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Health & Wealth

An Investor's Guide to Antimicrobial Resistance

An analysis of the economic costs, risks and opportunities

MSCI Sustainability Institute

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2020 Investor Action on AMR

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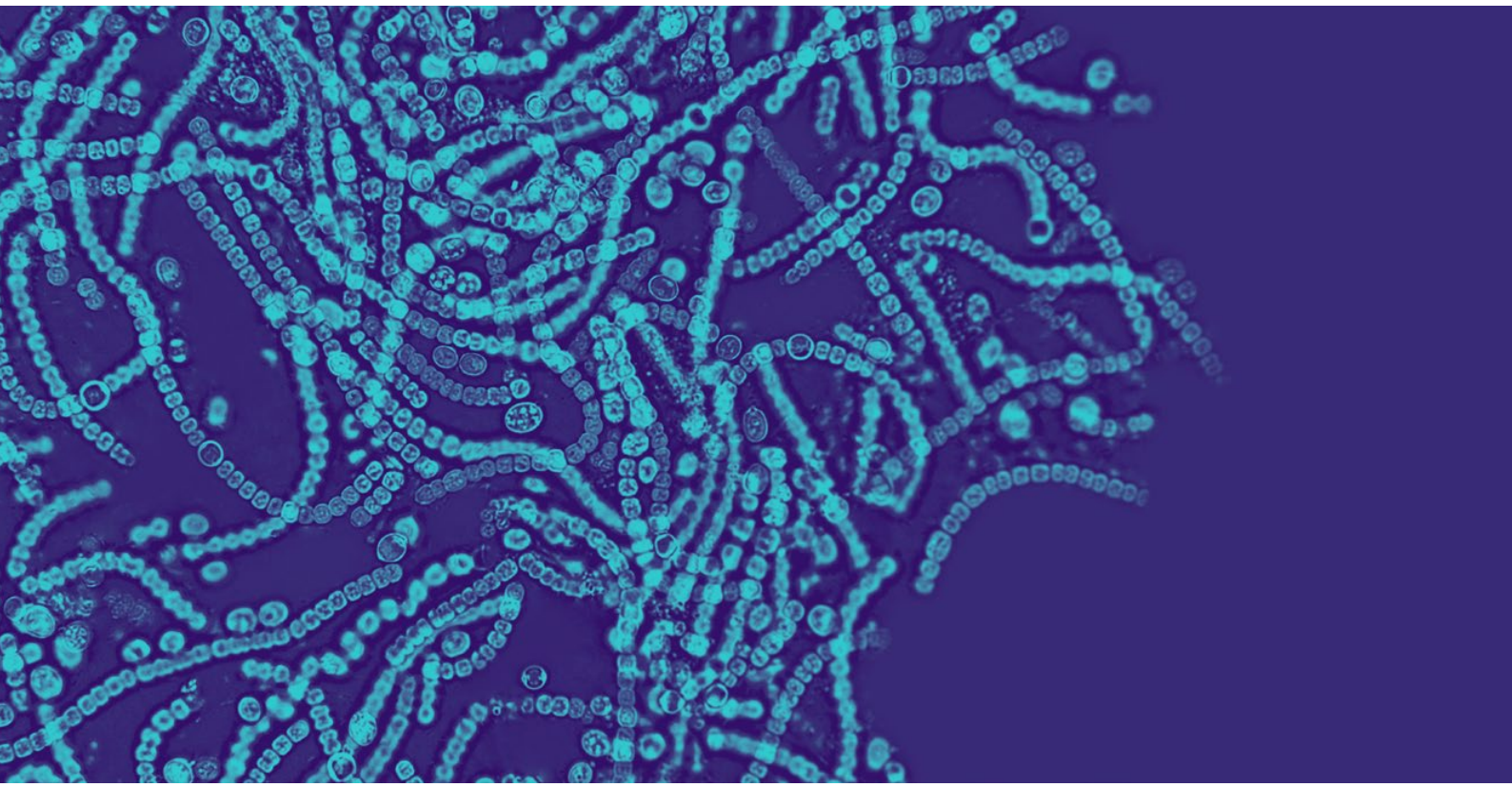
Executive *summary*

Antimicrobial resistance (AMR) occurs when pathogens withstand medicines that were specifically designed to eliminate them.[1]

The World Health Organization (WHO) identifies AMR as a critical threat to global health, with resistance rising to dangerously high levels worldwide. This trend affects public health across all demographics, making infections like pneumonia, tuberculosis and blood poisoning increasingly challenging and sometimes impossible to treat.

This guide provides an introduction to investment risks and opportunities tied to AMR. For investors, AMR underscores the urgent need for innovation in new antibiotics and alternative treatments, presenting both significant risks and potential opportunities across the investable universe.



Key findings

- The implications of AMR are significant, posing systemic risks. AMR transcends borders, with worsening resistance rates in low- and middle-income countries (LMICs) and posing a risk to high-income countries (HICs) as well. This underscores the necessity for holistic, global solutions to tackle the issue. By supporting sustainable practices and companies that are actively combating AMR, investors can contribute to global health solutions while mitigating the financial risks associated with this growing crisis.

- Though antibiotics have significantly reduced human deaths and illness from infections, boosted agricultural production and extended livestock longevity while reducing costs, their misuse and overuse have led to the rise of AMR.

- Coordinated global action is needed. As of 2022, AMR has been responsible for more deaths (1.27 million annually) than HIV/AIDS, malaria or most cancers. By 2050, AMR could lead to an estimated USD 1 trillion in additional healthcare costs, a 3.8% loss of global gross domestic product (GDP), and approximately 10 million deaths per year (11% of global deaths).

- Effective AMR containment strategies can yield substantial savings in both human and animal health sectors. Every dollar invested in infection prevention and control could save USD 1.10 - 1.30 in healthcare costs. For animal health, reducing antibiotic expenses can save USD 500 to USD 1,000 per farm annually, with additional savings from fewer veterinary consultations and increased productivity gains.

- Developing a new antibiotic can cost more than USD 1 billion and takes 10 to 15 years, but prevention and control of human morbidity and mortality can offset these costs. Introducing 18 antibiotics over 30 years could prevent 1.2 million deaths in the G7 and EU, offering investment return multiples ranging from 11-fold in the U.K. to nearly 28-fold in the U.S. and Japan.

    - Current AMR research is marked by an urgent need for novel antimicrobials, but the pipeline for innovative drug candidates remains sparse. As of December 2023, 97 products (57 antibiotics and 40 non-traditional antibacterials) were in clinical development, yet this is insufficient to tackle the growing AMR challenge.

- Most investments focus on basic research and early discovery phases, with significant gaps in funding for therapeutic and preventative alternatives such as vaccines.

- Small companies, which contribute 81% of antibacterial therapeutics in clinical testing, face significant funding gaps compared with other conditions like oncology. Despite initiatives like the AMR Action Fund, which aims to bring up to four new antibiotics to patients by 2030, more investment is needed to meet demand and foster innovation.

- While push funding — in which donors pay for research & development (R&D) through grants and bear the development risk — for AMR R&D has surged, additional annual funding of USD 250 million to USD 400 million is needed. Early-stage investments, like the PACE Initiative, support high-risk basic research, while late-stage investments, exemplified by CARB-X and the AMR Action Fund, target advanced clinical trials. Regulatory incentives and market-based mechanisms, such as the U.K.'s subscription model and the proposed U.S. PASTEUR Act, provide financial reasons for companies to invest in R&D.

- Investors have a unique opportunity to engage with investees to drive both individual and macro-level changes in combating AMR.

    - They can support regulation, incentivize research and development, and clarify sector roles and responsibilities.

    - By working collaboratively, investors can address existing gaps and promote sustainable practices. Understanding the economic impact, integrating AMR into investment decisions and supporting research and innovation are crucial. Investors can encourage sustainable operational practices and engage in multi-stakeholder initiatives like the Investor Action on AMR (IAAMR), which aims to build an AMR investor community and galvanize action to counter development of AMR.

AMR creates *financial risk*

AMR occurs when pathogens withstand medicines that were specifically designed to eliminate them. Resistance renders common antibiotic treatments ineffective and increases the risk of the spread of infectious diseases (and related morbidity and mortality).

Globally, resistance to antibiotics routinely used to treat common bacterial infections has increased. The trend of increasing resistance has also been observed for illnesses such as tuberculosis, Human Immunodeficiency Virus (HIV), malarial parasites and fungal infections.[2]

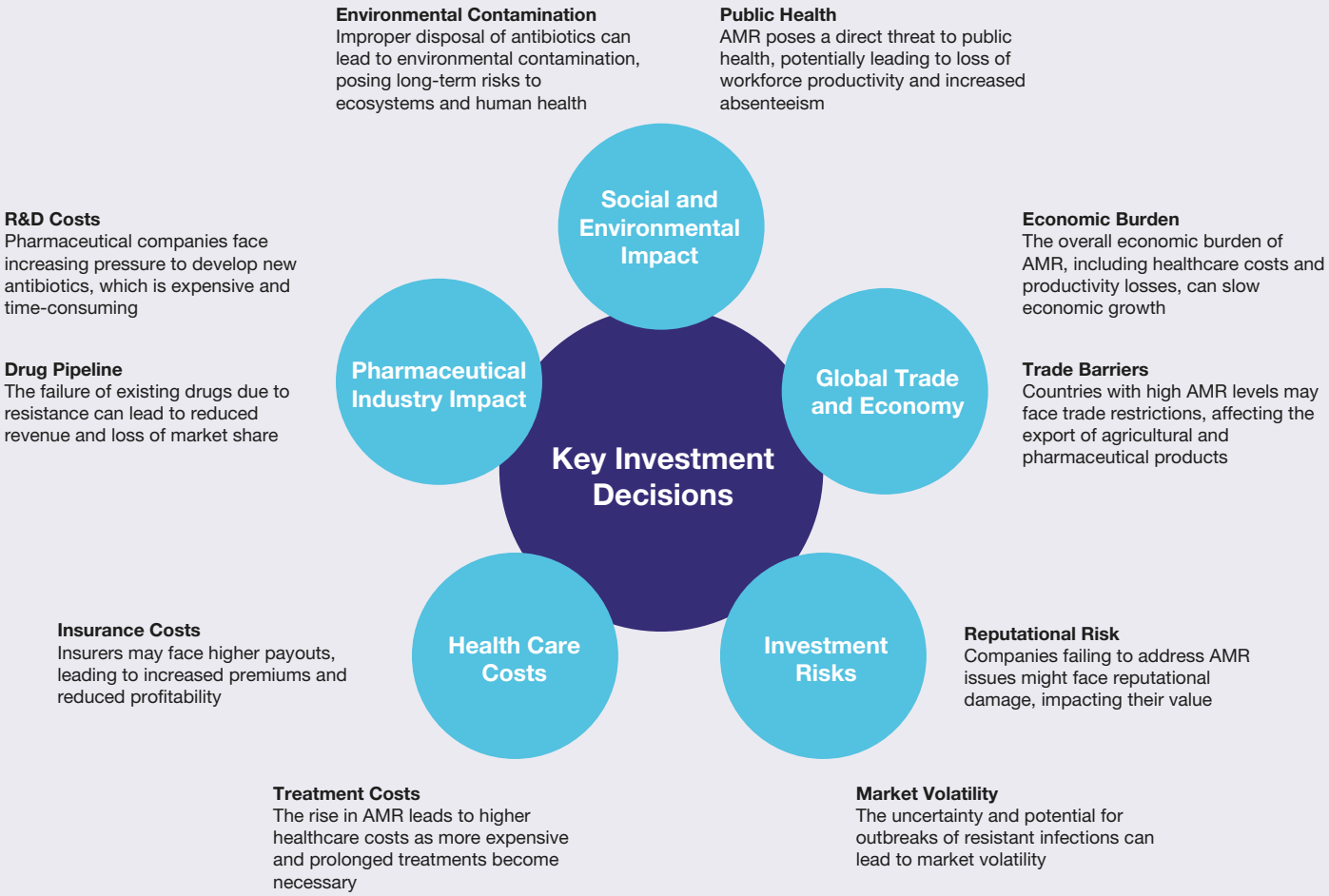
AMR is a natural process that results from genetic changes in pathogens. However, human activity, particularly the misuse and overuse of antimicrobials to prevent, control and treat human, animal and plant infections, is the primary driver of rising AMR. The lack of effective disease prevention and infection control in healthcare facilities and farms also plays a part. Waste from humans, animals and plants that have been treated with antimicrobials and effluent from antimicrobial manufacturing and wastewater treatment plants are also sources and transmission routes that create environmental hotspots of AMR.

