

Sustainable models to overcome the challenging economics of antimicrobial discovery and development

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

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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).

Meeting the Challenge of AMR



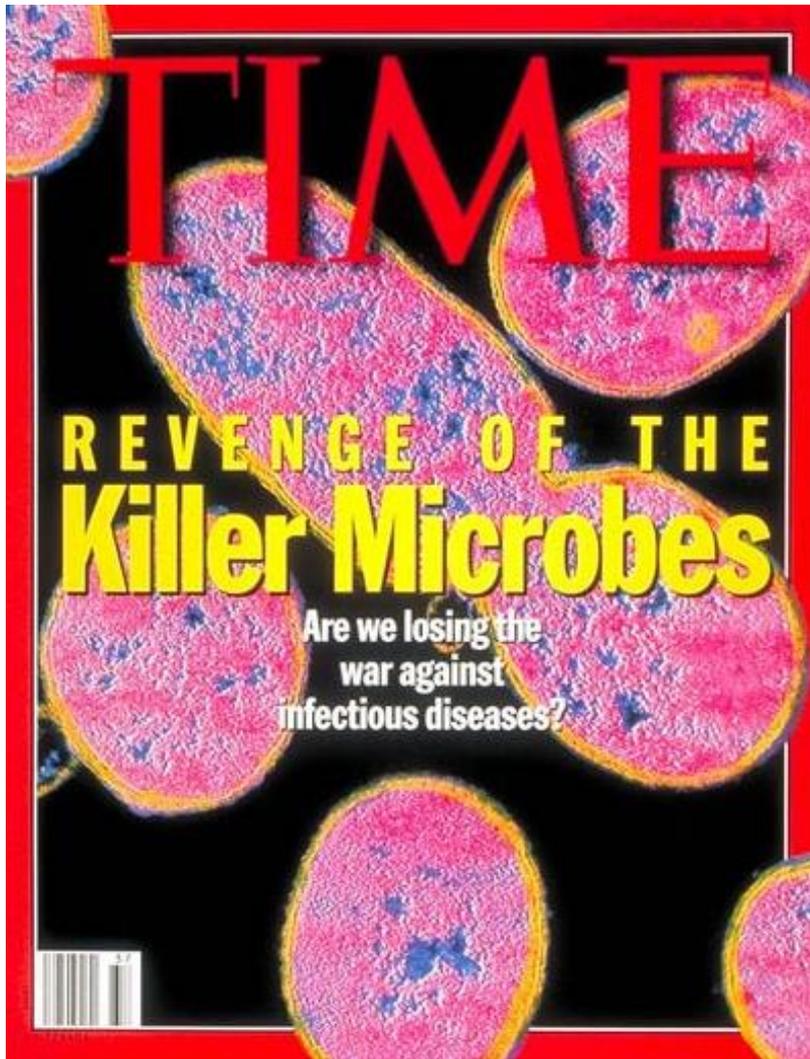
Speed up antimicrobial discovery and development

- New research and targets
- Novel vaccines, antibiotics, and alternatives
- Diagnostics
- Novel economic models



Slow down the emergence of resistance

- **Coordinated global effort**
 - Infection prevention
 - Diagnosis and surveillance
 - Antimicrobial stewardship
 - Prevent transmission
- **OneHealth + Ecological approach**



