Merck Highlights Ongoing Commitment to Developing Medicines Targeting Infectious Disease at 52nd Annual ICAAC

Release Date:
Wednesday, September 12, 2012 8:08 am EDT

Terms:
Research and Development News

Dateline City:
WHITEHOUSE STATION, N.J.

Merck (NYSE: MRK), known outside the United States and Canada as MSD, today reaffirmed its longstanding commitment to discovering and developing novel medicines in the global fight against infectious disease, and highlighted scientific data presented by researchers at the 52nd Annual Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) being held in San Francisco.

Building on its rich heritage, Merck scientists and their collaborators will present results from early-phase studies of novel investigational anti-infective drug candidates and new investigational formulations of a currently marketed product. Researchers will also present the latest findings from the Merck-sponsored Study for Monitoring Antimicrobial Resistance Trends (SMART), which has been tracking trends in antibiotic susceptibility of bacterial isolates collected from patients in different regions of the world since 2002.

"Infectious disease remains one of the most urgent global public health challenges we face, and growing resistance to some current therapies underscores the critical need for continued innovation in developing new medicines," said Robin Isaacs, M.D., vice president, infectious disease clinical research, Merck Research Laboratories. "At the same time, we must also look for ways to extend the utility of the therapies we have today."

At ICAAC, pharmacokinetic and safety data will be presented for two new investigational formulations of Merck's antifungal agent posaconazole: a once-daily solid oral tablet formulation and a once-daily intravenous (IV) formulation. Phase III studies with these new formulations are ongoing. NOXAFIL® (posaconazole) Oral Suspension is indicated for prophylaxis of invasive Aspergillus and Candida infections in patients, 13 years of age and older, who are at high risk of developing these infections due to being severely immunocompromised, such as hematopoietic stem cell transplant recipients with graft-versus-host disease or those with hematologic malignancies with prolonged neutropenia from chemotherapy. NOXAFIL also is indicated for the treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole.

In addition, researchers will present data for MK-7655, an investigational beta-lactamase inhibitor currently in Phase II development in combination with a marketed antibiotic. This combination has shown activity against bacterial isolates with class A and class C beta-lactamase-producing capabilities; such isolates, which are routinely resistant to many different classes of antibiotics, are increasing in prevalence worldwide.

Researchers will also present data from the SMART (Study for Monitoring Antimicrobial Resistance Trends) program. SMART was initiated by Merck in 2002 to monitor the in vitro susceptibility of clinical isolates to 12 commonly used antibiotics in different regions of the world to monitor changing trends in antibiotic susceptibility. SMART currently monitors antibiotic activity against gram-negative bacteria isolated from two common types of infection: intra-abdominal and urinary tract infections. Isolates have been collected from patients with complicated intra-abdominal infections since 2002 and from patients with complicated urinary tract infections since 2010. Among the new findings presented at ICAAC, researchers have found that there has been an increase in the percentage of common bacteria that produce enzymes called extended-spectrum beta-lactamasases, or ESBLs. ESBL-producing bacteria are often less susceptible to the activity of many of the currently available antibiotics.

Key data presentations at ICAAC 2012

**Antifungal**

**A-1934** Phase 1B Study of the Pharmacokinetics and Safety of Posaconazole (POS) Solid Oral Tablet in Patients at Risk for Invasive Fungal Infection (IFI); Duarte, RF et al.; poster session Halls A-C; Wednesday, Sept. 12, 2012, 9:15 AM - 11:15 AM

**A-1935** Effect of Concomitant Medications Affecting Gastric pH and Motility on Posaconazole (POS) Tablet Pharmacokinetics (PK); Kraft, WK et al.; poster session Halls A-C; Wednesday, Sept. 12, 2012, 9:15 AM - 11:15 AM

**A-1946a** Phase 1B Study of the Pharmacokinetics (PK) and Safety of Posaconazole (POS) IV in Patients (Pts) at Risk for Invasive Fungal Infection (IFI); Maertens, J et al.; poster session Halls A-C; Wednesday, Sept. 12, 2012, 9:15 AM - 11:15 AM

**Antibacterial**

**A-1934** Phase 1B Study of the Pharmacokinetics and Safety of Posaconazole (POS) Solid Oral Tablet in Patients at Risk for Invasive Fungal Infection (IFI); Duarte, RF et al.; poster session Halls A-C; Wednesday, Sept. 12, 2012, 9:15 AM - 11:15 AM

**A-1935** Effect of Concomitant Medications Affecting Gastric pH and Motility on Posaconazole (POS) Tablet Pharmacokinetics (PK); Kraft, WK et al.; poster session Halls A-C; Wednesday, Sept. 12, 2012, 9:15 AM - 11:15 AM