The threat to lives and livelihoods

AMR is a severe global health threat, causing 1.27 million deaths annually and contributing to an additional 3.7 million deaths. Most of these occur in LMICs, which account for about 90% of direct AMR deaths and more than 99.5% of AMR-related deaths in children under 5. As of 2022, AMR fatalities surpassed those from HIV/AIDS, malaria and most cancers.[3]

The World Health Organization has highlighted alarming resistance rates, at 42% for E. coli and 35% for MRSA (methicillin-resistant Staphylococcus aureus).[4] Despite lower per-capita antibiotic use, LMICs have higher AMR rates than HICs.[5] LMICs often experience more unregulated or inappropriate antibiotic use, thanks to access constraints often experienced in these countries.

AMR, like climate change, is a global issue, with rising resistance rates in developing economies posing risks to developed economies. This underscores the urgent need for comprehensive, worldwide solutions. For investors, AMR presents significant risks as well as opportunities, particularly in the development of new antibiotics and alternative treatments.



The threat to livestock

Escalating antibiotic resistance in livestock and aquaculture is a growing concern for the food supply-chain landscape. Currently, 73% of global antimicrobial sales are for livestock. This trend threatens future antibiotic efficacy, potentially affecting livestock productivity and profitability.[6]

In cattle, diseases such as bovine respiratory disease are showing high levels of resistance, while in poultry, antibiotic-resistant strains of Salmonella, E. coli and Campylobacter are causing stunted growth, early culling and higher mortality rates.[7] [8] In aquaculture, the rise of "super-resistant" bacteria complicates treatment and persists at farming sites even after antibiotic use stops.[9]

Intensive systems of production exacerbate these issues.[10] Lack of enforcement, poor hygiene and widespread unregulated antibiotic use all contribute to higher rates of antimicrobial resistance.[11] For global investors, this presents both challenges and opportunities, highlighting the need for innovation in sustainable farming practices and alternative treatments.

Addressing AMR requires coordinated global efforts, presenting both risks and opportunities for investors. By supporting sustainable practices and companies that are actively combating AMR, investors can contribute to global health solutions while mitigating financial risks associated with this growing crisis.

Stricter regulations on antibiotic use in agriculture may increase compliance costs and affect the bottom line for agribusinesses

There is an opportunity to invest in companies that prioritize sustainable farming practices and are proactive in addressing AMR, potentially offering long-term value and resilience against regulatory changes

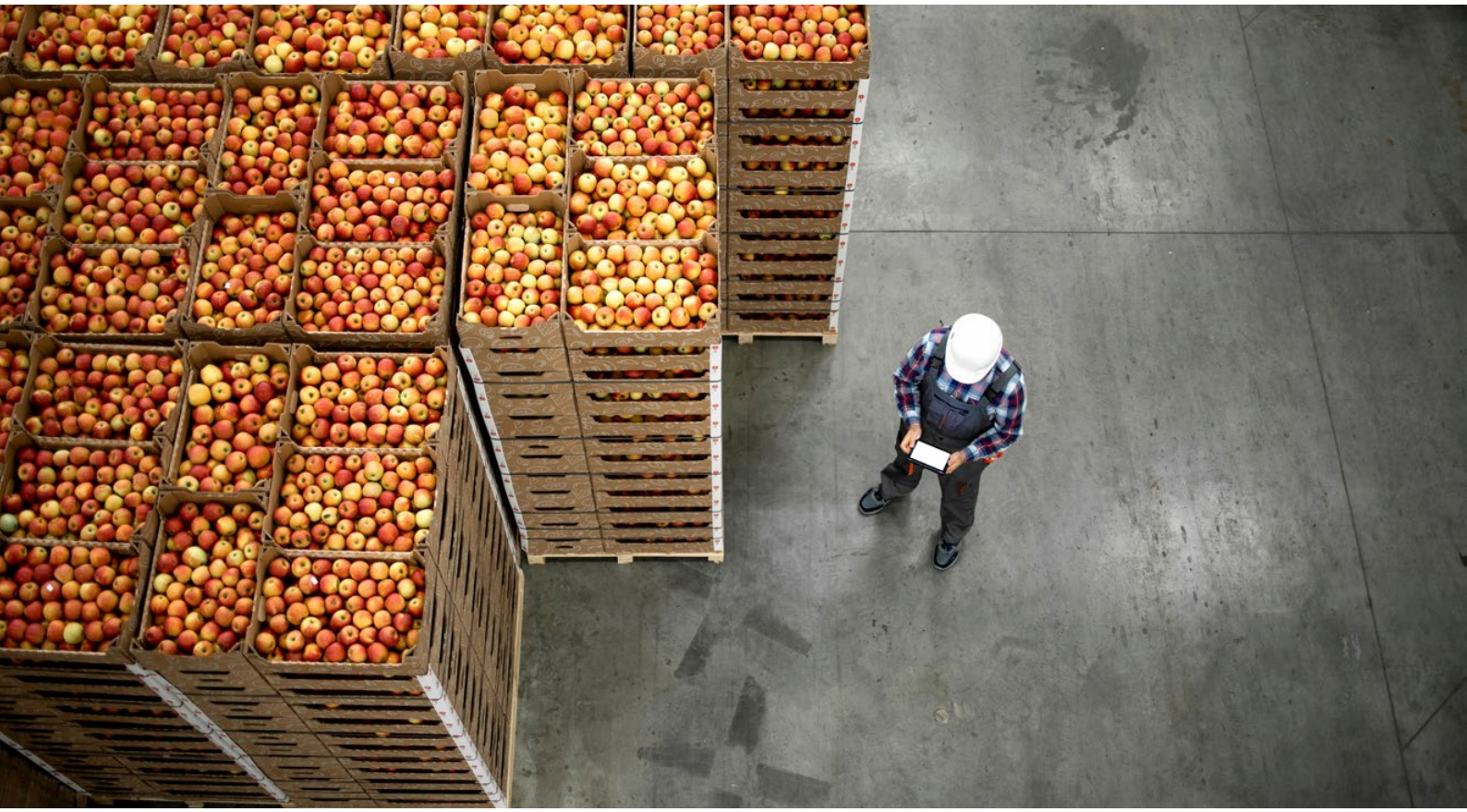
Increasing antimicrobial resistance in livestock and aquaculture can lead to increased mortality rates and reduced productivity, impacting the profitability of livestock industries

Disruptions in the food supply chain due to rising AMR can impact companies involved in food production, processing, and distribution, leading to potential market volatility.

Exposure, *risk & impact*

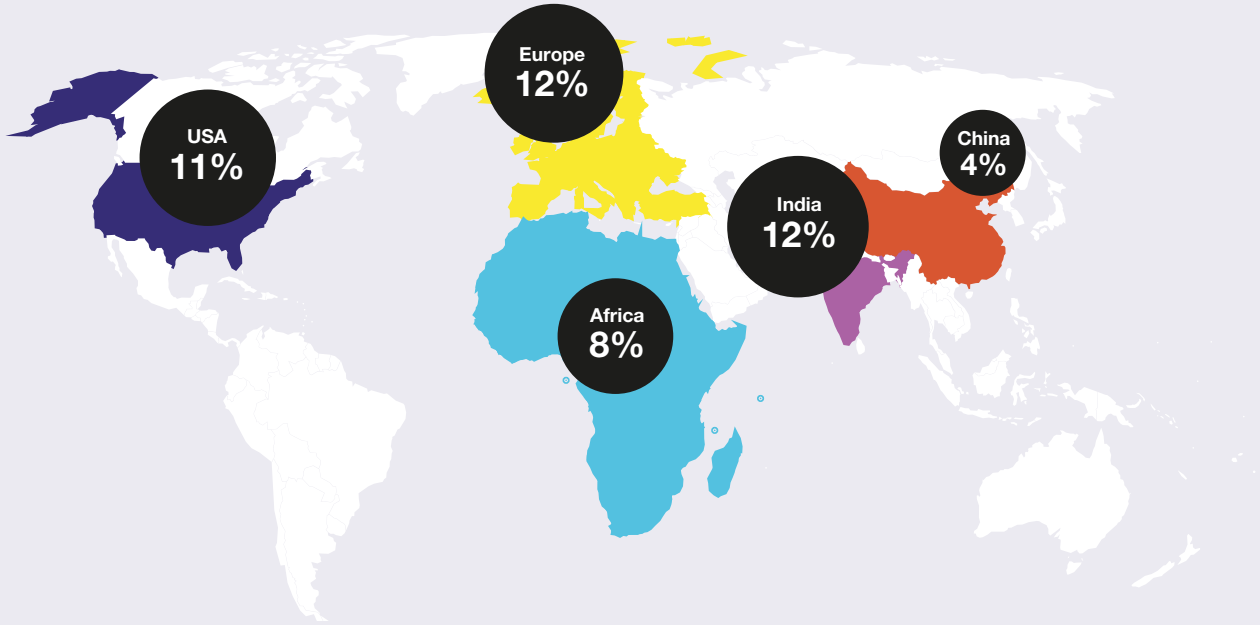
Almost 10% of global equity markets, or USD 14.6 trillion, is estimated to be exposed to AMR-related risks. Based on enterprise value (including cash), developed market companies are more exposed than their emerging market peers, on a valuation basis.

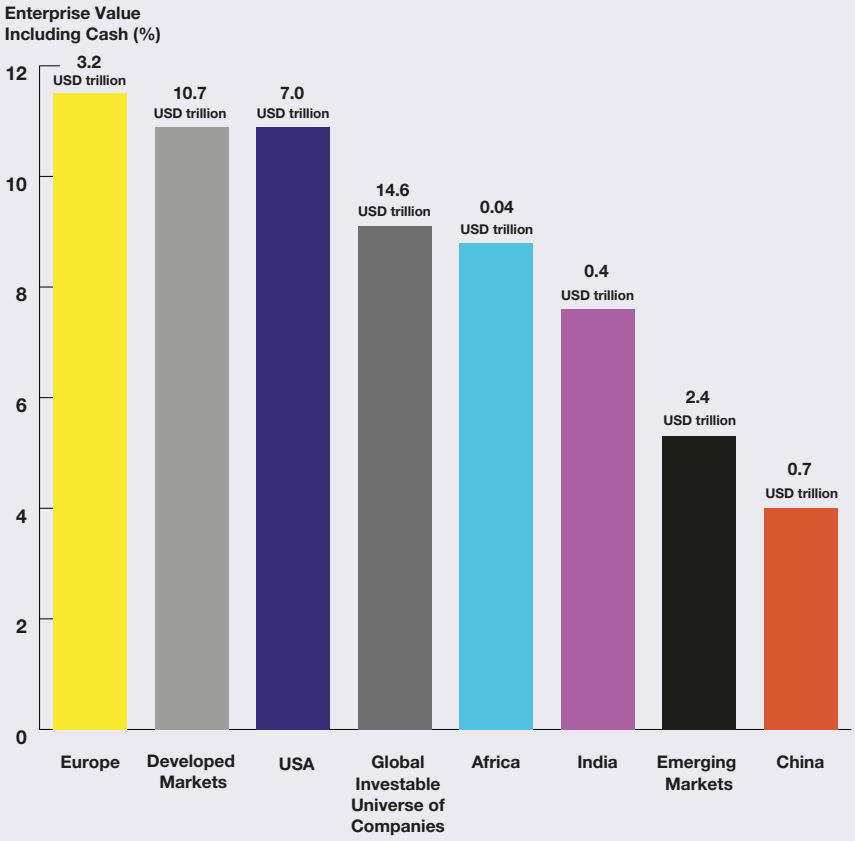
In absolute valuation terms, the U.S. investable companies universe is more exposed relative to any other region, followed by European companies. While market and economic risks are skewed toward the developed world, the health impacts are more prominent in developing nations.



Assets exposed to AMR related risks

Exhibit 1: Enterprise value including cash (EVIC) exposed to AMR risks – expressed as a percentage of the investable companies universe per region





Notes: Proportion of EVIC of each index derived from companies in the agricultural products and services, packaged foods and meats, food retail, restaurants, healthcare facilities, life & health insurance, managed healthcare, pharmaceuticals, biotechnology and life sciences tools and services GICS sub-industries.

Source: MSCI Sustainability Institute, June 18, 2024

Economic impact

According to World Bank estimates, by 2030, AMR could cause annual GDP losses ranging from USD 1 trillion to USD 3.4 trillion. By 2050, these losses could lead to a 3.8% reduction in global GDP, alongside an additional USD 1 trillion in healthcare costs.[12]

Developing countries may be particularly hard hit by 2050, potentially facing a 5% to 7% reduction in GDP. This could result in a cumulative global economic impact ranging from USD 100 trillion to USD 210 trillion.[13]

The overuse and misuse of antibiotics can also affect trade. Import bans due to indiscriminate antibiotic use and the presence of resistant pathogens can disrupt global supply chains. For example, 87% of global shrimp farming occurs in low- and middle-income countries in Asia. India exports half of its shrimp to the U.S., however, the U.S. Food and Drug Administration (FDA) frequently rejects these imports due to the detection of prohibited antibiotics or the presence of AMR. In January 2019, the FDA rejected 15% of shrimp shipments from India, and in 2021 it imposed a ban on the importation of raw shrimp from several other Asian countries.[14] Such import restrictions can extend across products, resulting in global food trade disruptions.

