

## Pfizer Policy Position on Antimicrobial Resistance (AMR)

The world is facing a large and growing problem due to infections caused by bacterial pathogens that are becoming increasingly resistant to existing antibiotics. Even minor infections from these organisms can become serious and may lead to death. Medical interventions that depend on antibiotics, such as surgery, are becoming more risky and may become more difficult in the future due to the dwindling pipeline of new antibiotics. The Davos Declaration signed by more than 100 companies and trade associations in January 2016, called for collective action to create a sustainable and predictable market for antibiotics, vaccines and diagnostics, that encourages appropriate use for new and existing treatments. As one of the original signatory companies of the Davos Declaration, Pfizer has joined other pharmaceutical companies in endorsing the Roadmap for Progress on Combating Antimicrobial Resistance. Pfizer endorses a six-part strategy to help address AMR: stewardship, manufacturing, surveillance, vaccination, a supportive regulatory framework, as well as incentives and new business models to support R&D and a sustainable marketplace. Antimicrobial stewardship practices can help to reduce the spread of antimicrobial resistance by applying greater oversight of appropriate antibiotic usage to enable more rational and judicious prescribing practices. Pfizer also believes that effective stewardship of antibiotics includes responsible manufacturing practices. Pfizer is committed to ensuring that the manufacture, use, and disposal of our products, including antibiotics, do not adversely affect human health or the environment. Regional and global surveillance of antibiotic resistance patterns are an important tool to assess both the nature and the scope of the problems as well as the effectiveness of our efforts to combat them. Vaccines serve as a significant tool to help prevent serious, life-threatening infections and therefore contribute to the responsible use of anti-infective drugs; therefore, efforts are needed across stakeholders to strengthen vaccine access and utilization. As part of the global effort to incentivize new antibiotic and vaccine R&D, there is a need to develop a tiered regulatory framework that allows either disease-based or pathogen-based label indications and promotes the most appropriate use of new agents. Renewed focus on anti-infective R&D efforts and support of the development of additional anti-infectives and vaccines will be critical in broadening the tools available to address antimicrobial resistance. Pfizer believes that the speed and the scope of R&D can be incentivized through a mix of novel business models and economic incentives.

### Background

Antimicrobial resistance is a global problem. Unlike almost every other class of drugs, antibiotics drive their own obsolescence by selecting antibiotic-resistant bacteria, even when used appropriately according to guidelines. These drug-resistant infections pose a significant public health and economic burden to healthcare systems due to the limited number of remaining treatment options.

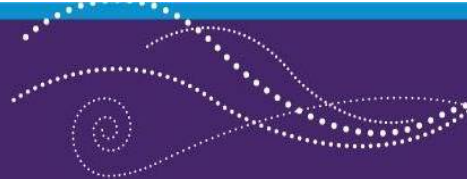
An industry Declaration on Antimicrobial Resistance was announced at the World Economic Forum in Davos, Switzerland on January 20<sup>th</sup> 2016 (Box 1). Pfizer along with over 100 companies and industry trade associations, from 18 different countries, signed the declaration. The Davos Declaration called for collective action to create a sustainable and predictable market for antibiotics, vaccines and point-of-care diagnostics, which encourages appropriate use of new and existing treatments. It also called for coordinated action to improve infection prevention, hygiene, stewardship, and conservation measures.

The pharmaceutical industry recognizes our responsibility and remains committed to playing a significant part in this long-term effort. Given the unique scientific, economic, public health and environmental challenges presented by AMR, collaboration between stakeholders is essential to maximize progress. Pfizer along with other pharmaceutical companies have developed the *Roadmap for Progress on Combating Antimicrobial Resistance*.

There are now several high profile efforts ongoing to address AMR globally. In the U.S., the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) was established in March 2015.<sup>1</sup> The role of PAC-CARB is to help develop and implement the National Strategy for Combating Antibiotic-Resistant Bacteria and the National Action Plan for Combating Antibiotic-Resistant Bacteria.<sup>2</sup>

In addition, the G7 countries released a Declaration on addressing antibiotic resistance at the G7 Health Ministers meeting in Berlin in October 2015.<sup>3</sup> During the Sixty-eighth World Health Assembly in May 2015,





the WHO released the Global Action Plan on Antibiotic Resistance.<sup>4</sup> More recently, the G7 and the G20 have released follow-up statements in support of the global efforts to combat AMR.

