



**MERCK**

INVENTING FOR LIFE

DELIVERING ON  
OUR COMMITMENTS:  
**MERCK'S ACTIONS  
TO ADDRESS  
ANTIMICROBIAL  
RESISTANCE**

January 2018

## MERCK'S LONGSTANDING COMMITMENT TO PREVENTING AND TREATING INFECTIOUS DISEASES

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For over 80 years, Merck has played a significant role in vaccine and antibiotic research and development (R&D). Today, Merck is one of only a few large pharmaceutical companies that has continued to pursue R&D to develop new medicines and vaccines that prevent and treat bacterial infections. Our broad portfolio spans both [human](#) and [animal health](#) and includes antibiotics, vaccines and novel approaches to reduce the need for antibiotics. We continue to invest in both early- and late-stage R&D.

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Since 2014, Merck has introduced two novel antibiotics, [SIVEXTRO® \(tedizolid\)](#) and [ZERBAXA® \(ceftolozane/tazobactam\)](#), as well as [ZINPLAVA® \(bezlotoxumab\)](#), a medicine used to reduce the recurrence of *Clostridium difficile* infection (CDI) in adults receiving antibacterial treatment of CDI and are at high risk of CDI recurrence. We continue to invest in further R&D to study the effectiveness of SIVEXTRO® and ZERBAXA® for the treatment of hospital-acquired bacterial pneumonia/ventilator-associated bacterial pneumonia.

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We are currently evaluating [MK-7655a](#), a combination of relebactam, a novel investigational  $\beta$ -lactamase inhibitor, and imipenem/cilastatin, an approved carbapenem antibiotic, in Phase 3 trials for the treatment of serious infections including complicated intra-abdominal infections, complicated urinary tract infections and hospital-acquired pneumonia.

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Merck is currently evaluating [V114](#), an investigational 15-valent pneumococcal vaccine designed to protect against *Streptococcus pneumoniae* infection and expand coverage beyond what is currently available.

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Merck is making significant investments to support antimicrobial stewardship (AMS) to improve patient outcomes and slow the development of AMR. Our company supports global AMR surveillance programs, the development of new diagnostic tools to detect resistance, expanded use of vaccines and AMS programs around the world.

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Merck is collaborating with hospitals around the world to develop and implement patient-centered AMS programs. Merck has collaborated with over [1,100 hospitals](#) in [28 countries](#) to develop and implement AMS programs since 2008. More than [10,000 health care providers](#) have been trained and over [500 tailored AMS focused hospital treatment pathways](#) have been implemented based on local hospital microbiological data.

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Merck's [Study for Monitoring Antimicrobial Resistance Trends \(SMART\)](#) is one of the world's largest AMR surveillance studies. Since its initiation in 2002, SMART has collected over [200,000 isolates](#) from [217 sites](#) in [63 countries](#) around the world. The company has collaborated with [OpGen, Inc.](#) to develop new rapid diagnostics to detect resistant bacteria. Merck will provide OpGen with access to its full archive of bacterial pathogens gathered through SMART. The company also makes these data available to the scientific community through the SMART database online.

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Merck Animal Health is commercializing or developing vaccines for all 15 prioritized animal diseases where vaccines can reduce antibiotic use in animals, as recognized by the [World Organization for Animal Health \(OIE\)](#). Producing over [90 billion animal health vaccine doses each year](#), Merck Animal Health is one of the [world's largest manufacturers of vaccines for animals](#). We have multiple initiatives to help farmers protect animal health and ensure a safe food supply.

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## DELIVERING ON OUR COMMITMENTS

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Recognizing that collective action is needed to address the growing global health threat of AMR, Merck has joined several industry initiatives. In January 2016, the company and over 100 biopharmaceutical, generic medicines and diagnostic companies, as well as key trade associations, launched a [joint declaration](#) at the World Economic Forum setting out bold commitments and calling for governments and industry to take action against AMR.

At the U.N. High-Level Meeting on AMR in September 2016, Merck and 12 other leading companies released the [Industry Roadmap for Progress on Combating AMR](#). This document laid out additional commitments to reduce the environmental impact from the production of antibiotics, help ensure antibiotics are only used by those who need them, improve access to antibiotics globally, and explore new opportunities for collaborations between the industry and public sector.

We are a founding board member of the [AMR Industry Alliance](#), comprised of signatories of these documents, to drive and measure industry progress against our commitments.

In October 2017, Merck Animal Health worked with [HealthforAnimals](#) to develop [global animal health commitments](#) related to the responsible use of antibiotics and investment into other areas of animal health and welfare.

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**Merck is committed to playing its part in the global response to AMR. We are working to deliver on these commitments. Four key areas of focus include:**



**ADVANCING  
ANTIBIOTIC  
R&D THROUGH  
COLLABORATIONS**



**IMPROVING  
APPROPRIATE  
ACCESS TO  
ANTIBIOTICS**



**REDUCING THE  
POTENTIAL  
IMPACT FROM  
THE PRODUCTION  
OF ANTIBIOTICS**



**ENSURING  
PROMOTIONAL  
ACTIVITIES  
SUPPORT AMS**

## ADVANCING ANTIBIOTIC R&D THROUGH COLLABORATIONS

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In spite of significant scientific, regulatory and economic challenges, Merck remains committed to advancing new vaccines and therapies to prevent and treat serious bacterial infections and fungal diseases with an unmet medical need. The company has collaborations spanning discovery through late-stage clinical development.

