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FOR IMMEDIATE RELEASE

The Medicines Company and SymBio Pharmaceuticals Establish Strategic Partnership for IONSYS® (fentanyl iontophoretic transdermal system) in Japan

PARSIPPANY, N.J. & TOKYO, JAPAN.--(BUSINESS WIRE) — Oct. 5, 2015-- The Medicines Company (Nasdaq: MDCO) and SymBio Pharmaceuticals Ltd. (4582: Tokyo), a Tokyo based specialty pharmaceutical company, today announced the establishment of a strategic partnership for IONSYS® (fentanyl iontophoretic transdermal system) in Japan.

The partnership includes an agreement granting SymBio an exclusive license in Japan to develop and commercialize IONSYS. IONSYS was approved by the U.S. Food and Drug Administration (FDA) on April 30, 2015, for the short-term management of acute post-operative pain in adult patients requiring opioid analgesia in the hospital. On September 25, 2015, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending marketing authorization for IONSYS. A phase I study for IONSYS targeting healthy Japanese patients has been completed.

Financial terms of the agreement, in addition to net sales royalties payable to The Medicines Company, include a $10 million upfront payment and certain regulatory and commercial milestones.

“This partnership further signals an important commitment of our company to pursue growth opportunities outside the United States through partnerships and to deliver innovation in the management of patients with acute post-operative pain to the Japanese market” said Glenn Sblendorio, President of The Medicines Company. “Through this partnership, IONSYS has the potential to become The Medicines Company’s first product to reach patients in Japan.”

“We are very excited to add IONSYS to our product portfolio. This product has the potential to change the management of pain in the hospital” said Fuminori Yoshida, Chief Executive Officer for SymBio. “We hope to take full advantage of an accelerated path to regulatory approval given that IONSYS has already completed a Phase I study in Japanese patients”.

About IONSYS® (fentanyl iontophoretic transdermal system)

INDICATION

IONSYS® (fentanyl iontophoretic transdermal system) CII, contains fentanyl, an opioid agonist. IONSYS is indicated for the short-term management of acute postoperative pain in adult patients requiring opioid analgesia in the hospital.

Limitations of Use:

- Only for use in patients who are alert enough and have adequate cognitive ability to understand the directions for use.
- Not for home use. IONSYS is for use only in patients in the hospital. Discontinue treatment with IONSYS before patients leave the hospital.
- IONSYS is for use after patients have been titrated to an acceptable level of analgesia using alternate opioid analgesics.

IMPORTANT SAFETY INFORMATION

WARNING: HOSPITAL USE ONLY; LIFE-THREATENING RESPIRATORY DEPRESSION; IONSYS REMS; ADDICTION, ABUSE, AND MISUSE; and CYTOCHROME P450 3A4 INTERACTION

Life Threatening Respiratory Depression

Use of IONSYS may result in potentially life-threatening respiratory depression and death as a result of the active drug, fentanyl. Only the patient should activate IONSYS dosing.

Accidental exposure to an intact IONSYS or to the hydrogel component, especially by children, through contact with skin or contact with mucous membranes, can result in a fatal overdose of fentanyl.

IONSYS is for use only in patients in the hospital. Discontinue treatment with IONSYS before patients leave the hospital.

IONSYS Risk Evaluation and Mitigation Strategy (REMS) Program

- Because of the potentially life-threatening respiratory depression resulting from accidental exposure, IONSYS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the IONSYS REMS Program.

Addiction, Abuse, and Misuse

- IONSYS exposes users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk before prescribing and monitor regularly for development of these behaviors or conditions.

Cytochrome P450 3A4 Interaction

The concomitant use of IONSYS with all cytochrome P450 3A4 inhibitors may result in an increase in fentanyl plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in fentanyl plasma concentration. Monitor patients receiving IONSYS and any CYP3A4 inhibitor or inducer.

Contraindications

- Significant respiratory depression
- Acute or severe bronchial asthma
- Known or suspected paralytic ileus and GI obstruction
- Hypersensitivity to fentanyl, cetylpyridinium chloride (e.g., Cepacol®), or any components of IONSYS