Health impact

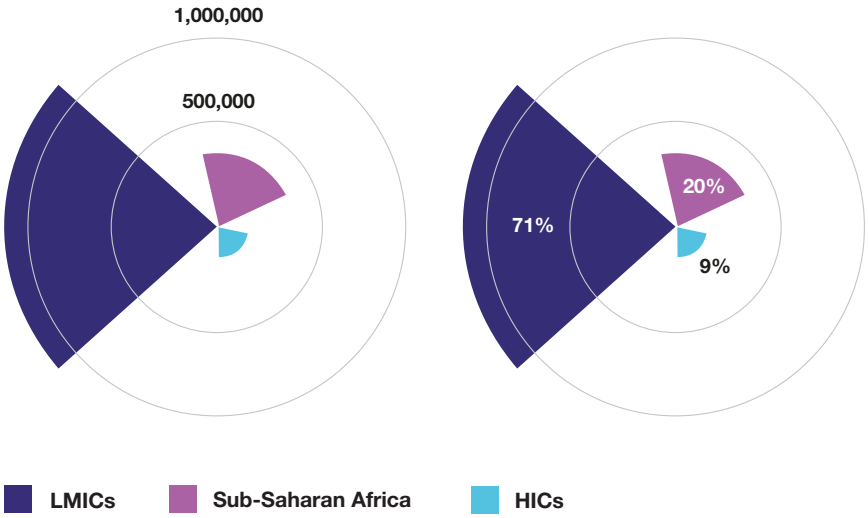
AMR was directly responsible for 1.27 million deaths worldwide in 2019, accounting for 2% of total global deaths.[15]

AMR also contributed to 4.95 million additional deaths that year. If not adequately controlled, AMR is projected to cause approximately 10 million deaths annually by 2050, representing an estimated 11% of global deaths.[15]

In LMICs, antibiotic-resistant bacteria led to a 58% increase in mortality rates from bloodstream infections, doubled the odds of Intensive Care Unit (ICU) admissions, extended hospital stays by an average of one week and increased direct medical costs by about USD 12,000 per case.[16] In 34 OECD and EU/EEA countries, resistant infections resulted in annual costs exceeding USD 28.9 billion and an additional 32.5 million hospital days, primarily due to prolonged hospitalizations.[17] In the U.S., the CDC estimates that AMR costs USD 55 billion annually, with USD 20 billion attributed to healthcare expenses and USD 35 billion to lost productivity.[18]

Chronic-disease and cancer patients are particularly vulnerable to infections, including those caused by resistant bacteria, due to their compromised immune systems. Furthermore, antibiotics are critical in controlling infections during standard medical procedures such as surgeries. Consequently, AMR may adversely affect the sales of non-antibiotic medications targeted at immunosuppressed patient groups (e.g., oncology, diabetes) and medical devices requiring surgical procedures. Investors should consider the significant financial and public health implications of AMR. As resistance continues to rise, the burden on healthcare systems and the associated costs are likely to escalate, potentially affecting various sectors, including pharmaceuticals and insurance segments.

Exhibit 2: Number of direct deaths caused by AMR by region (World Bank income classification)



Note: Direct deaths from AMR refers to fatalities that occur as a direct consequence of infections caused by bacteria, viruses, fungi or parasites that have developed resistance to antimicrobial treatments.

* Includes deaths due to other diseases, accidents and natural causes

Source: McDonnell, Anthony, Katherine Klemperer, Morgan Pincombe, Rachel Silverman Bonnifield, Prashant Yadav, and Javier Guzman. "A New Grand Bargain to Improve the Antimicrobial Market for Human Health." Center for Global Development, 2023.

COUNTRY GROUP	TOTAL DIRECT DEATHS FROM AMR	% OF TOTAL DEATHS FROM ALL CAUSES*
High-income countries	141,000	1.1%
Low- and middle-income countries	1,129,000	2.7%
Sub-Saharan Africa	317,500	2.4%

Livestock and environmental impact

The World Organization for Animal Health (WOAH) reported a 2% increase in global antibiotic use between 2019 and 2021.[19] By 2030, antimicrobial usage in animals is projected to rise by 8%.[20]

This increase has serious implications, particularly in the pig industry, where antimicrobial-resistant swine dysentery is becoming more prevalent. Traditional antibiotics are proving ineffective, leading to the use of alternatives such as WHO-classified medically important pleuromutilins.[21] However, emerging resistance to these drugs could result in significant livestock losses, with outbreaks reporting up to 90% morbidity and 30% mortality rates in weaned pigs.[22]

The World Bank estimates that AMR and its economic repercussions could reduce global livestock production by 3% to 8% by 2050. In LMICs, this reduction could reach 11% if AMR trends continue unchecked.[23] AMR transmission is a concern due to the proximity of humans and food-producing animals on farms.[24]

The presence of antibiotic residues and resistant bacteria in retail meat, eggs and dairy heighten the risk of AMR transfer through consumption. Additionally, food-producing animals that have been treated with antibiotics produce millions of tons of manure daily. This is often used as crop fertilizer, potentially spreading antibiotic residues and AMR through soil, water, air and, ultimately, to plants and animals.[25]

Exhibit 3a: AMR opportunities

Source: MSCI Sustainability Institute, Apr. 2, 2024

Exhibit 3b: AMR risks and impacts by sub-industry

GICS SUB-INDUSTRY	IMPACT	FINANCIAL RISKS
Agricultural products and services **Packaged foods and meats**	• Development of AMR in animals and plants • Environmental pollution due to antimicrobial effluents • Development of AMR in consumers & end-users due to antibiotics and resistant bacteria present in the food supply chain	• Veterinary cost increases due to AMR • Costs of compliance with regulatory demands on antibiotic use in animals, levels of antibiotics in the food supply chain, and reduction of antimicrobial presence in effluents • Export restrictions or bans for non-compliance with national regulations on antimicrobial content in food supply chain • Fines and loss of license to operate due to non-compliance with regulation • Market share loss due to reduced demand for antibiotic-treated animal protein • Productivity loss and supply chain disruption due to increased morbidity and mortality caused by AMR outbreaks • Higher insurance premiums due to AMR risks in own operations and supply chain
Food retail and restaurants	• Own operations - Development of AMR due to antibiotics and resistant bacteria present in the food supply chain	
Healthcare facilities	• Development of resistant infections in patients due to misuse and over prescription of antibiotics • Environmental pollution due to improperly treated hospital waste and antimicrobial effluents	• Increasing healthcare costs due to increased costs of patient care (length of hospital stay and intensity of treatment) and higher cost of backup or reserve antimicrobials • Reduced productivity due to increased morbidity and mortality caused by AMR outbreaks • Increased insurance premiums due to AMR risks in own operations
Pharmaceuticals (including veterinary pharmaceuticals) **Biotechnology** **Life sciences, tools and servcies**	• Development of resistant infections in patients and animals due to misuse and overprescription of antibiotics • Environmental pollution due to antimicrobial effluents	• Reduced sales of non-antibiotic therapeutics aimed at immunosuppressed patient groups (e.g. oncology, diabetes) and medical devices required for surgery • Costs of compliance with regulatory demands regarding antibiotic stewardship and reduction of antimicrobial levels in effluents • Fines and loss of license to operate due to non-compliance with regulation
Life and health insurance **Managed healthcare**		• Increased cost and frequency of claims due to increased AMR-related mortality and morbidity • Unexpected claim surges due to AMR outbreaks • AMR's detrimental impact on investment portfolios

The Global Industry Classification Standard (GICS) is the global industry classification standard jointly developed by MSCI and S&P Global Market Intelligence. "Global Industry Classification Standard (GICS®)" is a service mark of MSCI and S&P Global Market Intelligence.

Research & Development *landscape*

Current AMR research is marked by an urgent need for novel antimicrobials to address rising resistance; however, there is a notable dearth of innovative drug candidates in the research pipeline.

Current R&D status

As of December 2023, there were fewer than a hundred products in clinical development for priority pathogens, with a roughly equal split of antibiotics and non-traditional antibacterials.[26] Among these, just 12 antibiotics meet at least one of the four criteria for innovation.[27] Despite these developments, the current clinical pipeline and recently approved antibiotics are insufficient to address the escalating challenge of antimicrobial resistance.[28]

The active R&D pipeline for antibiotics significantly lags behind other conditions such as cancer, neuropsychiatric disorders and other non-communicable diseases. In fact, no new antibiotic classes have been discovered since the 1980s.[29] Although the FDA approved 164 direct-acting antibacterial new chemical entities (NCEs) from the early 1900s to 2019, innovation has slowed considerably, with only one new molecular target NCE approved between 1987 and 2022.[30]

Small companies are leading the charge in innovation, accounting for 81% of antibacterial therapeutics in clinical testing. However, investment in this sector is lagging, with antibacterial-focused biopharma receiving significantly less funding than other areas such as oncology. Additionally, clinical trial initiations for antibacterial NCEs have decreased by 33% in recent years, indicating a worrying trend for the future of antibacterial drug development.[31]

New vaccines may target specific population groups, such as patients undergoing surgery, to lower infection rates among these high-risk groups rather than the entire population.[32]

Challenges and potential solutions

According to the Access to Medicine Foundation, the antibiotic development landscape is in decline due to commercial viability concerns, leading to a scarcity of new treatments for priority pathogens. This leaves global populations vulnerable to severe drug-resistant infections.

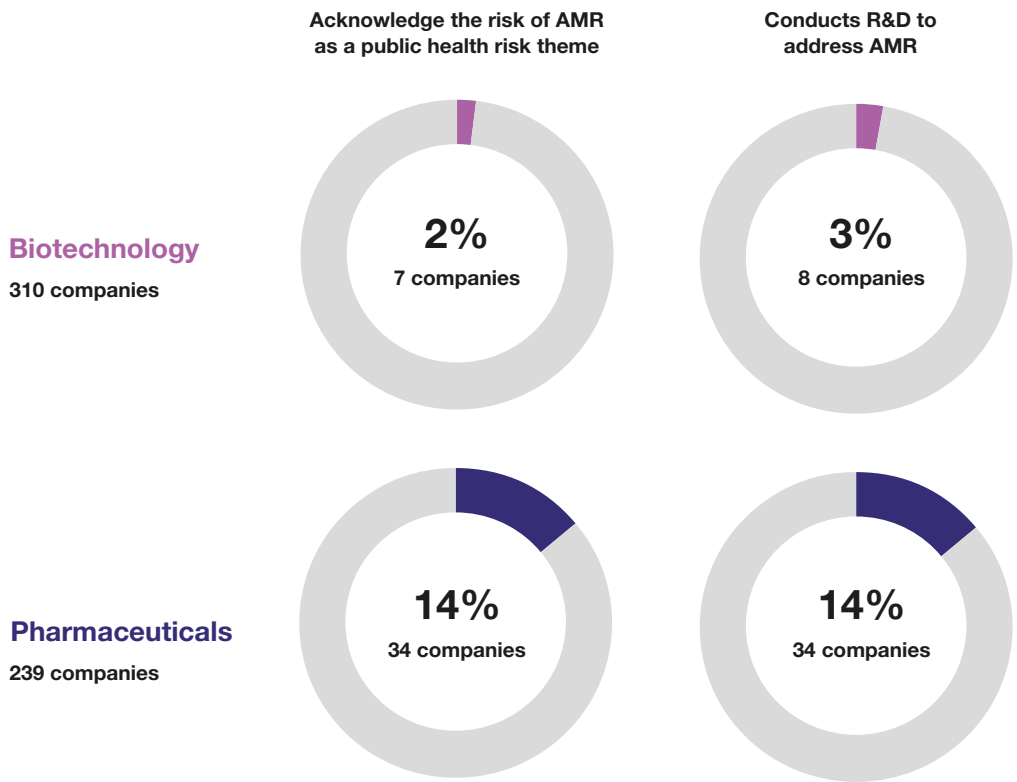
However, there are promising late-stage clinical development projects led by entities such as GSK, F2G, Innoviva, Venatorx and Pfizer, which could potentially provide treatments for these infections. These initiatives could significantly affect a wide range of patients globally.[33]

Investor implications

For investors, the antibiotic development sector presents both challenges and opportunities. While the current state of innovation and funding is concerning, the high unmet need for effective treatments of drug-resistant infections underscores the potential for significant returns on investment. Companies that can bring new and effective antibacterial therapies to market will not only address a critical global health issue but also stand to gain substantial market share in a field with limited competition. Investors should closely monitor advancements and support innovative projects that promise to address the growing AMR crisis, as these efforts are crucial for the future of global healthcare.