**Merck is collaborating with Prokaryotics, a small biotechnology company comprised of internationally renowned academics and collaborators, to develop, manufacture, and commercialize a collection of early pre-clinical programs and compounds with potential applications as novel antibiotics targeting Gram-positive and Gram-negative bacterial cell envelope enzymes.**

**Nearly 200,000 people die each year from multi-drug resistant tuberculosis (TB) and new treatments are desperately needed. Through the TB Drug Accelerator Program, Merck is sharing compound libraries and relevant data with scientists around the world. To date, almost 3 million small molecules have been screened for activity. In collaboration with others, we are further evaluating several candidates identified through initial screening.**

In addition to our own antimicrobial research efforts, Merck also collaborates with scientists worldwide. Through our Merck Innovation Network (MINt), we actively work with scientists to investigate novel therapeutic targets and develop novel tools and technologies. Merck has a number of ongoing collaborations with scientists at leading universities.

To facilitate scientific exchange, Merck scientists published approximately 150 peer-reviewed articles on antimicrobial-related studies (antibacterial and antifungal) in scientific journals in 2016.

## IMPROVING APPROPRIATE ACCESS TO ANTIBIOTICS

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We work to enhance affordable access to our new and existing antibiotics for patients who need them. We recognize the complex nature of expanding access to antibiotics globally, given the challenges of ensuring appropriate use and reducing the development of resistance. Merck is working to expand access to the antibiotic and antifungal medicines in our portfolio within the context of AMS.

We are working to achieve broad registration for our antibiotic and antifungal products. For example, just three years after U.S. Food and Drug Administration (FDA) approval, our most recently approved antibiotic, ZERBAXA® (ceftolozane/tazobactam), has been registered in nearly 60 countries with over 20 additional pending submissions; more than 30 of these are in low- and middle-income countries. For some of our older antimicrobial products like PRIMAXIN® (imipenem/cilastatin), Merck holds marketing authorizations in over 100 countries, including several low-income countries. As noted above, Merck is also supporting hospitals all over the world, particularly in developing countries, to strengthen their AMS programs. These efforts directly support appropriate use and access to antibiotics.

The company also continues to work with international organizations, governments and other stakeholders to identify and address specific access, market sustainability and supply bottlenecks for existing antibiotics, diagnostics and vaccines. In December 2016, Merck provided independent grants to:

**The Center for Disease Dynamics, Economics & Policy's Global Antibiotic Resistance Partnership to support expansion of its work to support the development of actionable policy proposals on AMR in low- and middle-income countries.**

**Florida International University to work with the Pan American Health Organization to develop regional guidelines for implementing AMS programs in Latin America and the Caribbean. These efforts aim to optimize both inpatient and ambulatory antimicrobial prescription practices.**

## REDUCING THE POTENTIAL IMPACT FROM THE PRODUCTION OF ANTIBIOTICS

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Merck is committed to understanding and managing the environmental impacts of our products, including the potential impact from the production of antibiotics. Over the past several years, we have committed over \$100 million to a water-infrastructure improvement initiative to install Active Pharmaceutical Ingredient (API)-treatment technology at our facilities. This assures that factory discharges do not contain residual pharmaceutical products that may present a risk to human health or the environment.

Merck is working to deliver on the commitments made in the [\*AMR Industry Roadmap\*](#) related to reducing the environmental impact from the production of antibiotics. We are currently reviewing the operations of our third-party suppliers to assess good practice in controlling releases of antibiotics into the environment. Merck is also working with other [\*AMR Industry Roadmap\*](#) signatories and key stakeholders, including independent technical experts, to establish a [common framework](#) for managing antibiotic discharge, develop a mechanism to transparently demonstrate that our supply chains meet the standards in this framework, and establish science-driven, risk-based targets for discharge concentrations.

## ENSURING PROMOTIONAL ACTIVITIES SUPPORT AMS

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In the 2016 *AMR Industry Roadmap*, we committed to “by the end of 2017, examine our promotional activities to ensure they align with the goal of advancing stewardship and eliminate those that do not to protect the utility of antibiotics by encouraging their correct use.” Based on guidelines from relevant organizations, including the World Health Organization (WHO) and U.S. Centers for Disease Control and Prevention (CDC), Merck developed a framework of AMS principles to guide the review of its promotional materials.

In September 2017, Merck developed and added a section on this framework to the mandatory e-learning training for all of the company’s certified medical reviewers. Merck is also taking steps to strengthen internal capacity to support AMS through new training requirements for all relevant employees, including promotion managers and brand teams working on antibiotics and antifungals.



**“ Merck remains deeply committed to working with governments, health care providers and others to drive antibiotic innovation, promote appropriate use and enhance access for patients. ”**

**– Kenneth C. Frazier, Chairman and Chief Executive Officer**





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

This document 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 2016 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)).