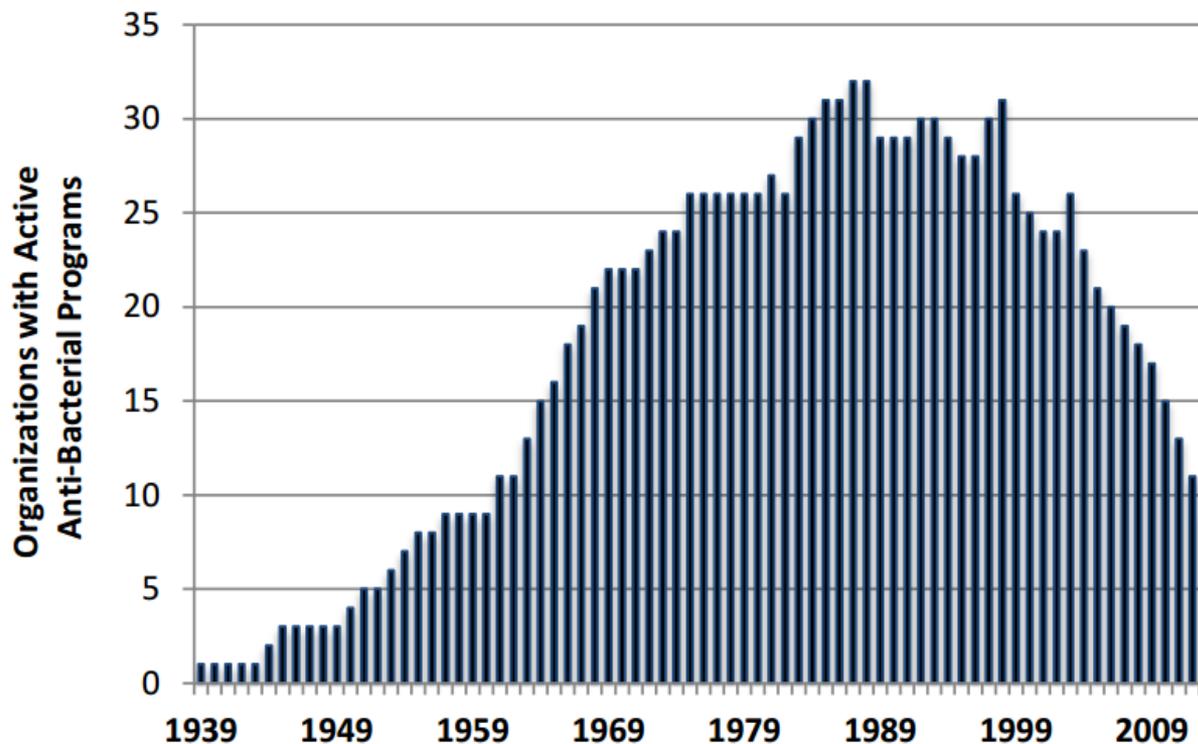
September 12, 1994



September 22, 2016

Decreased Activity in Antibiotic R&D

Active Corporate Antimicrobial Programs



Adapted from: Kinch MS et al. *Drug Discov Today* 2014; 19(9):1283-7

Antibiotic development presents significant challenges



SCIENTIFIC

Bacteria are resilient and constantly evolving

Narrow “therapeutic window”