**A-1946a** Phase 1B Study of the Pharmacokinetics (PK) and Safety of Posaconazole (POS) IV in Patients (Pts) at Risk for Invasive Fungal Infection (IFI); Maertens, J et al.; poster session Halls A-C; Wednesday, Sept. 12, 2012, 9:15 AM - 11:15 AM
A-008 MK-7655, A Novel β-lactamase Inhibitor (Bli), Elicits a Prolonged Post-Inhibitor Effect in P. Aeruginosa; Young, Ket al.; poster session Halls A-C; Sunday, Sept. 9, 11:30 AM - 1:30 PM

A-009 A Phase I Study Evaluating the Single-Dose Safety, Tolerability and Pharmacokinetics of an Intravenous Beta-Lactamase Inhibitor in Healthy Elderly Male, Elderly Female and Young Female Volunteers; James, P et al.; poster session Halls A-C; Sunday, Sept. 9, 11:30 AM - 1:30 PM

A-010 Pharmacokinetics of MK-7655, a Novel Beta-lactamase Inhibitor (Bli), in Combination with Imipenem/Cilastatin (IPM/CIL) in Subjects with Impaired Renal Function; Rizk, ML et al.; poster session Halls A-C; Sunday, Sept. 9, 11:30 AM - 1:30 PM

D-767 Broth Microdilution Quality Control Ranges for Testing the Imipenem/MK-7655 Combination (IMK) Against Key Organism Groups; Deane, Jet al.; poster session Halls A-C; Monday, Sept. 10, 11:15 AM - 1:15 PM

E-192 Activity of MK-7655 with Imipenem vs. β-Lactamase Producers; Livemore, DM et al.; poster session Halls A-C; Sunday, Sept. 9, 12, 11:30 AM - 1:30 PM

SMART Study

C2-100 Trends in Susceptibility and ESBL Production for Escherichia coli from Intra-abdominal Infections; SMART 2002-2011; Lob, S et al.; poster session Halls A-C; Sunday, Sept. 9, 11:30 AM - 1:30 PM

C2-120 Global Susceptibility and ESBL+ Rates of K pneumoniae from Intra-abdominal Infections - SMART 2011; Badal, R et al.; poster session Halls A-C; Sunday, Sept. 9, 11:30 AM - 1:30 PM


C2-702 In Vitro Susceptibilities of E. coli and K pneumoniae Isolated from Patients with Intra-abdominal Infections in China: Data from the Study for Monitoring Antimicrobial Resistance Trends (SMART) 2002-2011; Wang, W et al.; poster session Halls A-C; Monday, Sept. 10, 11:15 AM - 1:15 PM

L2-2107 Surveillance of Antimicrobial Susceptibility of Aerobic and Facultative Gram-Negative Bacilli Isolated from Patients with Urinary-Tract Infections in China: the 2010-2011 Study for Monitoring Antimicrobial Resistance Trends (SMART); Yang, Q et al.; poster session Halls A-C; Wednesday, Sept. 12, 9:15 AM - 11:15 AM

Selected safety information about NOXAFIL

Contraindications

NOXAFIL is contraindicated in persons with known hypersensitivity to posaconazole, any component of NOXAFIL, or otherazole antifungal agents.

NOXAFIL is contraindicated with sirolimus. Concomitant administration of NOXAFIL with sirolimus increases the sirolimus blood concentrations by approximately 9-fold and can result in sirolimus toxicity.

NOXAFIL is contraindicated with the CYP3A4 substrates that prolong the QT interval. Concomitant administration of NOXAFIL with the CYP3A4 substrates pimozaide and quinidine may result in increased plasma concentrations of these drugs, leading to QTc prolongation and rare occurrences of torsades de pointes.

NOXAFIL is contraindicated with HMG-CoA reductase inhibitors that are primarily metabolized through CYP3A4 (e.g., atorvastatin, lovastatin, and simvastatin) as increased plasma concentration of these drugs can lead to rhabdomyolysis.

NOXAFIL is contraindicated with ergot alkaloids. NOXAFIL may increase the plasma concentrations of ergot alkaloids (ergotamine and dihydroergotamine) which may lead to ergotism.

Warnings and Precautions

Concomitant administration of NOXAFIL with cyclosporine or tacrolimus increases the whole blood trough concentrations of these calcineurin inhibitors. Nephrotoxicity and leukoencephalopathy (including isolated deaths) have been reported in clinical efficacy studies in patients with elevated cyclosporine concentrations. Frequent monitoring of cyclosporine or tacrolimus whole blood trough concentrations should be performed during and at discontinuation of NOXAFIL treatment and the tacrolimus or cyclosporine dose adjusted accordingly.