### Box 1: Davos Declaration and AMR Industry Roadmap

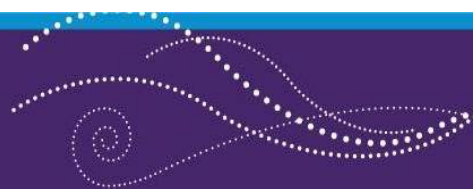
As a leading company supporting the 2016 Davos Declaration<sup>5</sup>, Pfizer welcomes the continued focus on AMR, as well as regional and international debate. This work has established a comprehensive agenda and challenges each key stakeholder group to act and contribute to managing the threat of resistance. As a part of the Roadmap for Progress on Combating Antimicrobial Resistance<sup>6</sup>, there are four key commitments on which the undersigning companies of this document will deliver:

1. Reduce the environmental impact from the production of antibiotics, including a review of the companies' manufacturing and supply chains, and working with stakeholders to establish a common framework for assessing and managing antibiotic discharge.
2. Play an important role ensuring antibiotics are only used by patients who need them, through continued doctor and patient education, examination of the companies' promotional activities, sharing of surveillance data with public health bodies and healthcare professionals, and collaboration with stakeholders to reduce uncontrolled antibiotic purchase.
3. Improve access to current and future antibiotics and vaccines globally, including working with stakeholders to strengthen health systems and address access bottlenecks; establishing new business models that balance access needs, appropriate use and adequate return to companies; and working to reduce the prevalence of substandard/counterfeit antibiotics in high risk markets.
4. Explore new opportunities for open collaborations between industry and the public sector to address challenges in the research and development of new antibiotics, vaccines and diagnostics, recognizing the value these bring to society

### Key Facts and Figures

- According to the World Bank, drug resistant infections could reduce world GDP by 2-3.5% by 2050.<sup>7</sup>
- In the United States, AMR bacteria cause at least 2 million infections each year. CDC estimates that 23,000 people die each year as a direct result of these infections.<sup>8</sup> Many more people die from other conditions that are complicated by an antibiotic-resistant infection.
- The National Action Plan for Combating Antibiotic-Resistant Bacteria states that stewardship practices could prevent 619,000 infections and 37,000 deaths from antibiotic-resistant bacteria in the US over the next five years.<sup>9</sup>
- A U.S. study found the mean cost per patient for hospitals treating methicillin-resistant *Staphylococcus aureus* (MRSA infections) is up to 40% greater than the cost for treating methicillin-sensitive *Staphylococcus aureus* (MSSA).<sup>10</sup>
- The economic burden created by antibiotic resistance in the U.S. is estimated at \$55bn (\$20bn in health service costs and \$35bn in lost productivity) per year.<sup>11</sup>
- Anti-microbial resistant infections cause over 25,000 deaths annually in Europe; hundreds of thousands more die in other regions.<sup>12</sup>
- In the EU, Iceland and Norway, the burden of additional hospital care due to AMR infections was estimated to be approximately €1.6bn in 2012.<sup>13</sup>
- In the EU, the economic burden associated with antibiotic resistant infections is estimated to be about €1.5 billion per year.<sup>14</sup>
- In India, 57% of the infections caused by *Klebsiella pneumoniae* were found to be resistant to one type of last-resort drug in 2014, an increase from 29% in 2008.<sup>15</sup>





## Pfizer AMR Policy Pillars

Pfizer endorses a six-part strategy to help address AMR: stewardship, manufacturing, surveillance, vaccination, regulatory framework, and incentives and new business models to support R&D and a sustainable marketplace:

- **Antimicrobial stewardship** practices can help to reduce the spread of antimicrobial resistance by applying greater oversight of antibiotic usage and enabling more rational and judicious prescribing practices.
- Pfizer is committed to ensuring that the **manufacture**, use, and disposal of our products, including antibiotics, do not adversely affect human health or the environment.
- **Regional and global surveillance** of antibiotic resistance patterns are an important tool to assess both the nature and the scope of the problems as well as the effectiveness of our efforts to combat them.
- **Vaccines** serve as a significant tool to prevent infections and therefore decrease the use of anti-infective drugs.
- A **tiered regulatory framework** that allows either disease-based or pathogen-based label indications and promotes the most appropriate use of new agents.
- **Incentives and novel business models** to support the development of additional anti-infectives and vaccines and strengthen a sustainable marketplace will be critical in broadening the tools available to address antimicrobial resistance.

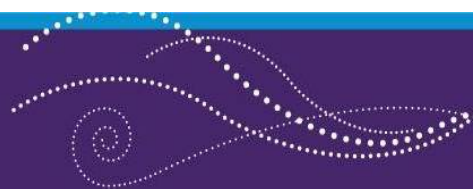
## Pfizer's Position: Antimicrobial Stewardship

Proper management of antibiotic use requires an evidence-based approach, prescriptively applied to discrete health care settings, and the individual patient's situation. Thus, it is necessary for infectious disease specialists, microbiologists, clinical pharmacists and other key caregivers to work together as a team. Pfizer believes that multiple strategies aimed at improving the appropriate use of anti-infectives should be employed at health care institutions and endorses strategies that ensure patient access to the medicines that treat serious infections. Pfizer and other pharmaceutical companies have developed and endorsed antibiotic stewardship strategies through the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). More details can be found on the IFPMA website at: <http://www.ifpma.org/innovation/anti-microbial-resistance.html>. Pfizer routinely sponsors and conducts medical education outreach for healthcare providers through a variety of mechanisms, including medical symposia and Pfizer sponsored preceptorships, to ensure appropriate utilization of antibiotics and improve infection prevention and control.

Pfizer recently partnered with the British Society for Antimicrobial Chemotherapy (BSAC) and the University of Dundee to launch the Massive Open Online Course (MOOC) on antimicrobial stewardship. This course helps health care professionals understand and address the global threat of antimicrobial resistance, focusing on how to responsibly use high-quality antibiotics safely in everyday practice. Over 5,000 healthcare professionals had completed the course, with over 39,000 registrants since September of 2015. Pfizer is currently providing support to BSAC for translation of the MOOC into Chinese, Russian and Spanish to enable broader global access to this antimicrobial stewardship (AMS) training. In addition, other e-modules focusing on the following topics: Gram Negative Bacteria, OPAT and IVOST are to be launched through this partnership later this year.

Pfizer has also partnered with BSAC and the University of Dundee to publish an interactive e-Book on Antimicrobial Stewardship (e-BAS). The e-BAS is aimed at a global audience of HCPs or policy-makers interested in learning about the principles of AMS and applying them to clinical practice. Core learning outcomes include understanding the definition, structure and implementation of AMS programs ["the toolkit"]; the value of measurement, metrics and feedback in evaluating AMS programs; and introducing real world examples to illustrate good AMS practices. Sign-off and publishing of the e-BAS is expected in December 2017.





## Pfizer's Position: Anti-Infective Manufacturing

In addition to Antimicrobial Stewardship measures, Pfizer also includes responsible manufacturing practices as part of its Pharmaceuticals In the Environment approach. Some reports have highlighted that some manufacturing practices may result in antibiotic active-pharmaceutical ingredient (API) in the environment, which under some circumstances may lead to AMR.

Pfizer is committed to ensuring that the manufacture, use, and disposal of our products, including antibiotics, do not adversely affect human health or the environment. We actively support measures to reduce the environmental impact from the production of antibiotics. As a signatory of the AMR Industry Roadmap Pfizer is seeking to create sound, robust solutions and to accelerate implementation of these solutions when possible.