DEVELOPMENT & REGULATORY

Complex regulatory pathways

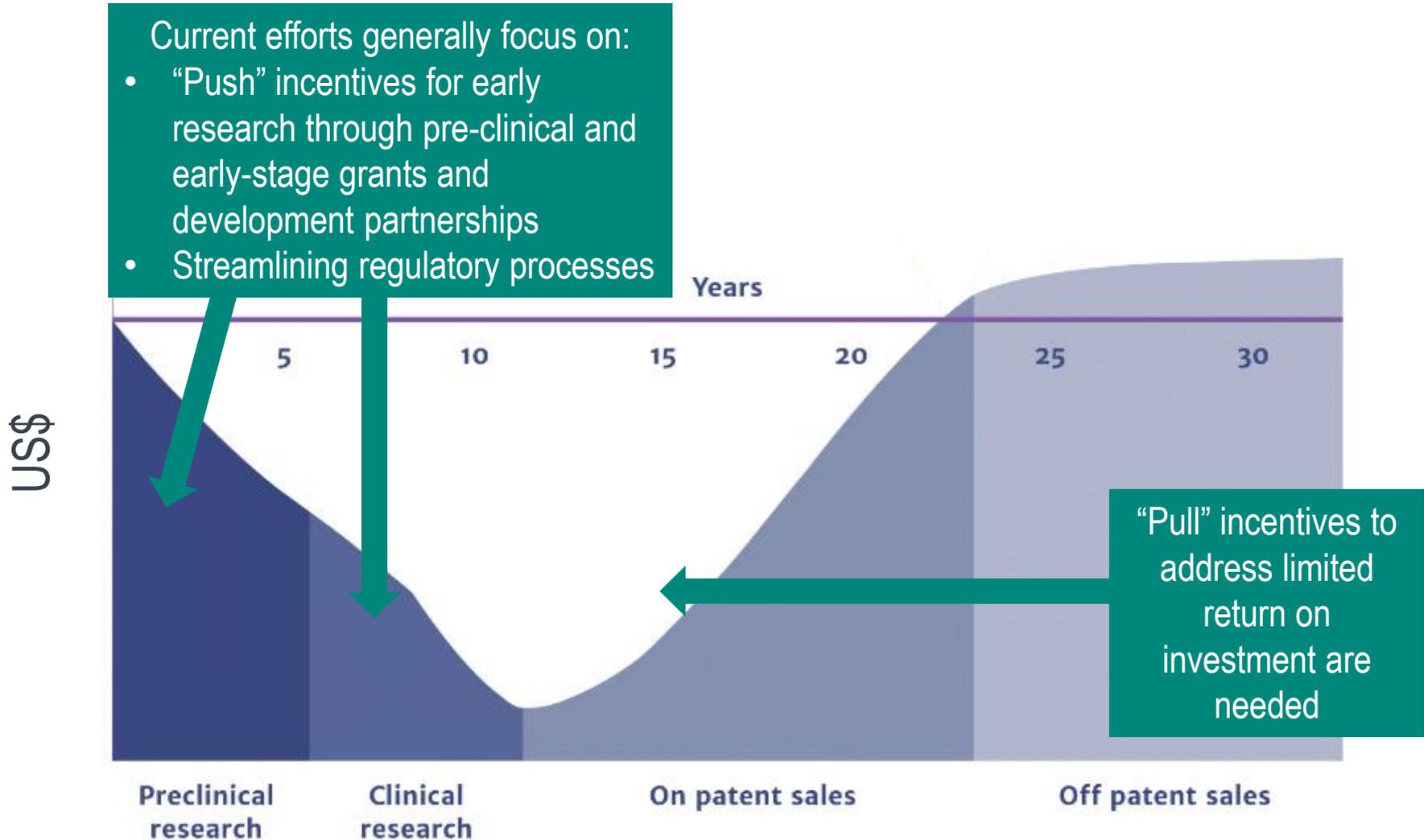
“Non-inferiority” clinical trials



ECONOMIC

Limited returns relative to other therapeutic areas

Challenging Economics of Current Model for Antibiotics



Multi-stakeholder efforts will be needed to deliver on the challenges outlined in the WHO Global Action Plan on AMR



IMPROVE
AWARENESS AND
UNDERSTANDING
OF AMR



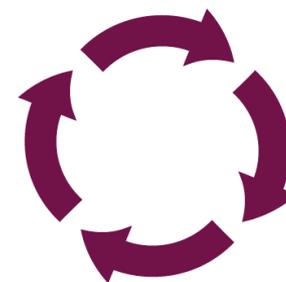
STRENGTHEN
SURVEILLANCE
AND RESEARCH



REDUCE THE
INCIDENCE
OF
INFECTIONS



OPTIMIZE
USE OF
ANTIMICROBIAL
AGENTS



ENSURE
SUSTAINABLE
INVESTMENT

The Private Sector Has an Important Role in Addressing AMR

Davos Declaration (January 2016) – over 100 companies and associations committed to:

- Increase investment in R&D
- Reduce resistance through appropriate stewardship
- Improve access to antibiotics and vaccines
- Called on governments to create a sustainable and predictable market

DECLARATION BY THE PHARMACEUTICAL, BIOTECHNOLOGY AND DIAGNOSTICS INDUSTRIES ON COMBATING ANTIMICROBIAL RESISTANCE

January 2016

Antimicrobials, and specifically antibiotics, play a crucial role in modern medicine. These precious medicines are often taken for granted and are not only necessary to treat life-threatening infections, but are also vital to underpin most common surgical procedures and many chronic treatments such as chemotherapy and HIV and transplant medicines. They also play a crucial role in the health of animals.

The increase in bacterial resistance to antibiotics has been dramatic, and combating this growth is a top priority for global policy and public health. There is a particular concern that antibiotics are losing effectiveness faster than they are being replaced by new, innovative drugs, including both antibiotics and alternative non-antibiotic approaches to treating and preventing infections.

This innovation gap has been examined extensively and is widely acknowledged to be the result of a combination of scientific as well as commercial barriers that have impeded antibiotic development over a number of years. The scientific difficulties are formidable and traditional R&D approaches have largely failed; companies, private and public, around the world have invested billions of dollars over the last 20 years to discover new antibacterials, yet no new class of antibiotic for Gram-negative infections has reached approval in over 40 years.

This situation poses a unique set of challenges. We will always need a supply of innovative new antibiotics, all antibiotics need to be used cautiously to conserve their effects and, in many countries, we still need to improve access to existing antibiotics.