Some azoles, including NOXAFIL, have been associated with prolongation of the QT interval on the electrocardiogram. In addition, rare cases of torsades de pointes have been reported in patients taking NOXAFIL. NOXAFIL should be administered with caution to patients with potentially proarrhythmic conditions. Rigorous attempts to correct potassium, magnesium, and calcium should be made in these patients before starting NOXAFIL.

Hepatic reactions (e.g., mild to moderate elevations in ALT, AST, alkaline phosphatase, total bilirubin, and/or clinical hepatitis) have been reported in clinical trials. The elevations in liver function tests were generally reversible on discontinuation of therapy, and in some instances these tests normalized without drug interruption and rarely required drug discontinuation. Isolated cases of more severe hepatic reactions including cholestasis or hepatic failure including deaths have been reported in patients with serious underlying medical conditions (e.g., hematologic malignancy) during treatment with NOXAFIL. Liver function tests should be evaluated at the start of and during the course of therapy. Discontinuation of NOXAFIL must be considered if clinical signs and symptoms consistent with liver disease develop that may be attributable to NOXAFIL.

Concomitant administration of NOXAFIL with midazolam increases the midazolam plasma concentrations by approximately 5-fold. Increased plasma midazolam concentrations could potentiate and prolong hypnotic and sedative effects. Patients must be monitored closely for adverse effects associated with high plasma concentrations of midazolam and
benzodiazepine receptor antagonists must be available to reverse these effects.

NOXAFIL has been shown to interact with several medications, including drugs that suppress the immune system, and these reactions may be serious. NOXAFIL is also a strong inhibitor of CYP3A4. Therefore, plasma concentrations of drugs predominantly metabolized by CYP3A4 may be increased by NOXAFIL. The product label should be consulted when other drugs are prescribed with NOXAFIL.

Co-administration of NOXAFIL with rifabutin, phenytoin, efavirenz, cimetidine and esomeprazole should be avoided unless the benefit outweighs the risk. Monitoring for toxicity and adverse events is recommended when tacrolimus, cyclosporine, ritonavir, atazanavir, vinca alkaloids, and calcium channel blockers and rifabutin are co-administered with NOXAFIL. Dosage adjustments should also be considered when tacrolimus, cyclosporine, vinca alkaloids, calcium channel blockers, and phenytoin are administered with NOXAFIL. Monitor plasma concentrations when co-administering digoxin, phenytoin, tacrolimus and cyclosporine with NOXAFIL. Monitor for breakthrough fungal infections when co-administering metoclopramide, fosamprenavir, rifabutin, phenytoin, cimetidine and esomeprazole with NOXAFIL.

The safety and effectiveness of NOXAFIL in patients below the age of 13 years old have not been established.

Adverse Reactions

The most common adverse reactions (>30%) in the prophylaxis clinical studies were fever, diarrhea, and nausea.

In clinical studies of OPC and refractory OPC (rOPC), the adverse reactions were more common in the pool of patients with rOPC. The most common adverse reactions (>5%) in the controlled OPC pool were diarrhea, nausea, headache, vomiting, and fever. The most common adverse reactions (>20%) in the rOPC pool were fever, diarrhea, nausea, vomiting, and coughing. The most common serious adverse reactions in rOPC patients included fever (13%) and neutropenia (10%).

About Merck

Today's Merck is a global healthcare leader working to help the world be well. Merck is known as MSD outside the United States and Canada. Through our prescription medicines, vaccines, biologic therapies, and consumer care and animal health products, we work with customers and operate in more than 140 countries to deliver innovative health solutions. We also demonstrate our commitment to increasing access to healthcare through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on Twitter, Facebook and YouTube.

Forward-Looking Statement

This news release includes “forward-looking statements” within the meaning of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Such statements may include, but are not limited to, statements about the benefits of the merger between Merck and Schering-Plough, including future financial and operating results, the combined company’s plans, objectives, expectations and intentions and other statements that are not historical facts. Such statements are based upon the current beliefs and expectations of Merck’s management and are subject to significant risks and uncertainties. Actual results may differ from those set forth in the forward-looking statements.

The following factors, among others, could cause actual results to differ from those set forth in the forward-looking statements: the possibility that all of the expected synergies from the merger of Merck and Schering-Plough will not be realized, or will not be realized within the expected time period; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; Merck’s ability to accurately predict future market conditions; dependence on the effectiveness of Merck’s patents and other protections for innovative products; and the exposure to litigation and/or regulatory actions.

Merck undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise. Additional factors that could cause results to differ materially from those described in the forward-looking statements can be found in Merck’s 2011 Annual Report on Form 10-K and the company’s other filings with the Securities and Exchange Commission (SEC) available at the SEC’s Internet site (www.sec.gov).

NOXAFIL® is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Whitehouse Station, N.J., USA.


Language: English

Ticker Slug:
Ticker: MRK
Exchange: NYSE