Pfizer supports measures to reduce environmental impact from production of antibiotics, and will:

1. Review our own manufacturing and supply chains to assess good practices in managing the release of antibiotic discharge into the environment;
2. Establish a common framework for managing antibiotic discharge, building on existing work such as the Pharmaceutical Supply Chain Initiative (PSCI), and start to apply it across our own internal manufacturing and external supply chain by 2018;
3. Work with stakeholders to develop a practical mechanism to transparently demonstrate that our supply chains meet the standards in the framework; and
4. Work with independent technical experts to establish science-driven, risk-based targets for discharge concentrations for antibiotics and good practice methods to reduce environmental impact of manufacturing discharges, by 2020.

Actions we are taking:

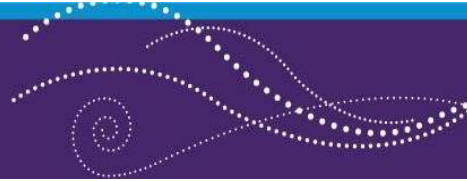
- Working through the AMR Alliance with other Roadmap signatory companies to establish science-driven, risk-based targets for discharge concentrations for antibiotics and a common framework for managing antibiotic discharge. Pfizer is seeking to create sound, robust solutions and to accelerate their implementation when possible.
- Pfizer is performing environmental reviews of our anti-infective suppliers, with a focus on pollution risks and waste water discharges, and we require improvement plans or supplier exit if the supplier is unable to meet expectations. Although the science is not agreed, as a precautionary measure and using existing published methodology, Pfizer is setting discharge limits that will minimize the manufacturing contribution to AMR.

## Pfizer's Position: AMR Surveillance

Understanding evolving bacterial resistance patterns enables physicians and healthcare providers in choosing appropriate antibiotic therapies for patients while also informing antimicrobial stewardship strategies.<sup>16</sup> In support of this effort, Pfizer sponsors a global antimicrobial surveillance program that monitors resistance patterns across more than 60 countries and enables real-time public access to these data.

The ATLAS (Antimicrobial Testing Leadership and Surveillance) program represents the integration of three global programs (TEST, AWARE, INFORM), and has generated 13 years of continuous global bacterial susceptibility data versus a panel of antibiotics. It includes source information from over 200 hospitals. Since 2004, publicly reported findings from these surveillance programs are available through over 50 published journal articles and over 750 medical congress presentations. Pfizer also provides access for healthcare providers to cumulative data through the ATLAS web site. The web site supports an interactive platform that enables physicians to evaluate data, conduct analyses, and export tables and figures that include parameters





such as organism, region, specimen source and *in vitro* susceptibility data. These *in vitro* surveillance data may be accessed at <https://atlas-surveillance.com>.

Recognizing that mobile devices and applications provide many benefits for healthcare professionals, Pfizer also offers ATLAS as a mobile application to enable rapid access to important resistance information.

Pfizer surveillance programs have evolved over the years to address the changing landscape of AMR. In addition to ATLAS, Pfizer has historically provided support for several independent surveillance programs including:

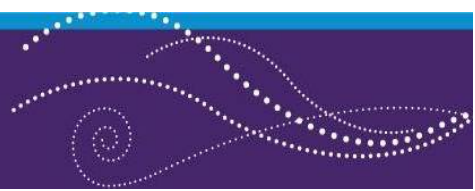
1. The LEADER (Linezolid Efficacy and Accurate Determination of Resistance) program, established in 2004, is a national (U.S.) initiative to monitor the activity of linezolid and comparator agents against target Gram-positive pathogens.
2. The ZAAPS (Zyvox Annual Appraisal of Potency and Spectrum) program has surveyed and documented the spectrum and activity of linezolid tested against non-U.S. Gram-positive pathogens for nine consecutive years (2004–12).
3. The SENTRY Antimicrobial Surveillance Program, which began in 1997 and is managed by JMI Laboratories, was designed to monitor the predominant pathogens and antimicrobial resistance for both nosocomial and community-acquired infections globally. Each year, the program surveys over 30,000 Gram-positive and Gram-negative organisms from medical centers participating in the global study.
4. In conjunction with the SENTRY program, Pfizer continues to support a global antifungal surveillance program focused on determining the frequency of occurrence of resistance among fungal pathogens causing infections in hospitalized patients. This global program includes 62 participating medical centers in the SENTRY Program, located in North America, Latin America, Europe, and the Asia-Pacific region. The antifungal global surveillance was in part supported by Pfizer Inc. and Astellas Pharma Global Development, Inc. It is currently an actively supported Pfizer program.
5. Pfizer also provides support for two China-based antibiotic resistance surveillance programs:
  - a. Since 2005, CHINET has investigated the anti-bacterial resistance and susceptibility rate of clinical isolates from major regions in China. Its 10-year report was just published, indicating the increased carbapenem resistance and the reduced MRSA incidence in China. It has accumulated around 600,000 isolates so far and will also expand its coverage to all regions within in 2017.
  - b. CHIFNET investigates the anti-fungal resistance and susceptibility rate from all the regions since 2009, with about 3,500 isolated collected.