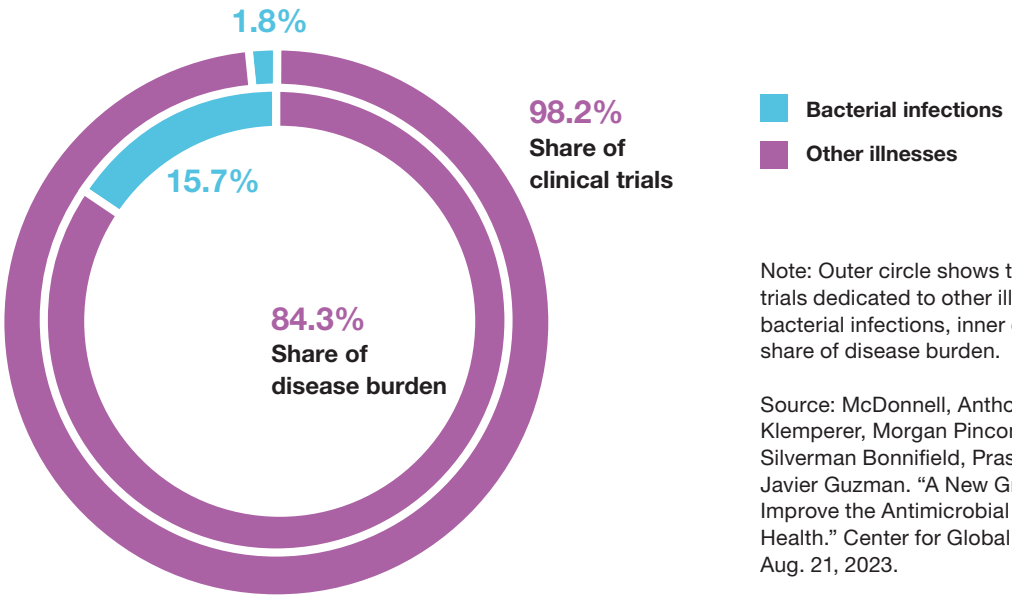
Most companies in the Biotechnology and Pharmaceuticals industry (constituents of the MSCI ACWI IMI, as of June 19, 2024) have not acknowledged AMR as a public health risk and are not conducting R&D in this area. This highlights the potential gap in the response to antibiotic resistance by the biopharma sector despite AMR evolving as a significant risk and an area for potential opportunities.

Exhibit 4: Biotechnology and pharmaceutical industry constituents of the MSCI ACWI IMI (n=549)



Source: MSCI ESG Research, as of June 19, 2024

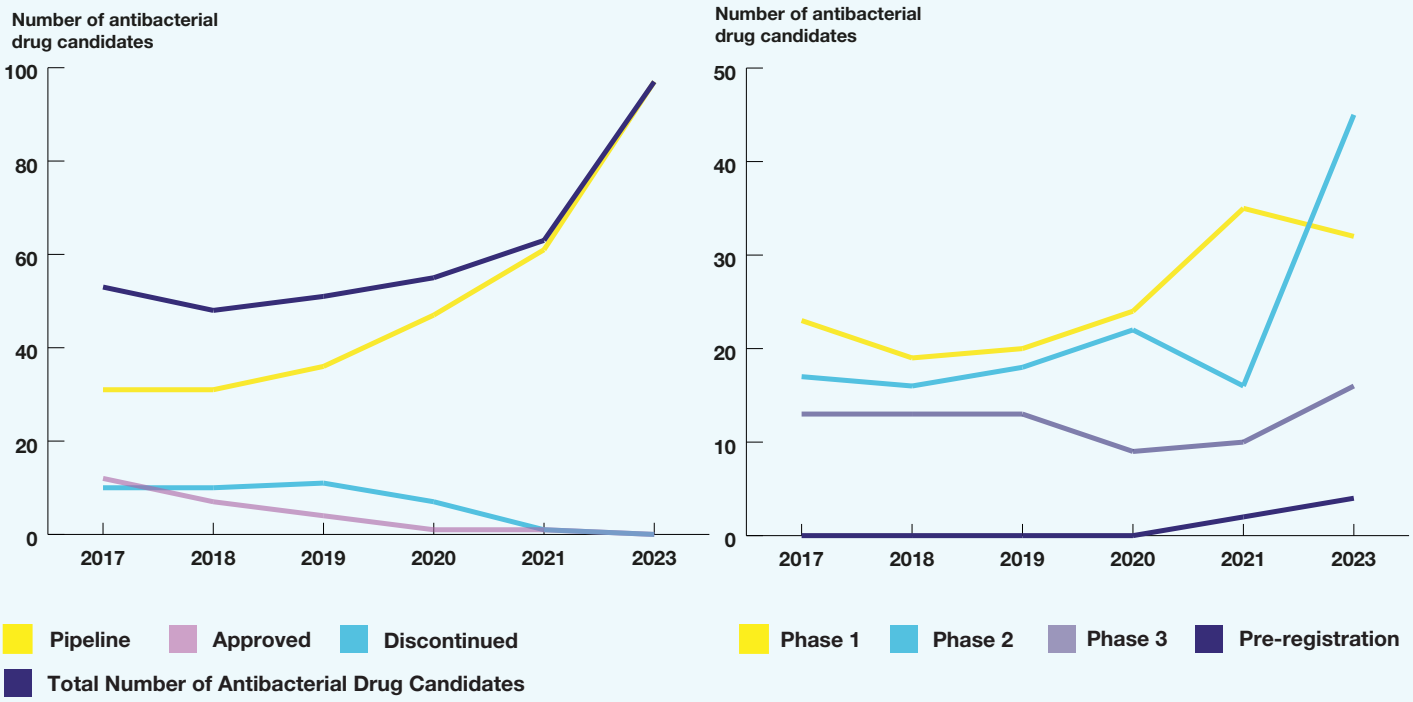
Exhibit 5: Mismatch between share of Phase II and Phase III clinical trials and global burden of disease for bacterial infections (N=13,605)



Note: Outer circle shows the share of clinical trials dedicated to other illnesses versus bacterial infections, inner circle shows the share of disease burden.

Source: McDonnell, Anthony, Katherine Klemperer, Morgan Pincombe, Rachel Silverman Bonnifield, Prashant Yadav, and Javier Guzman. "A New Grand Bargain to Improve the Antimicrobial Market for Human Health." Center for Global Development, as of Aug. 21, 2023.

Exhibit 6: WHO Antibacterial pre-clinical pipeline review



Sources: "Trend Analysis of Antibacterial Agents in the Pipeline (2017 - 2023)," World Health Organization, June 2024. "Antibacterial Products in Clinical Development for Priority Pathogens," World Health Organization, June 2022.

Funding for AMR R&D

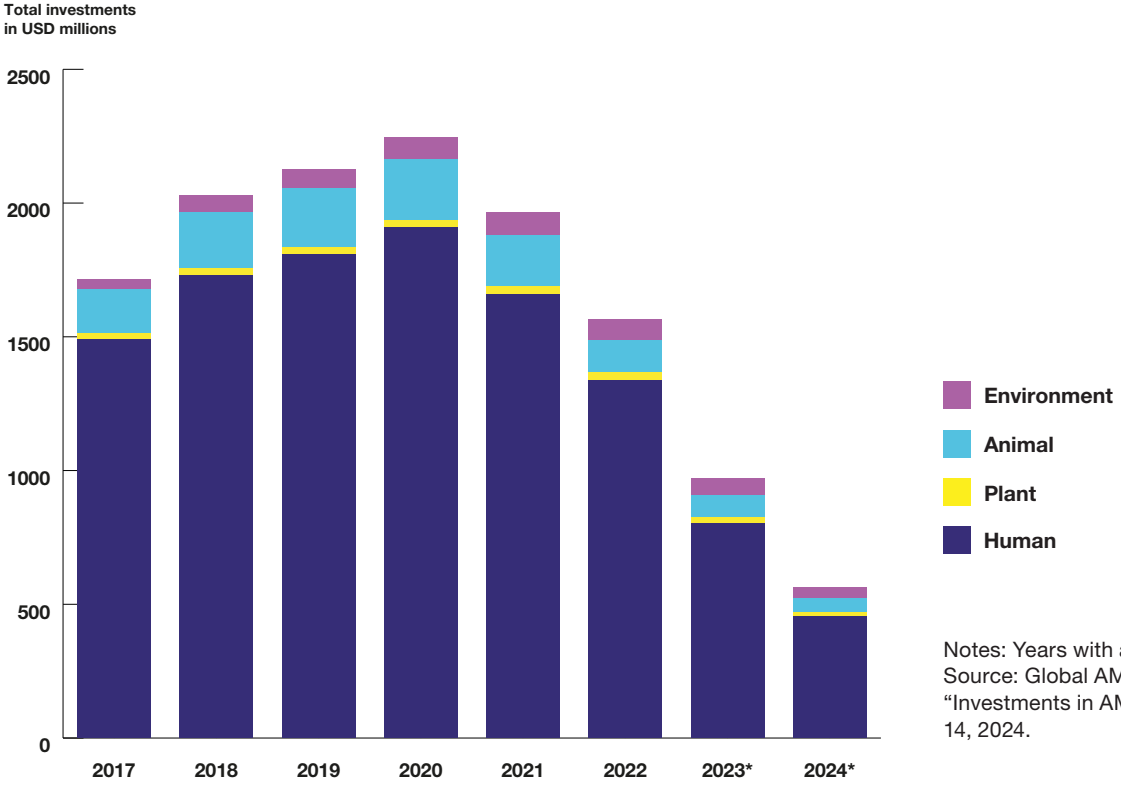
Current AMR funding overwhelmingly focuses on human health, which received approximately 85% of total funding between 2017 and 2024.[34] Animal health came a distant second with below 10% of funding devoted to this segment.

Public and private non-profit investments for AMR were chiefly focused on basic research which includes both fundamental scientific research and research geared towards product development (approximately 29% of total R&D investments in AMR).[35] The gap between therapeutic and preventative alternatives is widening with approximately 22% of total investments going to therapeutics and just 7.9% of investments towards vaccines and other preventive measures.[36] Similarly, diagnostics accounted for approximately 7.4% of total investments in AMR. Funding focused overwhelmingly on bacteria accounting for approximately 90% of total investments. Fungi and other agents including viruses had the remaining 10% split evenly between these two categories. Nearly 63% of funding focused on the early discovery phase of product-related research including preclinical stages. Development and trials took up the remaining funding.[37]

The AMR Action Fund, the world's largest public-private partnership investing in the development of new antimicrobials, aimed to bring up to four new antibiotics to patients by 2030. However, despite amassing USD 1 billion for investment to address AMR, the amount was still deemed insufficient to meet current demand and to innovate for meeting future demand.[38]

Innovators at small and medium-sized enterprises (SME) face financial 'valleys of death' until they secure investments to progress through the product development cycle. The lack of funding stalls development and may result in SME bankruptcy which results in the loss of a potential new drug. Examples include Achaogen and Melinta Therapeutics, both companies focused on the development of novel antibacterial agents and declared bankruptcy in 2019. To address the challenges, SMEs need a consistent financial and policy environment. This may include market entry rewards for successful product development or subscription models where governments provide regular payments in exchange for a guaranteed product supply. Additionally, regulatory changes are needed to streamline the approval of new products.[39]

Exhibit 7: Funding for AMR R&D



Notes: Years with asterisks are estimates.
Source: Global AMR R&D Hub Dashboard, "Investments in AMR R&D," Accessed June 14, 2024.

Economic case *for investment*

Developing new antimicrobials is expensive and can offer low returns.[40] While the estimated failure rate (95%) and the costs for research and development of antibiotics remain comparable to those of products targeting other disease areas, the antibiotics market faces some unique challenges that can limit its profitability.[41] [42]

Profitability challenges

- A key challenge in tackling AMR is the lack of financial incentives for manufacturers to invest in new antimicrobials. This is partly because antimicrobial use needs careful stewardship to maintain effectiveness, which makes volume-based sales with its associated profits inappropriate.[43] New antibiotics are primarily reserved for the treatment of resistant infections ('kept on the shelf') and are used sparingly and as a last resort. As a result, they have low unit sales but lifesaving implications.

- Discovery of new antibiotics and the complexity of antibiotic development and clinical trials also present challenges.[44] In contrast to orphan drug developers, antibiotic developers cannot use high unit-pricing strategies due to clinical trial design (difficulty in establishing superiority of newer antibiotics, as resistance is not extremely widespread yet) and reimbursement structures that reward prescribing cheaper antibiotics.[45]

- Antibiotics have a limited lifespan due to the emergence of drug resistance in contrast to most other drugs. Further, the duration of use of such drugs is short, compared with the use of drugs for non-communicable diseases such as diabetes.[46]

- The value of an antibiotic to patients and society at large is not aligned with its profitability. Standard cost-benefit modeling methods may not fully capture the true value of antimicrobials, as these methods often focus on immediate costs and benefits, such as the price of the drug and its effectiveness in treating a specific infection. They may not account for the broader societal benefits of having effective antimicrobials available, such as prevention of the spread of resistant infections, or enabling medical procedures like surgery that rely on effective infection prevention. As a result, current methods may undervalue antimicrobials, particularly in terms of protecting public health. This can lead to underinvestment in the development of new antimicrobials, which contributes to the challenges of AMR.

