



NEWS RELEASE

Results of Phase 2 Study of Merck's Investigational Beta-Lactamase Inhibitor Relebactam in Combination with Imipenem/Cilastatin Presented at ASM Microbe

6/20/2016

Pivotal Phase 3 Studies Ongoing in Treatment of Serious Bacterial Infections

Merck (NYSE:MRK), known as MSD outside the United States and Canada, today announced that a Phase 2 study of relebactam, the company's investigational beta-lactamase inhibitor, in combination with imipenem/cilastatin (an approved carbapenem antibiotic), in patients with complicated urinary tract infections, met its primary endpoint. The addition of relebactam is designed to restore activity of imipenem against certain imipenem-resistant strains of Gram-negative bacteria, including *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* carbapenemase (KPC)-producing Enterobacteriaceae.

The results were presented at the American Society for Microbiology's ASM Microbe 2016 meeting in Boston, June 16-20.

"New medicines are urgently needed to address the growing threat of antibiotic-resistant bacteria," said Dr. Amanda Paschke, director, infectious disease clinical research, Merck Research Laboratories. "We look forward to advancing our Phase 3 clinical program evaluating relebactam in combination with imipenem for use in the treatment of several complicated Gram-negative bacterial infections, and to continue to build on Merck's commitment to addressing infectious diseases."

In this multicenter, double-blind Phase 2 study, 302 adult patients with complicated urinary tract infections (51.7%) or acute pyelonephritis (48.3%) were randomized to receive either relebactam 250mg, relebactam 125mg, or



placebo, each given intravenously (IV) in combination with imipenem/cilastatin (IMI) 500mg every six hours for 4 to 14 days. Efficacy was evaluated at discontinuation of IV therapy (DCIV), early follow-up, and late follow-up. The primary endpoint was the proportion of microbiologically evaluable patients with a favorable microbiological response at DCIV, assessed by non-inferiority testing with a 15% margin. Results were similar across treatment groups: relebactam 250mg + IMI (95.5%) (n=67), relebactam 125mg + IMI (98.6%) (n=71), and placebo + IMI (98.7%) (n=75). Among microbiologically evaluable patients, 10.5% (n=25) had imipenem-resistant Gram-negative infections at baseline.

Safety analysis focused on adverse events occurring while on intravenous study therapy or during the 14 days following the end of therapy in all randomized patients who received at least one dose of intravenous study therapy. The most common adverse events (headache, diarrhea and nausea) occurred at similar rates across treatment groups: relebactam 250mg + IMI (7.1%, 5.1%, 4.0%), relebactam 125mg + IMI (3.0%, 2.0%, 6.1%), and placebo + IMI (4.0%, 4.0%, 4.0%), respectively.

Phase 3 Clinical Program of Relebactam/Imipenem/Cilastatin Ongoing

Two pivotal Phase 3 clinical studies of relebactam in combination with imipenem/cilastatin are currently ongoing and recruiting patients. One study compares treatment with imipenem/relebactam, as a fixed-dose combination, with piperacillin/tazobactam in patients with hospital-acquired bacterial pneumonia or ventilator-associated bacterial pneumonia. The primary hypothesis of this study is that imipenem/relebactam is non-inferior to piperacillin/tazobactam in the incidence rate of all-cause mortality. ([www.ClinicalTrials.gov Identifier: NCT02493764](https://www.ClinicalTrials.gov/ct2/show/study/NCT02493764))

A second study evaluates the efficacy and safety of imipenem/relebactam versus colistimethate sodium in combination with imipenem in the treatment of imipenem-resistant bacterial infections, including those caused by *Pseudomonas aeruginosa* and KPC-producing organisms. Infections evaluated in this study include hospital-acquired bacterial pneumonia, ventilator-associated bacterial pneumonia, complicated intra-abdominal infections and complicated urinary tract infections. ([www.ClinicalTrials.gov Identifier: NCT02452047](https://www.ClinicalTrials.gov/ct2/show/study/NCT02452047))

About Relebactam

Relebactam is an investigational, intravenous, class A and C, beta-lactamase inhibitor currently being evaluated in combination with imipenem/cilastatin for the treatment of certain complicated Gram-negative bacterial infections. In preclinical studies, relebactam administered in combination with imipenem demonstrated antibacterial activity against a broad range of Gram-negative and beta-lactam-resistant pathogens. The U.S. Food and Drug Administration (FDA) has designated this combination as a Qualified Infectious Disease Product (QIDP) with designated Fast Track status for the treatment of hospital-acquired bacterial pneumonia, ventilator-associated

bacterial pneumonia, complicated intra-abdominal infections and complicated urinary tract infections.

About Merck

For 125 years, Merck has been a global health care 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 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 health care through far-reaching policies, programs and partnerships. For more information, visit www.merck.com and connect with us on **Twitter**, **Facebook**, **YouTube** and **LinkedIn**.

Forward-Looking Statement of Merck & Co., Inc., Kenilworth, N.J., USA

This news release of Merck & Co., Inc., Kenilworth, N.J., USA (the “company”) includes “forward-looking statements” within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These statements are based upon the current beliefs and expectations of the company’s management and are subject to significant risks and uncertainties. There can be no guarantees with respect to pipeline products that the products will receive the necessary regulatory approvals or that they will prove to be commercially successful. If underlying assumptions prove inaccurate or risks or uncertainties materialize, actual results may differ materially from those set forth in the forward-looking statements.

Risks and uncertainties include but are not limited to, general industry conditions and competition; general economic factors, including interest rate and currency exchange rate fluctuations; the impact of pharmaceutical industry regulation and health care legislation in the United States and internationally; global trends toward health care cost containment; technological advances, new products and patents attained by competitors; challenges inherent in new product development, including obtaining regulatory approval; the company’s ability to accurately predict future market conditions; manufacturing difficulties or delays; financial instability of international economies and sovereign risk; dependence on the effectiveness of the company’s patents and other protections for innovative products; and the exposure to litigation, including patent litigation, and/or regulatory actions.

The company 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 the company’s 2015 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).

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