In 2017, Pfizer will continue to expand its leadership position in antibiotic surveillance and stewardship through several initiatives. Pfizer is a partner in the DRIVE-AB initiative, a public-private partnership/consortium that is funded by the European Innovative Medicines Initiative (IMI). The consortium includes activities in antibiotic use and stewardship, new economic models for antibiotic use, and management and communication.

### **Pfizer's Position: Vaccines and AMR**

In addition to the need for the development of new antibiotics and rational use of anti-infective drugs, experts agree that vaccines too play a vital role in the arsenal to address AMR.<sup>17</sup> Vaccines are typically administered to prevent infections from happening in the first place, which naturally leads to reducing the use — and misuse — of antibiotics. To date, several studies have demonstrated the beneficial role vaccines play in the reduction of AMR and Pfizer is committed to continue the development of new, innovative vaccines to help prevent serious disease globally.





Vaccines not only protect the vaccinated individual by direct immunization but also can protect others through indirect immunization (assuming the overall vaccination rate is high enough). In addition vaccines can also reduce disease caused by antimicrobial-resistant strains of bacteria.<sup>18</sup> It has been reported that the pneumococcal conjugate vaccine not only reduces the incidence of invasive antibiotic-resistant pneumococcal infections in young children receiving the vaccine, but it also reduces transmission of these strains to their younger siblings and to adults.<sup>19</sup> In a recent study done by the CDC, an examination of U.S. pneumococcal bacteria from surveillance sites across the U.S. demonstrated a decrease of multidrug – resistance in the strains covered by the vaccine in pediatric populations (<5 years).<sup>20</sup> The study specifically showed that there was a 93% and 86% reduction of isolates that were resistant to either single or multiple antibiotics, respectively. In separate recent analysis vaccine effectiveness using CDC data in the ≥5 years population of age by Suaya, et al., the incidence of invasive pneumococcal disease (IPD) caused by an antibiotic – resistant strain of pneumococcal bacteria decreased by up to 67% for three consecutive epidemiological years from 2010 to 2013.<sup>21</sup>

The CDC now advocates this concept that developing new vaccines can decrease rates of antibiotic-resistant infections.<sup>22</sup> A report titled, *Role of Vaccination in Reducing Antimicrobial Resistance*, was published by Vaccines Europe in 2013.<sup>23</sup> It cites evidence supporting the preventive use of antibacterial vaccines to protect individuals and communities against infectious disease, including those caused by resistant bacterial strains. The use of vaccines in routine national immunization programs along with the rational use of anti-infectives can produce synergistic gains in public health. By reducing the incidence of infections, vaccines can extend the clinical utility of anti-infectives. Fewer infections translate to fewer prescriptions for these drugs, and thus reduces the risk of antimicrobial resistance. We thus agree with the call for national immunization plans that ensure access to vaccinations for citizens of all ages that can benefit from them, as outlined by Vaccines Europe (2013).

Pfizer has made significant and substantial investments in vaccine R&D to develop new vaccines and to support several vaccines already in clinical usage.

