

# Jan7Pivotal Phase 3 Study of Merck's Investigational Beta-Lactamase Inhibitor Relebactam in Combination with Imipenem/Cilastatin Demonstrated Favorable Overall Response Against Certain Imipenem–Non-Susceptible Bacterial Infections

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Company Plans to Submit New Drug Application in the United States

Results Presented at ECCMID 2018 Annual Meeting

KENILWORTH, N.J., April 22, 2018 – Merck (NYSE: MRK), known as MSD outside the United States and Canada, today announced that a pivotal Phase 3 study of relebactam, the company's investigational beta-lactamase inhibitor, in combination with imipenem/cilastatin, demonstrated a favorable overall response in the treatment of certain imipenem–non-susceptible bacterial infections, the primary endpoint, with lower treatment-emergent nephrotoxicity (kidney toxicity), a secondary endpoint, compared to a Colistin (colistimethate sodium) plus imipenem regimen.

Based on these results, the company plans to submit a New Drug Application to the U.S. Food and Drug Administration seeking regulatory approval of a fixed-dose combination of imipenem/cilastatin and relebactam.

"Infections caused by Gram-negative bacteria continue to be a major problem for hospitalized patients. The prevalence of carbapenem-resistant pathogens is increasing globally, highlighting the need for effective new antibacterial agents with Gram-negative coverage," said Dr. Amanda Paschke, senior principal scientist, infectious disease clinical research, Merck Research Laboratories. "We look forward to advancing relebactam in combination with imipenem/cilastatin, and continuing to build on Merck's longstanding commitment in the fight against infectious disease."

Results of the RESTORE-IMI 1 study were presented at the 28th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) 2018 meeting in Madrid, Spain, April 21-24. The study was a multicenter, randomized, double-blind, comparator-controlled trial comparing the efficacy and safety of imipenem/cilastatin/relebactam (IMI/REL) versus Colistin plus imipenem/cilastatin (COL+IMI) in patients with imipenem-non-susceptible bacterial infections. Patients with hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP), complicated intra-abdominal infection (cIAI), or complicated urinary tract infection (cUTI) caused by one or more imipenem-non-susceptible (but Colistin- and IMI/REL-susceptible) pathogens, were randomized 2:1 to receive IMI/REL or COL+IMI in a double-blind fashion. Colistin dosing was based on medical literature, and was consistent with recent regulatory guidance. Study therapy duration was to be 5-21 days for cUTI and cIAI, and 7-21 days for HABP/VABP.

The primary endpoint of the study was favorable overall response (defined by relevant endpoints for each different infection type) in the microbiological modified intent-to-treat (mMITT) population (defined as patients having a qualifying baseline pathogen and having received at least one dose of study treatment). Secondary endpoints included favorable clinical response at Day 28, 28-day all-cause mortality, incidence of treatment-emergent nephrotoxicity, and incidence of adverse events.

In the study, 31 of 47 randomized and treated patients met mMITT criteria. Favorable overall response was comparable for the IMI/REL (71.4%; n=15) and COL+IMI (70.0%; n=7) treatment arms. Favorable clinical response at Day 28 was higher in the IMI/REL arm (71.4%; n=15) compared to the COL+IMI (40.0%; n=4) arm, and 28-day all-cause mortality was lower in the IMI/REL arm (9.5%; n=2) vs. COL + IMI (30.0%; n=3), respectively.

Among all treated patients, drug-related adverse events occurred in 16.1% of patients (n=31) in the IMI/REL arm compared to 31.3% of patients (n=16) in the COL+IMI arm. Treatment-emergent nephrotoxicity was lower with IMI-REL (10%; 3/29 patients) compared to COL+IMI (56%; 9/16 patients) (p=0.002).

## Second Pivotal IMI/REL Phase 3 study, RESTORE-IMI 2, ongoing

Merck is conducting a second pivotal Phase 3 clinical study, RESTORE-IMI 2, comparing treatment with imipenem/cilastatin/relebactam, as a fixed-dose combination, versus piperacillin/tazobactam in patients with hospital-acquired bacterial pneumonia or ventilator-associated bacterial pneumonia. The primary hypothesis of

this study is that imipenem/cilastatin/relebactam is non-inferior to piperacillin/tazobactam in the incidence rate of all-cause mortality ([www.ClinicalTrials.gov Identifier: NCT02493764](https://www.ClinicalTrials.gov Identifier: NCT02493764)).

## 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 more than a century, Merck, a leading global biopharmaceutical company known as MSD outside of the United States and Canada, has been inventing for life, bringing forward medicines and vaccines for many of the world's most challenging diseases. 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. Today, Merck continues to be at the forefront of research to advance the prevention and treatment of diseases that threaten people and communities around the world - including cancer, cardio-metabolic diseases, emerging animal diseases, Alzheimer's disease and infectious diseases including HIV and Ebola. For more information, visit [www.merck.com](http://www.merck.com) and connect with us on [Twitter](#), [Facebook](#), [Instagram](#), [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 2017 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](http://www.sec.gov)).

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