excited that ONIVYDE (nal-IRI) will now be available to people living with metastatic pancreatic cancer in the U.S. after they progress from gemcitabine-based therapy," said David Meek, Executive Vice President and President of Oncology at Baxalta. "Looking ahead, Baxalta continues to work toward marketing authorization in Europe with the goal of providing nal-IRI to patients in more countries around the world in need of new options."

PharmaEngine, Inc. (Taipei, Taiwan) holds the rights to commercialize ONIVYDE in Taiwan. PharmaEngine filed a New Drug Application (NDA) with the Taiwan FDA in May 2015.

Merrimack to Host Conference Call

Merrimack will host an investor conference call and webcast at 4:30 p.m., Eastern Time, today, October 22, where it will review the details of the approval. Investors and the general public are invited to listen to the call by dialing (877) 564-1301 (domestic) or (224) 357-2394 (international) five minutes prior to the start of the call and providing the passcode 67436538.

A listen-only webcast of the call can be accessed in the Investors section of Merrimack's website, investors.merrimack.com, and a replay of the call will be archived there for six weeks.

About the NAPOLI-1 Study

The NAPOLI-1 study was a randomized, open label Phase 3 study in patients with metastatic adenocarcinoma of the pancreas who received prior gemcitabine-based therapy, and was the largest Phase 3 study in this setting to date. The study evaluated ONIVYDE in combination with 5-FU and leucovorin administered every two weeks and as a monotherapy administered every three weeks. Each ONIVYDE containing arm was compared to a control arm of 5-FU and leucovorin. A total of 417 patients were randomized across the three arms. The primary endpoint of the study was overall survival. The ONIVYDE combination regimen demonstrated a significant increase in median overall survival versus 5-FU and leucovorin alone: 6.1 months vs 4.2 months ($p=0.014$, unstratified HR=0.68, 95% CI: [0.50-0.93]). The monotherapy regimen in this study did not show improvement over the 5-FU and leucovorin arm (HR=1.00, $p=0.97$ [unstratified log-rank test]). Patients were enrolled at 76 sites in North America, South America, Europe, Asia and Oceania.

About Pancreatic Cancer

Pancreatic cancer is rare and deadly. It accounts for only 3% of all cancer cases², but is the fourth leading cause of cancer-related death⁴, leading to a five year survival rate of only 7%¹. Each year an estimated 49,000 new cases are diagnosed in the United States¹, two-thirds of which are among people aged 65 or older⁵. There are an estimated 338,000 new cases diagnosed each year worldwide⁶.

The pancreas is composed of two main cell types: exocrine and endocrine. Exocrine tumors are the most common type of pancreatic cancer, accounting for 96% of all cases¹. Adenocarcinoma, a sub-type of exocrine tumors, comprises 95% of all exocrine tumors².

Because the signs and symptoms of pancreatic cancer are non-specific and may not appear until the disease has spread to other sites, approximately 80% of patients are not candidates for surgery⁴, instead receiving chemotherapy as the mainstay of their therapy. The majority of these patients receive gemcitabine-based therapy during either adjuvant/neoadjuvant treatment or during first- or second-line therapy for metastatic disease³. There is no consensus on the standard of care for patients with metastatic pancreatic cancer previously treated with a gemcitabine-based therapy.

About ONIVYDE™ [pronounced'ɒn - ih - vide \]

ONIVYDE, also known as MM-398 or "nal-IRI," is a novel encapsulation of irinotecan in a liposomal formulation. The activated form of irinotecan is SN-38, which functions by inhibiting topoisomerase I (an essential enzyme involved in DNA transcription and replication) and promoting cell death. **For more information please visit www.ONIVYDE.com.**

IMPORTANT SAFETY INFORMATION

INDICATION

ONIVYDE™ (irinotecan liposome injection) is indicated, in combination with fluorouracil (5FU) 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.

WARNINGS 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 1/117 patients in the ONIVYDE/5-FU/LV arm and 1/147 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 1 month after ONIVYDE treatment.

ADVERSE REACTIONS

- The most common ($\geq 20\%$) adverse reactions in which patients receiving ONIVYDE/5-FU/LV experienced a $\geq 5\%$ 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 $\geq 2\%$ 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 $\geq 5\%$ 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 1/2 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 ($\geq 2\%$) 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 1 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/m² intravenous (IV) infusion over 90 minutes every 2 weeks, administered prior to LV and 5-FU. The recommended starting dose of ONIVYDE in patients known to be homozygous for the UGT1A1*28 allele is 50 mg/m² administered by IV infusion over 90 minutes. There is no recommended dose of ONIVYDE for patients with serum bilirubin above the upper limit of normal. Premedicate with a corticosteroid and an anti-emetic 30 minutes prior to ONIVYDE. Withhold ONIVYDE for Grade 3/4 adverse reactions. Resume ONIVYDE with reduced dose once adverse reaction recovered to \leq Grade 1. Discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction and in patients with a confirmed diagnosis of ILD.

Do not substitute ONIVYDE for other drugs containing irinotecan HCl.

Please see full US [Prescribing Information](#) for ONIVYDE.

About Merrimack

Merrimack is a fully integrated biopharmaceutical company that views cancer as a complex engineering challenge. Through systems biology, which brings together the fields of biology, computing and engineering, Merrimack aims to decrease uncertainty in drug development and clinical validation, and move discovery efforts beyond trial and error. Such an approach has the potential to make individualized treatment of patients a reality. ONIVYDE, which was recently approved in combination with fluorouracil and leucovorin for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy, is Merrimack's first approved product. With four additional candidates in clinical studies, several in preclinical development and multiple biomarkers designed to support patient selection, Merrimack is

building one of the most robust oncology pipelines in the industry. For more information, please visit Merrimack's website at www.merrimack.com or connect on Twitter at @MerrimackPharma.

Forward-Looking Statements

To the extent that statements contained in this press release are not descriptions of historical facts, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements include any statements about Merrimack's strategy, future operations, future financial position and future expectations and plans and prospects for Merrimack, and any other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "hope" and similar expressions. In this press release, Merrimack's forward-looking statements include statements about the potential effectiveness and safety profile of ONIVYDE and Merrimack's expectations regarding the timing of availability of ONIVYDE. Such forward-looking statements involve substantial risks and uncertainties that could cause Merrimack's clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, availability of data from ongoing clinical trials, expectations for regulatory approvals, development progress of Merrimack's companion diagnostics and other matters that could affect the availability or commercial potential of Merrimack's drug candidates or companion diagnostics. Merrimack undertakes no obligation to update or revise any forward-looking statements. Forward-looking statements should not be relied upon as representing Merrimack's views as of any date subsequent to the date hereof. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Merrimack's business in general, see the "Risk Factors" section of Merrimack's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 10, 2015 and other reports Merrimack files with the SEC.

1. American Cancer Society. Cancer Facts and Figures 2015. Atlanta: American Cancer Society; 2015.
2. American Cancer Society. Pancreatic Cancer Overview. Atlanta: American Cancer Society; 2015.
3. Data presented at ASCO 2014 (Abrams et al.)
4. National Cancer Institute. Pancreatic Cancer Treatment -for health professionals (PDQ®). National Cancer Institute at the National Institutes of Health; 2015.
5. Surveillance, Epidemiology, and End Results Program. SEER Stat Fact Sheets: Pancreas Cancer; 2015. National Cancer Institute.
6. World Health Organization. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012; Lyon, Fr.: International Agency for Research on Cancer; 2012.

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