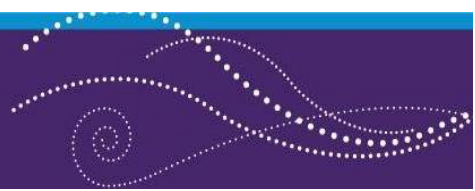
### **Pfizer's Position: Regulatory Framework**

In April 2017, the EMA, the U.S. FDA and the PMDA met to discuss how the three regulators can facilitate the development of safe and effective antibacterial medicines. The initiative responds to increasing global concerns over antimicrobial resistance and the lack of development of new antibiotics, with the objective of mapping existing similarities and differences in requirements in the three regions, and to work towards constructive proposals for further regulatory convergence.

As part of the global effort to incentivize new antibiotic and vaccine R&D, there is a need to develop a global, tiered regulatory framework that could allow either disease-based or pathogen-based label indications and which promotes the most appropriate use of new agents. Pfizer agrees in principle with several of the recommendations made by the IDSA (limited population antibacterial drugs), as included in the recently approved 21st Century Cures Act, and we support the consideration of adaptive non-inferiority trial designs greater consideration of preclinical and pharmacokinetic/pharmacodynamics data more flexible patient selection criteria, and greater acceptance of adaptive clinical trial designs. Specifically Pfizer supports a move to greater regulatory flexibility in the following areas:

- The use of non - inferiority trials for antibiotics due to ethical considerations, wherein the new drug must be shown to be non - inferior to the gold standard/standard of care treatment to minimize risk to patients. However, these complex trial designs require large numbers of patients and are difficult to run. It is also extremely challenging to demonstrate superiority for any discrete indication within the context of a non-inferiority trial. Regulatory flexibility is needed to support and develop appropriate trial designs for new antibiotics that may have the potential to demonstrate superiority sufficient for a label within the context of an ethically approved non-inferiority trial. The need for improved guidance on how clinical trial design can support the study of antibiotics in patients with a





confirmed antibiotic-resistant infection. Supporting this flexibility may demonstrate the value of a new antibiotic's potential to be especially effective at killing resistant strains, where it may otherwise not demonstrate increased efficacy in killing non-resistant strains.

- Greater use of surrogate end points such as pooling microbiological data across body sites, and augmenting that with non-clinical susceptibility and pharmacokinetic (PK) data.
- The use of adaptive clinical study design for AMR studies are more likely to demonstrate the safety and efficacy of the drug if one exists. Further these types of trials support quicker patient access to important antibiotics through trials that are more efficient, shorter duration, involve fewer patients,. Further, regulatory authorities could further support the use of real world data in an adaptive fashion to antibiotic development.
- A tiered regulatory framework that allows either disease-based or pathogen-based label indications and promotes the most appropriate use of new agents is currently under consideration. This could also be appropriate for vaccines that can be used to prevent infection by antibiotic – resistant bacteria, and/or antibiotic – sensitive bacteria in order to obviate the use of antibiotics.

### **Pfizer's Position: Incentives and New Business Models to Support R&D and a Sustainable Marketplace**

Health care professionals and other stakeholders agree that new innovative antibiotics need to be used sparingly in the early years of their commercial availability to ensure they are useful as later line agents for potential antibiotic resistant pathogens for a long period of time. As a result, multiple stewardship strategies aimed at improving the appropriate use of antibiotics are being employed. However, these stewardship measures challenge traditional health technology assessment techniques, as it is difficult to economically evaluate the importance of holding new antibiotics in reserve, particularly when combined with the fact that most existing antibiotics are generic and available at low cost. Overall, new antibiotics are faced with very challenging access dynamics and undervaluation, negatively impacting commercial availability. Consequently, new R&D incentives to strengthen investment and the antibiotic pipeline are needed along with novel business models to create more sustainable in-market dynamics.

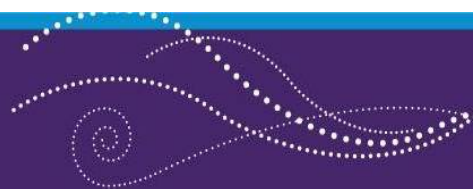
### **Incentives to Support Research and Development**

A report on antibiotic research, commissioned by the Swedish Government and issued by the London School of Economics and Political Science (LSEPS),<sup>24</sup> makes a broad recommendation for governments to create new incentives to promote the research and development of antibiotics in light of the growing concern over resistance to existing first line antibiotics. The LSEPS report differentiates current R&D incentives into two primary types – push and pull.

