June 30, 2016

NAPOLI-1 Data Demonstrates ONIVYDE® Regimen Maintains Quality of Life While Improving Overall Survival in Patients with Metastatic Pancreatic Cancer

The addition of ONIVYDE (irinotecan liposome injection) to fluorouracil and leucovorin significantly improves median overall survival and progression-free survival in patients with metastatic pancreatic cancer following gemcitabine-based therapy without compromising quality of life at 12 weeks when compared with fluorouracil and leucovorin alone
Quality of life analysis was presented at ESMO 18th World Congress on Gastrointestinal Cancer

CAMBRIDGE, Mass., June 30, 2016 /PRNewswire/ -- Merrimack Pharmaceuticals, Inc. (NASDAQ: MACK) today announced a newly presented analysis of the Phase 3 NAPOLI-1 data shows patients treated with ONIVYDE® (irinotecan liposome injection), also known as "nal-IRI," in combination with fluorouracil (5-FU) and leucovorin, maintain similar baseline quality of life at 12 weeks despite the addition of a second chemotherapeutic agent when compared to 5-FU and leucovorin alone. These findings were presented in an oral session by Dr. Richard Hubner, an investigator on the NAPOLI-1 trial and a Consultant Medical Oncologist at Christie NHS Foundation Trust, at the European Society for Medical Oncology (ESMO) 18th World Congress on Gastrointestinal Cancer in Barcelona, Spain.

Previously reported Phase 3 NAPOLI-1 data demonstrate that the ONIVYDE combination regimen significantly improves overall survival and progression-free survival when compared to 5-FU and leucovorin alone[1]. ONIVYDE in combination with 5-FU and leucovorin was approved by the U.S. Food and Drug Administration (FDA) in October 2015 for the treatment of patients with metastatic adenocarcinoma of the pancreas whose disease progressed after gemcitabine-based therapy. It is the first and only FDA-approved therapy in this setting and was recently designated category 1 status by the National Comprehensive Cancer Network.

"This quality of life analysis of the NAPOLI-1 data underscores the significant clinical benefit the ONIVYDE regimen provides to a patient population with few treatment options," said Dr. Richard Hubner, investigator on the NAPOLI-1 trial and Consultant Medical Oncologist at Christie NHS Foundation Trust. "Fluorouracil and leucovorin is recognized as a well-tolerated therapy for metastatic pancreatic cancer patients. The addition of ONIVYDE, a second chemotherapeutic agent, to this treatment regimen demonstrated significant improvement in median overall survival, progression-free survival and overall response rate[2] with little or no impact on baseline quality of life at 12 weeks, as shown in this analysis. This further supports the growing recognition that the ONIVYDE combination regimen is a clinically beneficial treatment option for metastatic pancreatic cancer patients who have progressed on gemcitabine-based therapy."

Methodology and Results:

Effects of nal-IRI (MM-398) ± 5-fluorouracil on quality of life (QoL) in NAPOLI-1: A phase 3 study in patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) previously treated with gemcitabine-based therapy (Abstract O-004)

Quality of life was assessed using the European Organization for Research and Treatment of Cancer quality of life core questionnaire, which includes functional scales (physical, role, cognitive, emotional and social), symptom scales (appetite loss, constipation, diarrhea, dyspnea, fatigue, insomnia, nausea and vomiting and pain), and a global health and quality of life scale.

Patients completed the European Organization for Research and Treatment of Cancer quality of life core questionnaire at treatment start, every 6 weeks and 30 days post-follow-up visit. A total of 154 patients (ONIVYDE in combination with 5-FU and leucovorin, n=71; 5-FU and leucovorin, n=83) comprised the population for this analysis. Sixty-nine percent (49/71) of

patients in the ONIVYDE combination regimen group and 53% (44/83) in the 5-FU and leucovorin group had evaluable data at 12 weeks. No substantial differences are identified in the percentage of patients exhibiting improved, stable or worsening quality of life in the global health status, functional scale or symptom scale scores between the two study arms. The analysis demonstrates that in the NAPOLI-1 study, evaluable patients treated with the ONIVYDE combination regimen were able to maintain quality of life over 12 weeks and there were no significant differences versus the 5-FU and leucovorin-treated patients in quality of life response despite the addition of a second chemotherapeutic agent.

About Pancreatic Cancer

Pancreatic cancer is a rare and deadly disease with only 7% of all patients surviving five years or longer[3]. There are approximately 50,000 patients diagnosed with pancreatic cancer each year in the United States[4], the overwhelming majority of which have adenocarcinoma[5]. Globally there are approximately 338,000 new cases each year[6]. 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[7], but are left with no standard of care therapy upon progression. ONIVYDE in combination with 5-FU and leucovorin is approved in the United States and Taiwan for these patients whose disease has progressed following gemcitabine-based therapy.

About ONIVYDE® [pronounced ** 'on - ih - vide **\]

ONIVYDE® (irinotecan liposome injection), 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. ONIVYDE was approved by the U.S. FDA in combination with fluorouracil and leucovorin for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy. For full prescribing information, including Boxed WARNING, please visit www.ONIVYDE.com.

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.

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 (≥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 1/2 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 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/m^2 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/m^2 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 ≤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 U.S. Prescribing Information for ONIVYDE.

Global Partnerships

In 2014, Merrimack and Shire plc entered into an exclusive licensing agreement for the development and commercialization of ONIVYDE outside of the United States and Taiwan. Shire's marketing authorization application for the treatment of patients with metastatic adenocarcinoma of the pancreas who have been previously treated with gemcitabine-based therapy is currently under review with the European Medicines Agency. PharmaEngine, Inc. (Taipei, Taiwan) holds the rights to commercialize ONIVYDE in Taiwan and received the Taiwan FDA approval of ONIVYDE in October 2015.

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. Merrimack's first commercial product, ONIVYDE® (irinotecan liposome injection), was approved by the U.S. FDA in October 2015. 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 quality of life of patients receiving 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 May 2, 2016 and other reports Merrimack files with the SEC.

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[1] Wang-Gillam A, et.al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomized, open-label phase 3 trial. *The Lancet*. Vol. 387, No. 10018, p545-557, 6 Feb 2016

[2] Wang-Gillam A, et.al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomized, open-label phase 3 trial. *The Lancet*. Vol. 387, No. 10018, p545-557, 6 Feb 2016

[3] American Cancer Society. Cancer Facts and Figures 2016. Atlanta: American Cancer Society; 2016

[4] American Cancer Society. Cancer Facts and Figures 2016. Atlanta: American Cancer Society; 2016

[5] American Cancer Society. Cancer Facts and Figures 2016. Atlanta: American Cancer Society; 2016

[6] World Health Organization. GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012; Lyon, Fr.: International Agency for Research on Cancer; 2012

[7] Data presented at ASCO 2014 (Abrams et al.)

To view the original version on PR Newswire, visit:http://www.prnewswire.com/news-releases/napoli-1-data-demonstrates-onivyde-regimen-maintains-quality-of-life-while-improving-overall-survival-in-patients-with-metastatic-pancreatic-cancer-300292469.html

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