The combination of low per-unit sales and low cost per unit led to an exodus of large pharmaceutical players from the antibiotics market. Small and medium-sized companies accounted for approximately 90% of new antibiotics in development as of 2019.[47] These companies struggle to finance their products in the late clinical stages of drug development and at the regulatory approval phase.[48] The absence of a profitable market and limited development pipelines pose significant challenges to investment in combating AMR. However, AMR's impact on asset values can lead to systemic risks across various industries.

Potential Savings from AMR containment
Potential savings exist from effective AMR containment strategies: In the human health sector, each 1 USD allocated to investments in infection prevention and control could yield USD 1.10 to USD 1.3 0 in savings in healthcare expenditure, depending on the type of intervention and setting.[49]

In terms of animal health, reductions in antibiotic expenses were estimated to save approximately USD 500 to USD 1,000 per farm annually.[50] Fewer veterinary consultations and treatments would save between USD 200 and USD 500 per case.[51] Reduced mortality would save between USD 10 to USD 20 per animal.

Cost-effectiveness of investing in AMR prevention and control
R&D costs: On average, it can take 10 to 15 years and cost more than $1 billion to develop a new antibiotic. The mean estimated R&D outlay for antibiotics is over $300 million, but when accounting for opportunity costs and the price of failure, it can increase to $1.3 billion per drug.[52]

Prevention and control costs
The attributable cost of resistant infection ranges from USD 2,371 to USD 29,289 (adjusted for 2020 price) per patient episode; the mean excess length of hospital stay is 7.4 days, the likelihood of death for patients with resistant infection was 1.844 and readmission was 1.492.[53]

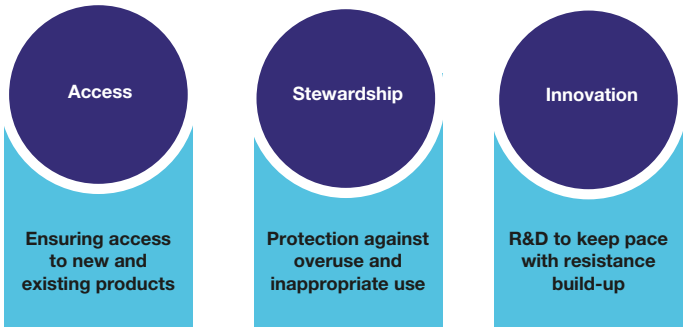
Returns on investment in AMR solutions
The introduction of 18 antibiotics over 30 years, with a total commitment of USD 4.5 billion for each drug, would prevent almost 1.2 million deaths in the G7 and the E.U. alone. The return on investment would be substantial, ranging from an 11-fold return in the U.K. to an almost 28-fold return in both the U.S. and Japan over a 30-year period.[54]

Investment *opportunities*

AMR was a significant public health threat even before the COVID-19 pandemic, which exacerbated the issue by accelerating antibiotic misuse. Investors, having reassessed their strategies in light of COVID, must now recognize the potential impact of AMR on their investments. They are uniquely positioned to leverage their influence to protect societies, economies and the long-term value of their portfolios.

By supporting initiatives to combat AMR, investors can drive substantial change by capitalizing on opportunities for strategic investments through innovative finance models and funding coalitions. Blending different sources of capital can create a more robust investment landscape.

Exhibit 8: Three pillars of opportunity – factors needed for a sustainable antimicrobial market



Source: McDonnell, Anthony, Katherine Klemperer, Morgan Pincombe, Rachel Silverman Bonnifield, Prashant Yadav, and Javier Guzman. "A New Grand Bargain to Improve the Antimicrobial Market for Human Health." Center for Global Development, 2023.

Furthermore, investors may leverage growth opportunities in emerging markets and LMICs. These regions offer a conducive environment for clinical trial enrollment that enables relevant populations to benefit from testing. Partnerships with organizations, such as SECURE, can ensure increased access to antimicrobials in these regions as well.[55] Commercialization plans need to be coupled with access planning frameworks in LMICs.

Current scenario for AMR funding

The pharmaceutical industry has seen a surge in push funding for antimicrobial R&D. However, the WHO and the Global AMR R&D Hub have reported that small biotech companies and research groups require additional push funding to replenish a weak clinical pipeline. It is estimated that the annual push funding is less than USD 200 million, and an additional annual push funding amount of USD 250 million to USD 400 million is still required to bridge the current gap.[56]

The following approaches may be employed to encourage the R&D of new antibacterial agents:

Investment in research: Early-stage investment is crucial for supporting the basic research necessary to discover novel therapeutics. This phase often requires significant funding, as it involves high-risk basic science that may not lead to immediate commercial products. Governments and private entities can provide grants and venture capital and can establish public-private partnerships to fund this early research. An example of early-stage investment is the Pathways to Antimicrobial Clinical Efficacy (PACE) Initiative, backed by an investment of approximately USD 18.75 million each from Innovate UK and LifeArc. This initiative aims to bolster the pre-clinical AMR pipeline by funding U.K.-based early-stage R&D projects in medical discovery and diagnostics.

Investment in development: Late-stage investment targets the phase of advanced clinical trials and regulatory approval processes. Strategic alliances and partnerships, such as those fostered by CARB-X, a global partnership funding late-stage antibacterial development projects, are examples.

CARB-X, since its inception in 2016, has allocated USD 398.2 million to product developers for 92 R&D initiatives. The AMR Action Fund, a global alliance of biopharma companies, philanthropic contributors and multilateral development banks, anticipates investing more than USD 1 billion in small biotech firms' projects over the coming decade. Europe's largest public-private collaboration, New Drugs for Bad Bugs, made investments in eight projects (for a total of USD 710 million) between 2013 and 2021.[57]

Funding may also seek to address other aspects of AMR prevention such as stewardship and preventative products and services. These include preventative alternatives to antimicrobials for food-producing animals such as diagnostic tools, gene editing to prevent disease, teat sealant medication and vaccine (bacterial and viral) development.[58] In addition, alternatives for poultry animals include prebiotics, antimicrobial peptides, herbal medications, vitamins and minerals, and plant extracts.[59] In aquaculture, specifically salmon and shrimp, novel alternatives include nutritional products (probiotics), bacteriophages and newer aquaculture techniques like Biofloc.[60] [61]

Apart from the above, regulatory and market-based approaches may also help channel funding for novel therapeutics and increase market attractiveness post-approval:

Regulatory incentives: Regulatory incentives to facilitate the development and approval of new drugs may include fast-track designation, priority review and extended exclusivity periods, which can significantly reduce the time and cost associated with bringing new antibacterials to market.[62] [63] [64] The U.S. Generating Antibiotic Incentives Now (GAIN) Act, for instance, extends exclusivity for certain antibiotics. Regulators may also decrease the time and cost for products to reach patients by clarifying, optimizing and converging regulatory requirements across indications and geographies.[65]

Market-based mechanisms (pull incentives): Market-based mechanisms ensure a market for new antibacterial drugs, providing a financial reason for companies to invest in R&D. These can include advanced market commitments, subscription models and prize funds.[66] The U.K.'s "subscription-style" payment model for antibiotics is an innovative approach that pays pharmaceutical companies upfront for access to their antibiotic product, based on the product's value rather than the quantity used. In the U.S., the Pioneering Antimicrobial Subscriptions to End Up surging Resistance (PASTEUR) Act of 2023 would grant upfront payments to antibiotic developers with new antibiotics that address unmet need and add significant clinical value.[67]

Reimbursement reform: Reimbursement reform involves changing how healthcare providers are compensated for using new antibiotics. This can encourage the adoption of new treatments and promote responsible antibiotic use. Adjusting hospital reimbursement rates and implementing value-based pricing are examples of reimbursement reform. The Medicare New Technology Add-on Payment (NTAP) program for new antimicrobial products is one such reform initiative.[68] The Swedish government also tested a new reimbursement model to ensure availability of new antibiotics: The pilot continued as of 2023.

Exhibit 9: Examples of initiatives in antibacterial research and development

Preclinical Research:	Clinical Trial:	Late-stage R&D:
Supporting early-stage R&D	**Enhancing clinical trial conduct**	**Supporting late-stage R&D**
• CARB-X	• ECRAID	• GARDP
• JPIAMR	• COMBACTE	• AMR Action Fund
• REPAIR Impact Fund	• ALRG	• BARDA BSA
	• CTTi	• IDFF

Notes: CARB-X – Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator. JPIAMR – Joint Programming Initiative on Antimicrobial Resistance, ECRAID – European Clinical Research Alliance on Infectious Diseases, COMBACTE – Combatting Bacterial Resistance in Europe – Networks, ARLG – Antibacterial Resistance Leadership Group, CTTi – Clinical Trials Transformation Initiative, GARDP – Global Antibiotic Research and Development Partnership, BARDA BSA – Broad Spectrum Antimicrobials programme, IDFF – InnovFin Infectious Diseases Finance Facility
Source: Global AMR R&D Hub Dashboard, "Incentives for Antibacterial R&D." Accessed June 14, 2024

Late-stage investment and market-based mechanisms remain the most attractive avenues for investors. Late-stage investments, exemplified by initiatives such as CARB-X and the AMR Action Fund, offer a more immediate pathway to market, reducing the high risks associated with early-stage research. These projects are closer to commercialization, providing investors with clearer timelines and potential returns.

Additionally, market-based mechanisms like the U.K.'s subscription-style payment model and the U.S. PASTEUR Act offer substantial financial incentives and guaranteed markets for new antibacterial drugs. These models not only ensure a stable revenue stream for pharmaceutical companies but also align with investor interests by mitigating market uncertainties and providing predictable returns.

Call to *action*

Investors have a unique opportunity to engage with investee companies at an individual level and to influence macro-level changes. They can demonstrate an appetite for appropriate regulation of harmful business practices, drive incentives for R&D and improve clarity around the roles and responsibilities of different sectors. By working collaboratively, investors can help identify and address existing gaps.

- **Understanding the economic impact:** Investors recognize that failure to tackle AMR could result in significant economic losses.
- **Integrating AMR into investment decisions:** The concept of incorporating an "AMR lens" into investment decisions involves both risk management and the identification of opportunities to invest in companies and initiatives that are part of the solution to AMR. It considers the impact of investments on AMR and avoids investments that exacerbate it.
- **Supporting research and innovation:** Investors can play a pivotal role in driving the research and development of new antibiotics, diagnostics and alternative treatments. This is particularly relevant for investors in the pharmaceutical and biotech industries. By providing the necessary funding, investors can help accelerate the pace of innovation and commercialization of solutions.
- **Engagement with investee companies:** Investors may engage with the companies to encourage adoption of sustainable operational practices and make use of freely available data on business practices provided by organizations such as FAIRR or the Access to Medicine Foundation as two examples.
- **Participation in multi-stakeholder initiatives:** Such platforms can provide valuable insights into the systemic risks and opportunities associated with AMR, and guide investment decisions toward more sustainable and resilient business models. The Investor Action on AMR (IAAMR) is one such collaborative effort that aims to address the systemic risks caused by AMR. With USD 14 trillion in combined assets, the 22 investor partners of IAAMR aim to integrate AMR considerations into their investment decisions. This approach involves either adopting an AMR lens when making investment decisions or engaging with investee companies on AMR-related issues. IAAMR also serves as a platform for policy engagement. It has outlined seven key policy recommendations for global leaders to help them tackle AMR and the group's previous efforts have gained recognition from the G7 finance ministers.[69] This initiative continues to take part in public-policy discussions, particularly in the lead-up to the UN General Assembly's High-Level Meeting on AMR in September 2024.

Exhibit 10: IAAMR's essential asks for tackling AMR

Science-based Guidance and Targets

- Establish an independent panel, modelled on the IPCC, for regular scientific assessments on AMR.
- Develop an international framework, like the Montreal Protocol or Paris Agreement, with science-based targets for cohesive AMR action.

Stewardship and One Health

- Commit to reducing antibiotic use in agriculture and end routine use for growth promotion and group prophylaxis.
- Adopt legislation to set maximum residue limits for antibiotics in wastewater and manage residues from livestock manure and wastewater treatment systems.

Integrated Surveillance

- Support a globally integrated surveillance system for AMR and antibiotic use, aligning data across humans, animals, and the environment, and mandate accurate reporting of antibiotic use in animal agriculture.