- Push incentives focus on removing barriers to the developer, largely by decreasing the costs for investments in R&D. These incentives tend to impact the earlier stages of the development process, and include R&D tax credits and grants.
- Pull incentives involve the commitment of financial reward after a technology has been developed, and include intellectual property extensions, advanced marketing commitments, monetary prizes, and market entry rewards.
- Regulatory incentives<sup>25</sup> include approaches to accelerated assessment and approvals, such as the Generating Antibiotic Incentives Now (GAIN) Act, the Limited Patient Antibiotic Drug Act (LPAD), and 21<sup>st</sup> Century Cures.

Important reports from the German Guard Initiative,<sup>26</sup> the AMR Review on Antimicrobial Resistance,<sup>27</sup> the Duke-Margolis Center for Health Policy,<sup>28</sup> the Pacific Research Institute<sup>29</sup>, the Office of Health Economics<sup>30</sup>, and Precision Health Economics<sup>31</sup> have been released, each advocating for the need for significant market-based incentives to increase R&D investments in AMR, including novel intellectual-property based approaches. A transferable IP exclusivity extension for the development of an antibiotic drug that in turn





could be applied to a different drug in that company's portfolio could create meaningful incentives for antibiotic development.

Pfizer believes that a mix of different and complementary incentives is needed to encourage increased AMR-focused antibiotic and vaccine development within the framework of the regulatory and IP systems applicable to the particular jurisdiction.<sup>32</sup>

- Novel IP mechanisms such as transferable market exclusivity with appropriate stewardship and access provisions for society could be one of the most impactful incentive mechanisms to support R&D and a sustainable marketplace. An important feature of this type of incentive is that it does not require any upfront government monies and it is sustainable over the long term. This incentive has the added benefit that a significant portion of manufacturer revenue is generated from the transferable IP exclusivity, not the volume of antibiotic sold – an important policy element. The other advantage of the transferable exclusivity is that similar to other development programs, it puts the risk of R&D on the companies and only rewards success.
- In the EU the equivalent of GAIN incentives (additional 5 years' regulatory exclusivity or IP protection for the product itself) may be useful as well as one year of exclusivity transferable to another product.
- Transferable Priority Review Vouchers (tPRV): In the U.S. the tPRV provides the option to transfer a priority review to a higher value asset; these have been used successfully in the United States. Since transferable priority review vouchers can be exchanged or “sold” between companies, this feature creates a strong incentive. tPRVs should be supported by the U.S. legislature because of the potential positive impact on antibiotics R&D.
- R&D Tax Credits: Tax credits have appeal as they can help to significantly decrease the financial burden of R&D. They have been successfully used as part of the Orphan Drug Act, so are already proven incentives.
- Diagnostics: Regulatory and economic incentives should also include the development of diagnostic assays, which can differentiate antibiotic-resistant from antibiotic-sensitive strains of bacteria, and will be a key enabler for the development and usage of targeted, new generation antibiotics.

Active discussions are currently underway in the U.S. and EU on how regulatory changes envisioned by the GAIN Act in the U.S. would be applied to the European regulatory system. This could include the automatic acceptability of new antibiotic drug and vaccines into EU accelerated regulatory schemes (PRIME and Adaptive Pathways).

One other incentive that has recently been raised is a “pay or play” levy proposed by The Review on Antimicrobial Resistance, which would tax companies not involved in anti-infective R&D. We do not believe this is the right solution. Taxes can add significant inefficiencies including, in this case, attracting less qualified companies to the area and unfairly targeting biopharma companies for a broad, complex challenge that involves all of the health care system. In addition, there is real potential for such a tax to shift R&D resources away from other critical public health needs.

