GARDP
Global Antibiotic Research & Development Partnership

GLOBAL CHALLENGES

ANTIBIOTIC DISCOVERY

DISCOVERING THE NEXT GENERATION OF INNOVATIVE ANTIBIOTICS

Antibiotic resistance is now beginning to outpace antibiotic development. Over the past several decades, drug-resistant infections have continued to spread, while the pipeline for new antibiotics has been drying up. Research shows that what is lacking is a sufficient number of antibiotic treatments, especially innovative treatments, to tackle the most difficult-to-treat Gram-negative infections posing the greatest threat to public health.

According to a 2025 review, less than ten percent of treatments in the current antibiotic clinical pipeline target the most serious of the World Health Organization (WHO) priority pathogens in an innovative way.[1] That means that few potential treatments in the current pipeline can help replace antibiotics lost to resistance.

This situation is alarming given that antibiotic resistance is already one of the world's biggest killers, contributing to more than 4.7 million deaths in 2021. With the rise and spread of Gram-negative bacterial infections, that number is now expected to rise sharply, increasing by more than 70% from 2025 to 2050.[2] To prevent this crisis scenario and address the public health threat, we must have a multi-faceted response, including greater investments in the discovery of innovative antibiotics.

INVESTING IN DISCOVERY RESEARCH

Antibiotics revolutionized modern medicine, but nearly all of the antibiotic classes that we rely on today were discovered before 1980. In recent decades, antibiotic discovery has been plagued by many of the same problems as the antibiotic pipeline more generally: reduced investment by pharmaceutical companies and fewer antibiotic researchers. In comparison to other disease areas, antibiotic discovery research also faces exceptionally high failure rates due to scientific and commercial challenges, including the need for high doses with low toxicity along with the expectation of an unusually low cost of goods.

For researchers targeting Gram-negative bacteria in particular, the challenge is even more formidable. These bacteria are equipped with a double cell membrane that shields against antibiotics. Even when antibiotics manage to get past this barrier, Gram-negative bacteria have specialized resistance mechanisms that may disable or eject them. To be able to overcome these sophisticated defence systems in the future, what's needed is a new arsenal of antibiotic treatments with never-before-seen modes of action and other novel tactics. What's needed, in other words, is innovation.

GARDP'S INNOVATIVE ANTIBIOTIC DISCOVERY RESEARCH

The Global Antibiotic Research & Development Partnership (GARDP) works to discover, develop and enable appropriate access to antibiotics to address public health needs. Its discovery and exploratory research zeroes in on innovative antibiotics by searching for new antibiotic substances and identifying previously unexploited bacterial vulnerabilities, among other approaches. These efforts drive toward a common goal of delivering innovative preclinical candidates that may become next-generation antibiotics to tackle drug resistance (see Figure 1).

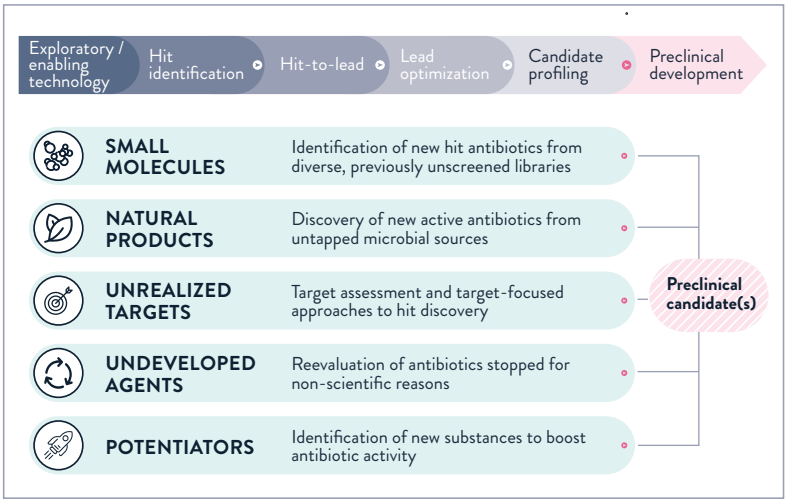
[1] WHO. 2025 Antibacterial agents in clinical and preclinical development: an overview and analysis.
[2] Global burden of bacterial antimicrobial resistance 1990–2021: a systematic analysis with forecasts to 2050. Naghavi, Mohsen et al. The Lancet, Volume 404, Issue 10459, 1199 – 1226.

HARNESSING INNOVATIVE ANTIBIOTIC DISCOVERY RESEARCH FOR PUBLIC HEALTH NEEDS

Current antibiotic discovery research often involves non-traditional, experimental approaches that focus on narrow or niche indications. GARDP's discovery research, in turn, focuses on solutions for high-burden regions by placing public health need and affordability at its centre. It prioritizes innovative, small-molecule antibiotics capable of providing rapid, systemic treatment for the most difficult-to-treat infections, in particular those caused by deadly *Klebsiella pneumoniae* and *Acinetobacter baumannii*. The ideal treatments would be usable in low- and middle-income countries, where AMR-related deaths are greatest. They would not require cold chains for stability, would have low manufacturing costs and could be effective when administered orally. These characteristics would help enable rapid adoption and access in diverse healthcare settings, including low-resource settings with limited diagnostics.

To advance this ambitious public-health-first approach to discovery research, GARDP works in collaboration with experts around the world using the latest technologies, such as custom-built high-throughput screening and AI modelling. It identifies and optimizes potential antibiotics that have activity against the most serious multidrug-resistant pathogens in a highly iterative and collaborative process that drives toward candidate profiling for preclinical development.

Figure 1: *GARDP discovery research to identify innovative preclinical candidates*



IN FOCUS: GARDP'S DISCOVERY OF UNREALIZED TARGETS

Every organism has vulnerabilities that might be taken advantage of—an Achilles heel. Antibiotics can target these vulnerabilities, including specific molecules or pathways, to kill or disarm harmful bacteria. But over time these bacteria evolve to become immune to the drugs designed to kill them—they are resistant. The "unrealized targets" workstream in GARDP's discovery research focuses on previously unexploited vulnerabilities in drug-resistant bacteria. As part of this workstream, GARDP is working with partners on an innovative antibiotic that targets a protein essential for the survival of *Klebsiella pneumoniae*, which causes deadly bloodstream and other types of infections. The aim is to optimize this innovative antibiotic into a preclinical candidate that can be further developed as a treatment for drug-resistant *Klebsiella* and other pathogens belonging to the Enterobacterales order.

GARDP works with Institut Pasteur Korea to execute high-throughput screening for innovative antibiotics.
Photo credit: Institut Pasteur Korea

GARDP, H3D at the University of Cape Town, and Ersilia are building AI models to identify new antibiotics.
Photo credit: H3D