Funding the Development of New Antimicrobials

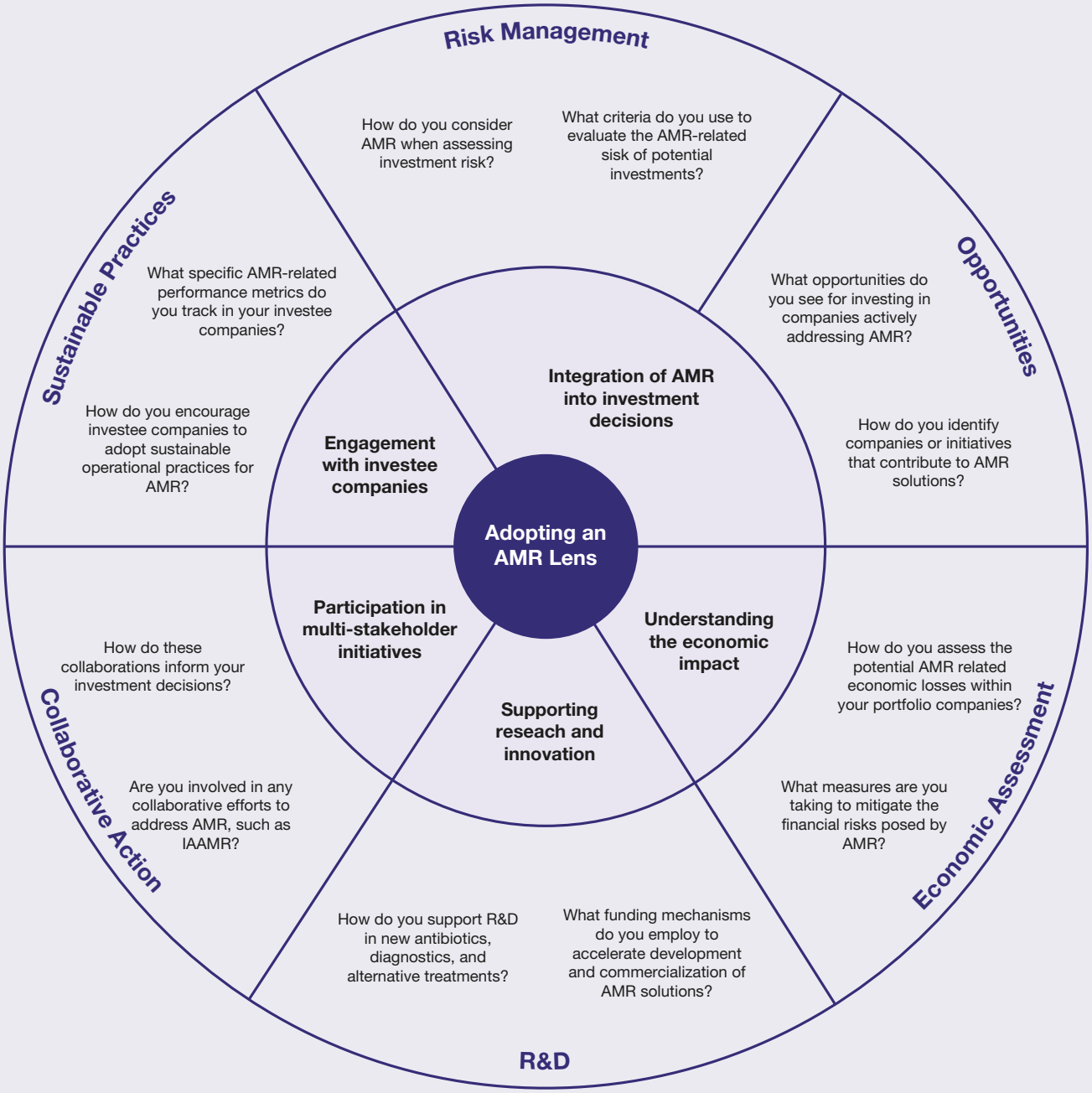
- Promote R&D of new antimicrobials and alternatives, targeting priority pathogens and considering the needs of LMICs. Encourage nations to implement push and pull incentives to ensure future antimicrobial development.

Global Equitable Access

- Address the lack of equitable access to antimicrobials by establishing a multilateral fund for LMICs, engaging with generics and biosimilars markets, supporting national action plans, improving surveillance, and mandating early access planning in R&D collaborations.

Source: "Investor Action on AMR (IAAMR) Public Investor Statement." IAAMR. May 22, 2024.

Exhibit 11: Examples of questions investors may ask when adopting an 'AMR' lens




Adopting an AMR Lens By Industry
Biopharmaceutical Sector
Animal Agriculture and Meat Production Sector
Healthcare Sector
Environmental Management
Global Surveillance Systems
Access & Stewardship
How do you ensure that biopharma companies have access and stewardship plans for new antimicrobials particularly in LMICs?
What criteria do you use to assess the stewardship strategies of pharmaceutical companies?
Reduction of Antibiotic Use
How do you engage with companies to reduce the inappropriate use of antibiotics in animal agriculture?
What strategies do you promote for improving hygiene and preventative measures and adopting alternative treatment methods?
Strategic Alliances
How do you engage with meat producers to support responsible antibiotic use?
How do you evaluate the effectiveness of these alliances in reducing AMR risks?
Waste Management
How do you engage with companies to adopt environmentally sustainable practices in antibiotic manufacturing?
What standards or certification schemes do you rely on to verify responsible waste management practices?
Responsible Administration
What resources do you use to evaluate healthcare providers' performance on AMR?
How do you promote responsible antimicrobial medication use among healthcare providers?
Risk Planning
How do you invest in global surveillance systems to manage AMR risks?
How do these investments contribute to global risk planning and the safe use of novel antibiotics?
Innovation
How do you support the innovation of new medications and diagnostic technologies to combat AMR?
What investment models do you use to promote R&D in antimicrobial resistance?

By industry:

Livestock and aquaculture sector
Engagement in this area may be geared toward the reduction of inappropriate antibiotic use, improving hygiene and adding preventative measures and alternative treatment methods to prevent the development of AMR in food supply chains. This is crucial for both large corporations and SMEs within the food and animal-health industries.

With the intensification of antibiotic regulations and the shift toward responsible antibiotic use, investors could potentially engage with companies to promote adherence to stewardship best practices.[70]

The International Finance Corporation (IFC), an arm of the World Bank Group, is actively involved in the animal protein sector through investment and focused advisory work. They review operational practices and provide clients benchmarking on good industry practices, including the use of veterinary services and antibiotics.[71]

Company engagement should encourage the adoption of a comprehensive antibiotics policy that restricts routine non-therapeutic use of medically important antibiotics. Other areas include supplier engagement to identify and implement treatment alternatives and preventative measures (improving biosecurity, animal husbandry, nutrition, and vaccination) to reduce inappropriate antibiotic use.[72] Consumer-facing companies, including retailers and restaurant businesses, play a critical role in supporting suppliers to improve practices and in monitoring compliance.

Healthcare sector
Investors may engage with healthcare providers using tools and databases to help evaluate their performance on responsible administration of antimicrobial medications. The private healthcare sector also presents opportunities, particularly through the support of health service providers. Strengthening health systems to enable appropriate antibiotic use in LMICs is another potential opportunity to expand in emerging markets. For example, the IFC has developed a Quality Assessment Tool used to assess health service companies on various clinical governance and patient safety criteria. Enhancing such tools to incorporate best practices for implementing policies, protocols and training about antimicrobial drug use could be a potential area of interest for investors.[73]

Biopharmaceutical sector

These enterprises have substantial opportunities to innovate new medications and diagnostic technologies, such as rapid tests that facilitate informed prescription decisions.

Initiatives that decouple financial gains from the sales volume of novel drugs could serve as a catalyst for intensified research into AMR.[74] Development finance institutions may have a strong role in creating push incentives for companies to engage in antimicrobial R&D by uncoupling profits for novel antimicrobials from the actual sales volumes.[75] Other modes of investment include Product Development Partnerships (PDPs), biopharmaceutical accelerators, impact investing and public-private collaborations.

For sustainable solutions to take hold, comprehensive and detailed access and stewardship plans must be embedded in companies' antimicrobial innovation, ahead of a product's market approval.[76]

In response to pull incentives, biopharmaceutical companies may be engaged to prioritize R&D in critical areas that cater to global needs, elevate production quality standards and supply chains, and guarantee the availability of drugs in all countries.[77] Other areas for investment include alternatives to antimicrobials such as vaccines, diagnostics and alternative therapies.

Other avenues for engagement include stewardship for responsible antibiotic use and enhanced waste management through environmentally sustainable practices to prevent the emergence and spread of AMR. This is particularly important for relatively large corporations.[78] The British Standards Institution, in collaboration with the AMR Industry Alliance, has developed a certification scheme.[79] This program is noteworthy because it provides third-party independent verification that the antibiotic waste released into the environment by companies that manufacture antibiotics and their raw ingredients is appropriately controlled.[80] In addition, the WHO is currently developing a more comprehensive set of guidelines for managing and reporting effluence from antibiotic manufacturing. These guidelines, which are not yet finalized, will be developed by an independent organization, providing an added layer of credibility and impartiality.[81]

A report by the Access to Medicine Foundation highlights the importance of structured advance access planning, which is not a standard practice across companies.[82] While all companies mentioned in the report were conducting clinical trials in low- and middle-income countries (LMICs) and indicated some level of post-trial access commitments, these commitments are not always detailed and clear. Stewardship strategies were generally lacking, with only some surveillance and data-sharing strategies in place. This emphasizes the need for both large pharmaceutical companies and SMEs active in antimicrobial R&D to pursue access and stewardship planning for all late-stage clinical projects.

Partnerships are vital in scaling efforts and broadening access and stewardship plans. SMEs rely heavily on partners to help commercialize products and drive global access. Collaborations with publicly funded entities like the Global Antibiotic Research & Development Partnership (GARDP) can help SMEs pursue access on a wider scale through licensing agreements.

Investment in global surveillance systems may present financial opportunities tied to global risk planning, particularly in managing AMR outbreaks. This strategy may also provide a pathway for the safe use of novel antibiotics, rather than limiting their use to prevent resistance development. The use of reserve antibiotics, traditionally effective in hospitals and developed countries, can be expanded through adaptive R&D and infrastructure development to create a more responsive and robust system for managing and mitigating the AMR risks in LMICs. This approach could facilitate the launch of other high-potential candidates in LMICs, thereby creating a more inclusive global health landscape.

Case *studies*

Case study 1:

Mirova

The French asset manager Mirova has focused on improving the health of people, animals and ecosystems and promoting sustainable agriculture at its investee companies.

Approach:

With global meat production accounting for 70% of all antibiotic use and projected to increase by 11.5% between 2017 and 2030, companies exposed to animal health products must demonstrate efforts to transition toward more sustainable agriculture. Mirova's two-pronged approach involved the identification of companies that can make a positive contribution through the One Health approach and through engagement with companies to foster a positive impact.

Mirova opined that most companies exposed to antibiotics use were still in the early stages of AMR stewardship. So it focuses on stewardship efforts, notably to support the transition of farmers toward less antibiotics-intensive agriculture. However, transparency on measures implemented is still limited, and, as investors, tools to truly identify the impact of investments in combating AMR were limited. Hence, its focus is on the development of alternatives (Ecolab, Zoetis) and addressing this risk at various stages of the supply chain (Zoetis).

Investments:

- **Ecolab:** Farm disinfectants used in the prevention of animal diseases may reduce antibiotic use in animals. However, Mirova identified that the use of biocides, such as disinfectants and sanitizers in animal production, may lead to the development and spread of AMR within the food chain. Ecolab, which acquired CID Lines, a provider of livestock biosecurity and hygiene solutions, is exposed to AMR as a result.[83] Mirova engages with Ecolab to prioritize prevention products that are alternatives to the use of antibiotics. Projects that Mirova supports include CID Lines' development of a diagnostic tool for animal health, and a partnership with Ghent University to promote a biosecurity approach to livestock through the European biosecure project.

- **Zoetis:** Zoetis' livestock products segment accounted for 35% of its FY 2022 revenue and the share of revenue from livestock antibiotic sales within this segment decreased to 12% in 2022 from 22% in 2018. Instead, Zoetis pivoted to develop vaccines and other alternative diagnostic products to minimize the need for antibiotics in animal populations. Examples include vaccines developed for porcine and poultry disease and a sequencing tool for veterinarians and producers to track and monitor infection. The estimated share of revenue from prevention and diagnostics in Zoetis' livestock segment is between 10% to 20%. Further, Zoetis is also conducting research for emerging infectious diseases and transboundary diseases.

Case study 2:

The Council on Ethics of the Swedish National Pension Funds

How can investors engage with companies to adopt responsible antibiotic use policies and sustain momentum for investments to address AMR?

Approach:
The Council on Ethics of the Swedish National Pension Funds influences companies to address systemic sustainability risks, in collaboration with other investors. Their goal is to raise AMR awareness and encourage change through engagement with relevant companies and stakeholders.

- **Engagement Initiatives:** Since 2023, they have participated in FAIRR's AMR-related initiatives on animal pharmaceuticals and restaurant antibiotics to encourage responsible antibiotic use across the animal protein value chain. Engagement dialogues with, and assessment of, the 19 focus companies covered by the initiatives continues in 2024 and beyond, as does follow-up on outcomes.