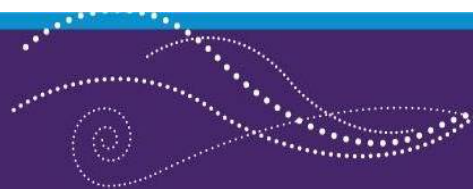
Pfizer believes that we should be working with industry partners, healthcare providers and governments towards incentives that support additional investment and innovation in this critical challenge in ways that work synergistically within the global healthcare environment.

### **Business Models to Support a Sustainable Marketplace for New Antibiotics**

One new business model which has been discussed and endorsed in principle by several external stakeholders is one based on the concept of insurance. Essentially, in exchange for making the new antibiotic available in a market, payers agree to provide companies upfront and/or annual negotiated payments at a fixed price or preset fee. Antibiotics are either purchased in addition to the annual fee or a certain volume may be covered by that fee. This model may also include a revenue limit/cap in the event of large demand requirements due







to a catastrophic resistant infection outbreak. From the health care system perspective, this ensures the availability of the new antibiotic and manages the unpredictability of resistance levels while at the same time improving budget predictability. The company is insured against the commercial risk of very low use at launch as it will at least receive the upfront/annual fee regardless of the volume of antibiotic used.

Pfizer supports further development and future pilots of this new business model as an important element in the battle against antimicrobial resistance. It is important to note though, that our external discussions and our internal analysis suggest that in and of itself, this new business model will not dramatically increase the returns associated with the long term research and development of new antibiotics. A mix of different and complementary incentives will still be needed to encourage increased AMR-focused R&D to the extent necessary, to help solve this global problem. Pfizer remains committed to developing real world pilots of new business models that eventually could become a new standard for reimbursing new antibiotics.

<sup>1</sup> <http://www.hhs.gov/ash/advisory-committees/paccarb/about-paccarb/index.html>

<sup>2</sup> [https://www.whitehouse.gov/sites/default/files/docs/national\\_action\\_plan\\_for\\_combating\\_antibiotic-resistant\\_bacteria.pdf](https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf)

<sup>3</sup> G7 Berlin Declaration at: <http://www.ip-watch.org/weblog/wp-content/uploads/2015/10/G7-Health-Ministers-Declaration-AMR-and-EBOLA-final-Scan-mit-Unterschriften.pdf>

<sup>4</sup> WHA Global Action Plan on antimicrobial resistance. [http://apps.who.int/gb/ebwha/pdf\\_files/WHA68/A68\\_ACONF1Rev1-en.pdf](http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_ACONF1Rev1-en.pdf)

<sup>5</sup> Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance January 2016. [https://amr-review.org/sites/default/files/Declaration\\_of\\_Support\\_for\\_Combating\\_AMR\\_Jan\\_2016.pdf](https://amr-review.org/sites/default/files/Declaration_of_Support_for_Combating_AMR_Jan_2016.pdf)

<sup>6</sup> Industry Roadmap for Progress on Combating Antimicrobial Resistance – September 2016. <http://www.ifpma.org/wp-content/uploads/2016/09/Roadmap-for-Progress-on-AMR-FINAL.pdf>

<sup>7</sup> Adeyi, Olusoji O.; Baris, Enis; Jonas, Olga B.; Irwin, Alec; Berthe, Franck Cesar Jean; Le Gall, Francois G.; Marquez, Patricio V.; Nikolic, Irina Aleksandra; Plante, Caroline Aurelie; Schneidman, Miriam; Shriber, Donald Edward; Thiebaud, Alessia. 2017. final report. Washington, D.C. : World Bank Group. <http://documents.worldbank.org/curated/en/323311493396993758/final-report>

<sup>8</sup> Centers for Disease Control and Prevention Antibiotic Resistance Threats in the United States, 2013. Available at: <http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf>

<sup>9</sup> The National Action Plan for Combating Antibiotic-resistant Bacteria available at:

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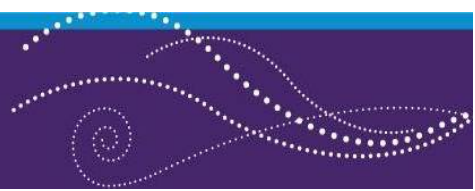
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