Warnings and Precautions

- Interactions with CNS depressants: Hypotension, profound sedation, coma, respiratory depression, and death may result if IONSYS is used concomitantly with alcohol or other central nervous system (CNS) depressants (e.g., sedatives, anxiolytics, hypnotics, neuroleptics, other opioids). Monitor patients closely if co-administration is required.
- Risk of Injury During MRI: IONSYS contains metal parts and must be removed and properly disposed of before a Magnetic Resonance Imaging (MRI) procedure. Monitor any patients wearing IONSYS with inadvertent exposure to an MRI for signs of central nervous system and respiratory depression.
- Risk of IONSYS Use During Other Procedures or Near Certain Equipment: Use of IONSYS during cardioversion, defibrillation, X-ray, CT, or diathermy can damage IONSYS and should be removed and properly disposed of before these procedures. Avoid contact with synthetic materials (such as carpeted flooring) to reduce the possibility of electrostatic discharge and damage to IONSYS. Avoid exposing IONSYS to electronic security systems to reduce the possibility of damage to IONSYS. Use of IONSYS near communications equipment (e.g., base stations for radio telephones and land mobile radios, amateur radio, AM and FM radio broadcast and TV broadcast radio) and Radio Frequency Identification (RFID) transmitters can damage IONSYS. If exposure to the above procedures, electronic security systems, electrostatic discharge, communications equipment, or RFID transmitters occurs, and if IONSYS does not appear to function normally, remove IONSYS and replace with a new IONSYS.
- Topical Skin Reactions: Topical skin reactions may occur with use of IONSYS and are typically limited to the site application area. If a severe skin reaction is observed, remove IONSYS and discontinue further use.
- Use in Elderly, Cachectic, and Debilitated Patients: Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients. Monitor such patients closely especially when IONSYS is used concomitantly with other drugs that depress respiration.
- Use in Patients with Chronic Pulmonary Disease: Monitor patients with significant chronic obstructive pulmonary disease or cor pulmonale, and patients having a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression for respiratory depression, particularly when initiating therapy with IONSYS. Consider the use of alternative non-opioid analgesics in these patients if possible.
- Hypotensive Effect: IONSYS may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume, or concurrent administration of certain CNS depressant drugs (e.g., phenothiazines or general anesthetics). Monitor these patients after initiating IONSYS. Avoid the use of IONSYS in patients with circulatory shock as IONSYS may cause vasodilation that can further reduce cardiac output and blood pressure.
- Patients with Head Injury or Increased Intracranial Pressure: IONSYS is not suitable for use in patients who are not alert and able to follow directions. Monitor patients using IONSYS who may be susceptible to the intracranial effects of CO_2 retention (e.g., those

with evidence of increased intracranial pressure or brain tumors) for signs of sedation and respiratory depression, particularly when initiating therapy with IONSYS. Avoid use of IONSYS in patients with impaired consciousness or coma. IONSYS may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure. Opioids may obscure the clinical course of patients with head injury.

- Use in Patients with Gastrointestinal Conditions: IONSYS is contraindicated in patients with gastrointestinal obstruction, including paralytic ileus. Fentanyl may cause spasm of the sphincter of Oddi. Monitor patients with biliary tract disease, including acute pancreatitis for worsening symptoms. Opioids may cause increases in serum amylase.
- Use in Patients with Convulsive or Seizure Disorders: IONSYS may aggravate convulsions in patients with convulsive disorders and may induce or aggravate seizures in some clinical settings. Monitor patients with a history of seizure disorders for worsened seizure control during IONSYS therapy.
- Bradycardia: IONSYS may produce bradycardia in some patients. Monitor patients with bradyarrhythmias closely for changes in heart rate, particularly when initiating therapy with IONSYS.
- Hepatic Impairment: Insufficient data are available on the use of IONSYS in patients with impaired hepatic function. Monitor for signs of sedation and respiratory depression in patients with hepatic impairment.
- Renal Impairment: A clinical pharmacology study with intravenous fentanyl in patients undergoing kidney transplantation has shown that patients with high blood urea nitrogen level had low fentanyl clearance. Monitor for signs of sedation and respiratory depression in patients with renal impairment.

Adverse Reactions

Most common (frequency ≥2%) headache, hypotension, nausea, vomiting, anemia, dizziness, application site reaction-erythema, pruritus, and urinary retention.

About The Medicines Company

The Medicines Company's purpose is to save lives, alleviate suffering and contribute to the economics of healthcare by focusing on 3000 leading acute/intensive care hospitals worldwide. Its vision is to be a leading provider of solutions in three areas: serious infectious disease care, acute cardiovascular care, and surgery and perioperative care. The company operates in the Americas, Europe and the Middle East, and Asia Pacific regions with global centers today in Parsippany, NJ, USA and Zurich, Switzerland.

The Medicines Company Forward-Looking Statements

Statements contained in this press release about The Medicines Company that are not purely historical, and all other statements that are not purely historical, may be deemed to be forward-looking statements for purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Without limiting the foregoing, the words "believes," "anticipates," "expects," "hopes," and "potential" and similar expressions, are intended to identify forward-looking statements. These forward-looking statements involve known and unknown risks and uncertainties that may cause the Company's actual results, levels of activity, performance or achievements to be materially different from those expressed or implied by these forward-looking statements. Important factors that may cause or contribute to such differences include whether our product candidates will advance in the clinical trials process on a timely basis or at all, whether physicians, patients and other key decision makers will accept clinical trial results, whether the Company or its partners will make regulatory submissions for its product candidates on a timely basis or at all, whether its regulatory submissions will receive approvals from regulatory agencies on a

timely basis or at all, the Company's or its partner's ability to successfully compete with potential competitors which may discover, develop or commercialize competing products more successfully than we do, and such other factors as are set forth in the risk factors detailed from time to time in the Company's periodic reports and registration statements filed with the Securities and Exchange Commission including, without limitation, the risk factors detailed in the Company's Quarterly Report on Form 10-Q filed with the SEC on August 7, 2015, which are incorporated herein by reference. The Company specifically disclaims any obligation to update these forward-looking statements.

About SymBio

SymBio Pharmaceuticals Ltd. was established in March, 2005, by President and CEO, Fuminori Yoshida, who previously served concurrently as Corporate VP of Amgen Inc. and founding President of Amgen Japan. The company's underlying corporate mission is "delivering hope to patients in need" as it aspires to be a leading global biopharmaceutical company dedicated to addressing underserved medical needs.