- **Partnerships and Sectorwide Initiatives:** In 2024, they joined the Investor Action on Antimicrobial Resistance (IAAMR) to raise AMR risk awareness and leverage investor influence. Currently, 22 leading institutional investors, representing USD 14 trillion in assets, are involved in this initiative.

- **Expectations and Recommendations:** Ahead of the UN General Assembly's second high-level meeting on AMR in September 2024, they endorsed a public statement, developed by IAAMR's founding collaborators. The statement calls for global leaders to manage AMR adequately by adopting a "One Health" approach and establishing an independent panel modeled on the IPCC.

Case study 3:

WHEB Asset Management

How can investors address the prevention and stewardship aspects of combating AMR?

Approach:
WHEB investment strategy avoids exposure to companies involved in the agricultural use or overuse of antibiotics. Instead, they invest in companies reducing AMR transmission through infection prevention and control (IPC). Effective IPC interventions can reduce healthcare-associated infections by 35% to 70%.[84]

Investments:

- Under WHEB's health theme, the company invests in STERIS, which offers hygiene and sterilization products and services for hospitals, medical device manufacturers, biopharmaceuticals, food safety and industrial markets. The company's products and services prevent microbial contamination, particularly in healthcare settings where the risk of infection is high.

- In addition, WHEB invests in Agilent and ThermoFisher, which manufacture equipment used to analyze and test environmental samples for microbes. WHEB also invests in Novo Nordisk, which donated USD 75 million to the AMR Action Fund.

- Under WHEB's water theme, the company invests in Ecolab and Xylem, which provide supply water and wastewater treatment services and technologies to the biopharmaceutical industry. These contribute to the reduction of antibiotics in industrial effluents and consequent environmental contamination. In addition, WHEB also invests in Veralto, which provides treatment technologies to the municipal wastewater industry. This contributes to the reduction of AMR by controlling environmental contamination due to human waste. The companies also provide microplastic removal services from wastewater. This is an indirect solution: AMR can be up to three times higher in wastewater containing microplastics, as they provide more favorable conditions for bacterial growth.[85]

Case study 4:

Legal & General Investment Management

How can investors influence companies to implement effective AMR policies and strategies?

Approach:
Legal & General Investment Management (LGIM) focuses on systemic engagement themes that address global sustainability challenges. As part of this commitment, LGIM actively engages with companies to promote responsible antibiotic use and mitigate the risks of antimicrobial resistance.

- McDonald's, as one of the largest purchasers of beef and pork, has significant influence on animal husbandry standards across its supply chain.[86] In 2021, LGIM, along with other shareholders, co-filed a proposal at McDonald's annual general meeting (AGM) asking the board to evaluate the environmental and public-health costs of antibiotic use in the company's supply chain. LGIM supported this resolution and a similar proposal the following year, publicly declaring its support in advance. They also engaged directly with McDonald's, urging increased AMR stewardship efforts. In 2023, LGIM co-filed a resolution under The Shareholder Commons, asking McDonald's to comply with WHO guidelines on antimicrobial use in food-producing animals.[87] [88] The resolution, supported by nearly a fifth of shareholders, was refiled for voting at the 2024 AGM but was allowed by the U.S. Securities and Exchange Commission (SEC) to be omitted by McDonald's from its proxy materials on the grounds that the company already has substantially implemented the proposal.[89]

- Support for other shareholder resolutions: LGIM consistently supports shareholder resolutions aimed at improving AMR stewardship at various companies including Tyson Foods, Hormel Foods and Abbott Laboratories.

- In 2024, LGIM published its first health policy, which outlines required AMR-related actions for companies in various sectors. The policy indicates LGIM's commitment to supporting AMR-related shareholder resolutions and holding boards or individual directors accountable for strategies, products and supply chains that negatively affect AMR management. Ahead of the UN General Assembly's second high-level meeting on AMR in September 2024, LGIM endorsed a public investor statement developed by IAAMR.

Case study 5:

Aviva

Aviva's stewardship efforts around antimicrobial resistance (AMR) have intensified, reflecting the company's concerns regarding the public health and financial implications of AMR, particularly due to its investments in food retail and production, pharmaceuticals and biotechnology companies, and health insurance.

Approach:
During World Antibiotic Awareness Week in 2022, Aviva launched a white paper titled Confronting a Permacrisis. This paper outlined, for the first time, the complex links between AMR, climate change, and biodiversity. It argued that climate change and nature loss are contributing to conditions that allow certain pathogens to spread, while antimicrobials—an essential tool in the fight against disease—are becoming less effective.

In the last 18 months, Aviva has focused its company engagements on the agricultural and water pollution impacts of AMR.

Aviva has also:

- Provided evidence at the All-Party Parliamentary Group on AMR and the All-Party Parliamentary Group on Water Sanitation, advising on policies the UK government could enact to combat AMR.

- Successfully used its influence, as recognized by Professor Dame Sally Davies, to convince G7 finance ministers to collaborate with investors, policymakers, and companies to mitigate AMR.

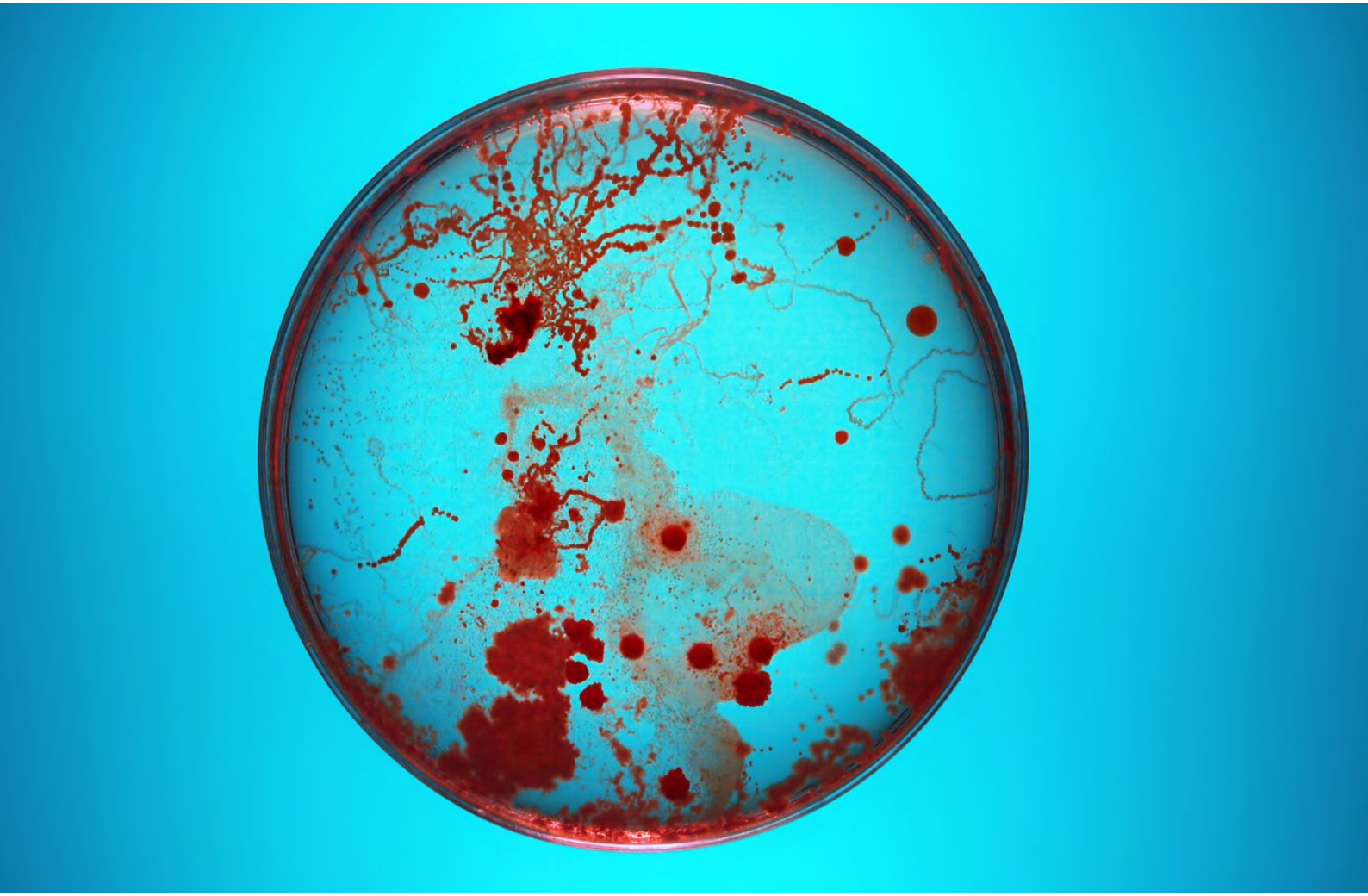
- Presented to the Global Leaders Group on AMR, chaired by the Prime Minister of Barbados and the Prime Minister of Bangladesh, on the role of finance in tackling AMR, and called for the establishment of an independent panel on AMR evidence, similar to the IPCC.

In May 2024, the UK Government announced funding of £10 million over the next five years to help establish a global independent scientific panel for AMR, modelled on the success of international panels such as the Intergovernmental Panel on Climate Change (IPCC). An Aviva Investors delegation will attend the UN General Assembly high-level meeting on AMR in September 2024 to share insights on what an independent panel could look like, based on Aviva's experience with the IPCC as investors.

Conclusion

Investors are encouraged to recognize the critical role of the private sector in addressing AMR at both the company and policy levels.

By fostering an environment conducive to research and development, and by implementing sustainable practices, businesses can contribute significantly to the global effort to mitigate the threat posed by antimicrobial resistance.



This is a collective effort, requiring more than just government interventions alone.

It is now imperative for the financial sector to mobilize and contribute to the solution.

Appendix

Exhibit 12: Antibiotic resistance rate in humans for critical pathogens as of 2017

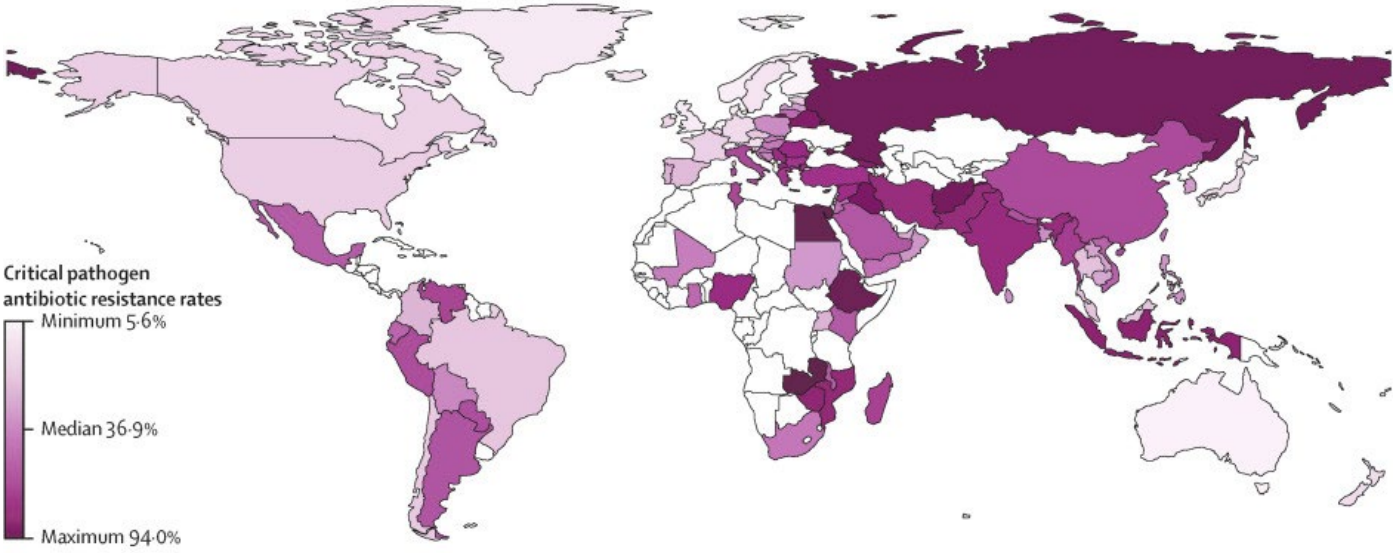
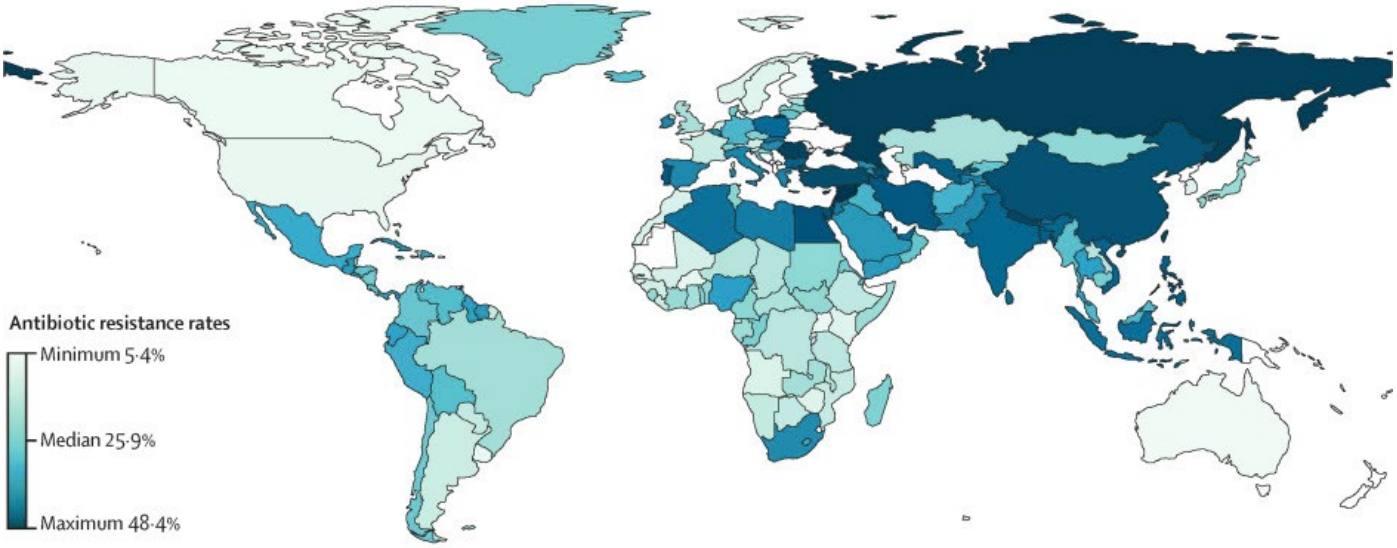