We welcome the economic analysis of Jim O'Neill's Review on Antimicrobial Resistance (AMR), which quantifies both the costs and investments needed. The challenges are clearly substantial and call for transformational changes from many stakeholders. The pharmaceutical, biotechnology, and diagnostics industries have an important role to play, and we are committed to doing our part. Leadership from other sectors is also required, and we welcome the initiative of the Review on AMR, as well as the attention of governments and politicians world-wide (including the recent G7 Berlin declaration), and the leadership of key international organizations (WHO, OIE, FAO, ECDC, US CDC), public funding bodies (NIH, BARDA, the European Commission, and IMI), and charitable foundations (Wellcome Trust, BMGF, and Pew Charitable Trusts), amongst others.

We similarly welcome those steps already taken by key regulatory authorities around the world, such as the US Food and Drug Administration (FDA) and European Medicines Agency (EMA), to enable antibiotic development in advance of widespread resistance, and we support a continuation of these efforts to ensure greater harmonisation of regulatory processes internationally.

* WHO – World Health Organization; OIE – World Organization for Animal Health; FAO – Food and Agriculture Organization of the United Nations; ECDC – European Centre for Disease Control; US CDC – United States Centers for Disease Control; NIH – US National Institutes of Health; BARDA – US Biomedical Advanced Research and Development Authority; IMI – European Innovative Medicines Initiative; BMGF – Bill & Melinda Gates Foundation.

Roadmap on Progress on Combatting AMR (September 2016) – 13 leading companies committed 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
- Explore new opportunities for collaborations between the industry and public sector

Incentives Are Needed to Promote Antibiotic R&D

There is no “one size fits all” solution

- Mix of “push” and “pull” incentives
- Market-based models that reward successful innovation
- Predictable and sustainable funding mechanisms
- Recognition of societal value of novel antibiotics
- Reduce Tension between cost and stewardship



Actions Needed to Incentivize Antibiotic R&D across the Product Life Cycle

Build on existing mechanisms

- Reimbursement Reform
 - R&D Tax Credits
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Explore novel incentive models

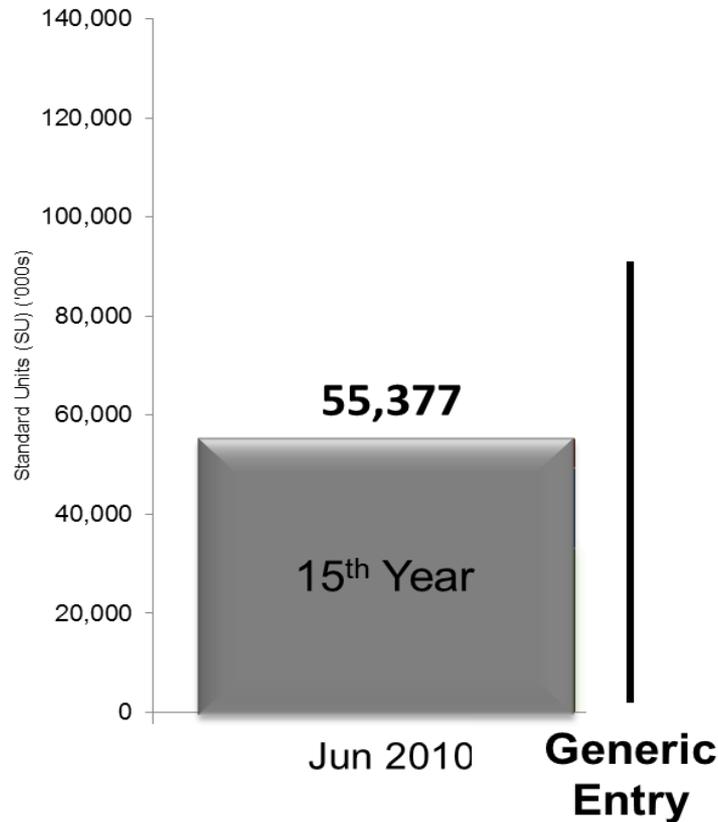
- Reward innovation earlier in product life cycle (competitive return on investment)
- Decrease proportion of manufacturer revenue from volume of sales

These models could include:

- Market entry rewards in key markets
- Transferable exclusivity

The Tension between Cost and Stewardship... A Real World Example

Leading Gram-Negative Molecule

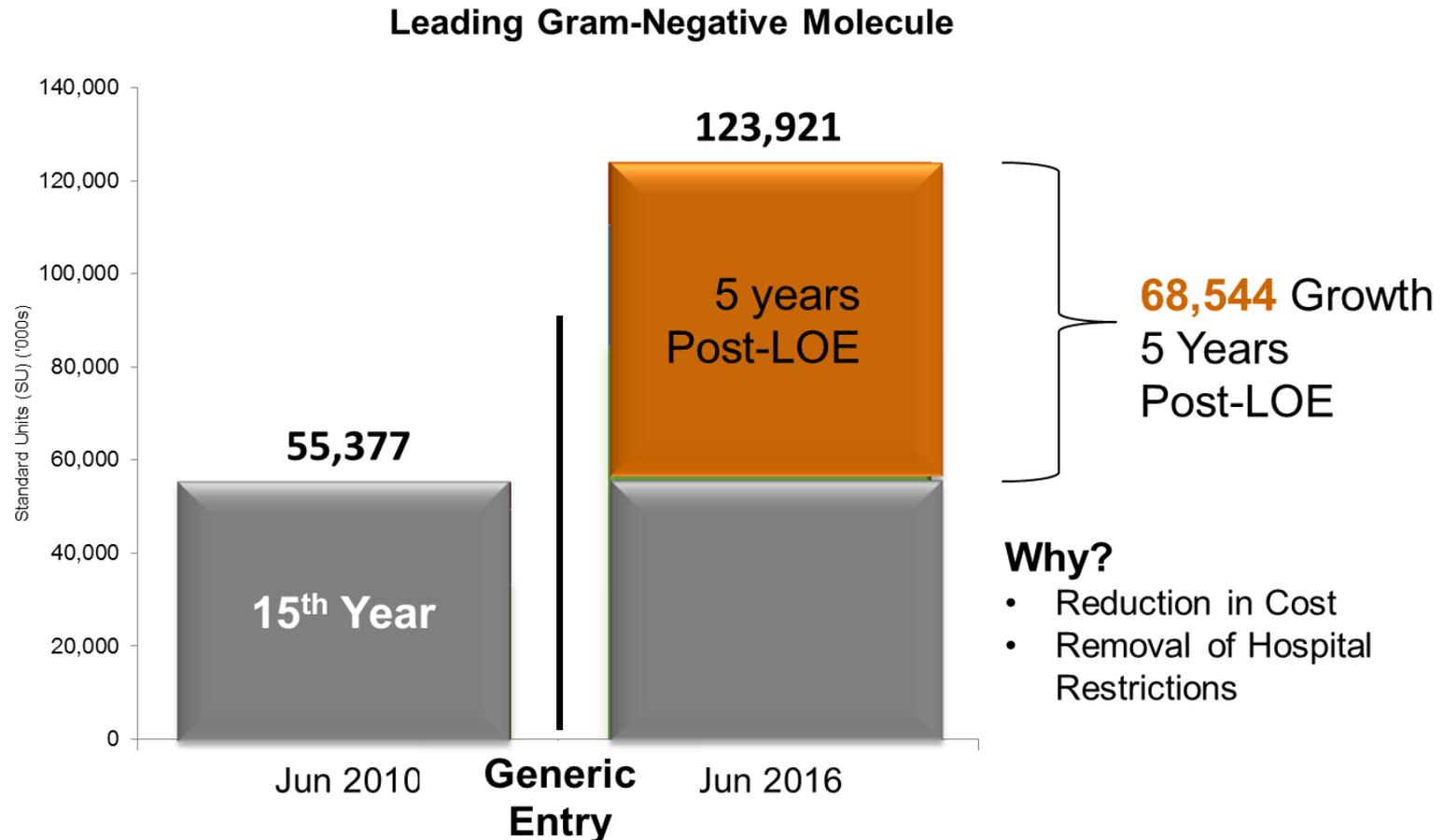


What is the impact of generic entry



Source: QuintilesIMS Midas/ France GERS

The Tension between Cost and Stewardship... A Real World Example



Source: QuintilesIMS Midas/ France GERS

Industry is Committed to Supporting Antimicrobial Stewardship and Enhanced Global Access

- Incentive models can be refined to reinforce antimicrobial stewardship and complement efforts to slow resistance
- Programs to support appropriate use of and access to antibiotics should be developed and implemented in collaboration between industry, governments and others
- Industry committed to work with stakeholders to expand global access to antimicrobials based on success in HIV, vaccines, and reproductive health

The Way Forward

Capitalize on the current momentum to deliver concrete action on AMR for patients worldwide

Collaborate with key stakeholders – governments, industry, civil society and others – to address this critical unmet need

Transform the societal perception of the value of antibiotics, addressing today's reimbursement challenges and advancing novel incentive models