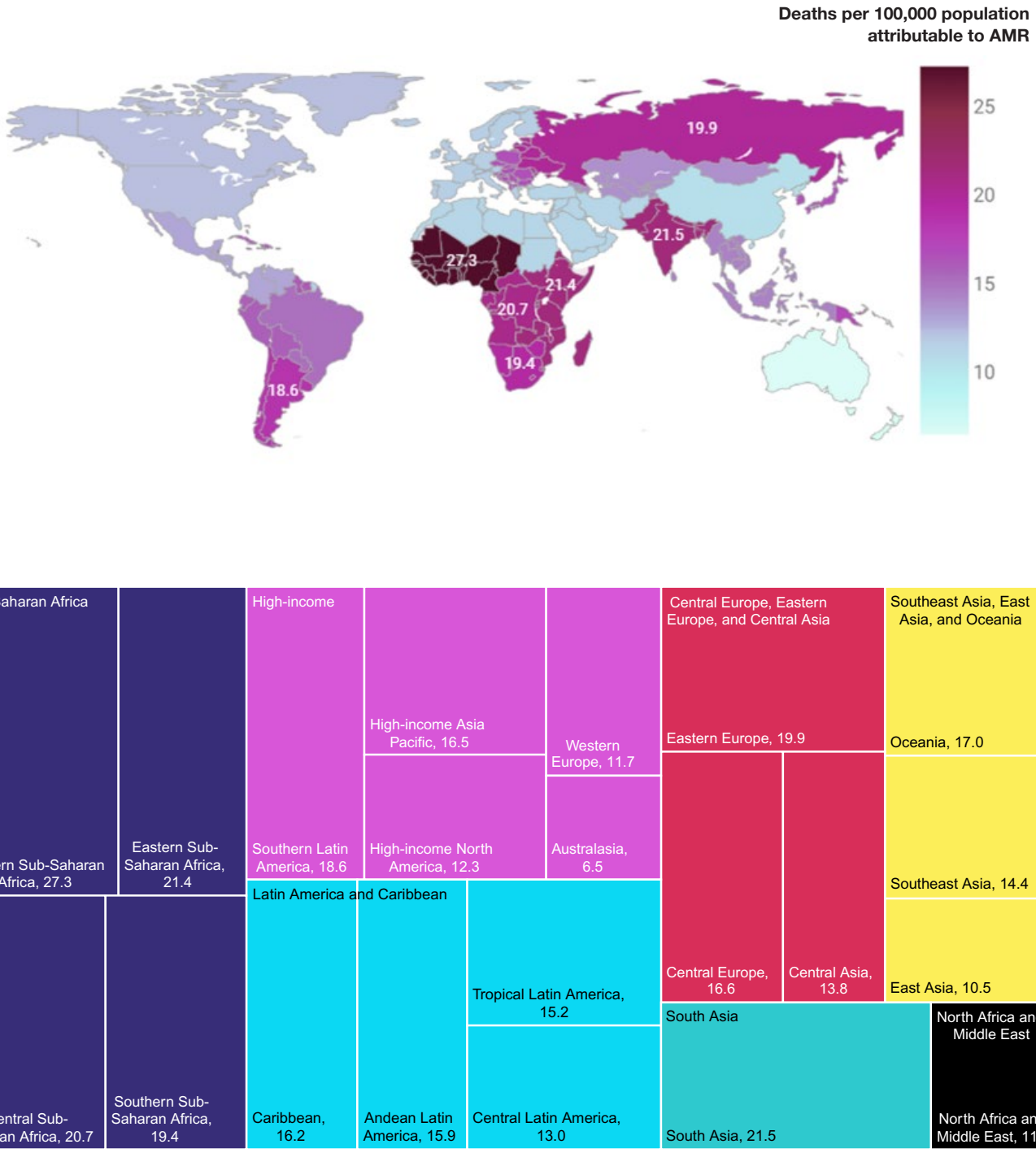
Exhibit 13: Antibiotic resistance rate in animals as of 2019



Note: Countries in white do not have data

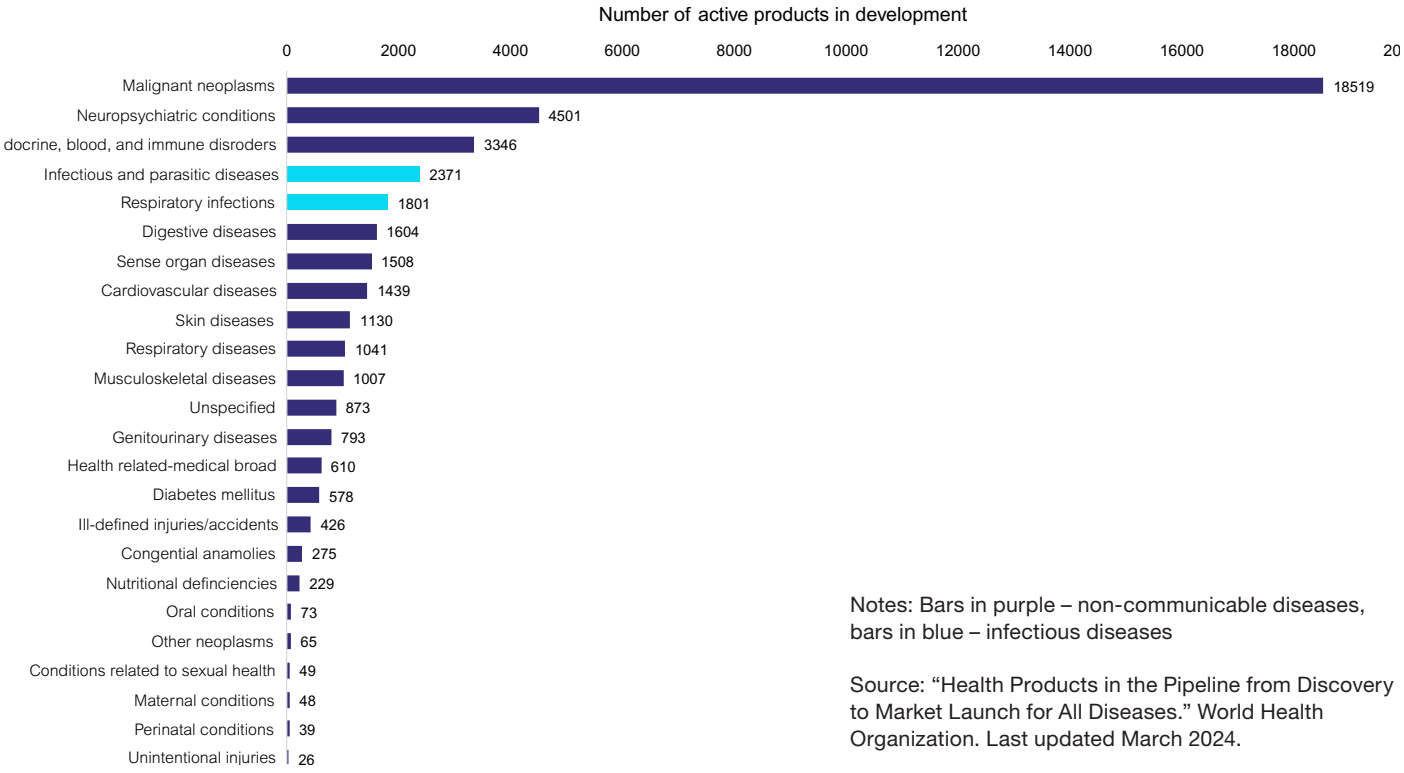
Source: Allel, Kasim, Day, Lucy, Hamilton, Alisa, Lin, Leesa, Furuya-Kanamori, Luis, Moore, Catrin E., Van Boeckel, Thomas, Laxminarayan, Ramanan, Yakob, Laith. "Global Antimicrobial-Resistance Drivers: An Ecological Country-Level Study at the Human–Animal Interface." The Lancet Planetary Health 2023. Accessed June 6, 2024.

Exhibit 14: Deaths per 100,000 population attributable to bacterial antimicrobial resistance by Global Burden of Disease region, 2019



Source: "VizHub - MICROBE." Institute for Health Metrics and Evaluation. Accessed April 2, 2024.

Exhibit 15: Number of active products in development by sub -category



Notes: Bars in purple – non-communicable diseases, bars in blue – infectious diseases

Source: "Health Products in the Pipeline from Discovery to Market Launch for All Diseases." World Health Organization. Last updated March 2024.

Exhibit 16: Global costs and benefits, over 10 years and over 30 years

	Total cost (discounted)	Lives saved	DALYs saved	Value of DALYs saved	Benefit: cost ratio
10-year	USD 11.7 billion	518,000	19.5 million	310.6 billion	27:1
30-year	USD 38.9 billion	9,933,000	374.5 million	4,874.2 billion	125:1

Source: Silverman Bonnifield, Rachel, and Adrian Towse. "Estimating the European Union's Return on Investment from an Ambitious Program to Incentivize New Antibiotics." CGD Brief, December 2022.

World Health Organization: The overall burden of disease is assessed using the disability-adjusted life year (DALY), a time-based measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health, or years of healthy life lost due to disability.

Exhibit 17: EU Return on Investment estimates under different scenarios

	10 – year EU[a]	30-year EU[a]	10-year global[b]	30-year global[b]
Base-case	4:1	18:1	27:1	125:1
No growth in AMR deaths (0% per year)	3:1	12:1	23:1	82:1
Fast Growth in AMR Deaths (5% Per Year)	5:1	35:1	34:1	237:1
Slower resistance growth to new antimicrobials (1% per year)	4:1	20:1	27:1	136:1
Faster resistance growth to new antimicrobials (5% per year)	4:1	15:1	25:1	100:1
Lower drug efficacy scenario (2% death reduction per drug at peak efficacy)	2:1	7:1	11:1	50:1

Source: Silverman Bonnifield, Rachel, and Adrian Towse. "Estimating the European Union's Return on Investment from an Ambitious Program to Incentivize New Antibiotics." CGD Brief, December 2022.

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1 Pathogens are disease-causing agents such as bacteria, viruses, fungi and parasites. Antimicrobials (antibiotics, antivirals, antifungals and antiparasitics) are drugs that destroy pathogens. See "Antimicrobial Resistance - World Health Organization (WHO)." https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance. Accessed April 2, 2024.

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4 The percent of samples that tested non-susceptible or resistant to certain antimicrobials.

5 See Sustainable Development Goal – SDG Target 3.d.2 – Proportion of bloodstream infection due to methicillin-resistant Staphylococcus aureus (MRSA) (%) and Proportion of bloodstream infection due to Escherichia coli resistant to third-generation cephalosporins (%).

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In January 2020 at the World Economic Forum Annual Meeting in Davos, the Access to Medicine Foundation, the FAIRR Initiative and the UK Department of Health and Social Care launched the Investor Action on AMR (IAAMR) initiative. The initiative aims to build and support a global AMR investor community to galvanise and leverage investor efforts to mitigate the development of AMR. IAAMR is currently supported by 22 investors representing USD 14 trillion in assets.

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