ACTIVITY REPORT

2021

EXECUTIVE SUMMARY

Global Antibiotic
Research & Development
Partnership



EXECUTIVE SUMMARY 2021

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MESSAGE

FROM THE BOARD CHAIR & EXECUTIVE DIRECTOR

For the first time, scientists have undertaken in-depth research to record all lives lost to antibiotic resistance worldwide. A recent study in *The Lancet* highlighted the 1.27 million deaths that occurred in 2019 due to antimicrobial resistance¹ (AMR) – more than malaria and HIV/AIDS – and made the case for greater access to effective antibiotics for all people. The importance of GARDP's mission could not be more evident.

Throughout 2021, our programmes made notable progress in accelerating the development of new treatments where they are the most urgently needed: neonatal sepsis, sexually transmitted infections and serious bacterial infections in hospitalized adults and babies.

The issue of access is highly critical. We are working to ensure that new and existing antibiotic treatments like zoliflodacin and cefiderocol are made available and affordable globally, including in low- and middle-income countries (LMICs). Patient need – not money or location or social status – should determine whether or not a patient receives an effective antibiotic treatment.

2021 was also an important year in terms of political engagement to counter antibiotic resistance. In

June and December, declarations by the G7 Health and Finance Ministers drew attention to this vital issue.

In 2021, we were honoured to have been granted a privileged status by the Swiss Federal Council, which recognizes the major role we play in the fight against antibiotic resistance. We are one of a few international foundations that have been granted such status since the Swiss Host State Act took effect in 2008.



Ramanan Laxminarayan GARDP BOARD CHAIR

We are very grateful for our partners' new and renewed funding commitments. By the end of 2021, GARDP had invested over €75 million since our inception in 2016 to develop treatments for drugresistant infections and make them accessible.

Together with our partners, GARDP is ramping up efforts to fight antibiotic resistance and meet this great health challenge of our time.



Manica Balasegaram
GARDP EXECUTIVE DIRECTOR



MISSION

PRESERVING THE POWER OF ANTIBIOTICS

Every one of us will need antibiotics at some point during our lifetime. Not only do we all use them, but antibiotics are the foundation of modern medicine. They are used for surgeries, oncology care, medical implants, to name a few. Our ability to push forward the frontiers of healthcare is made possible by our ability to push back dangerous bacteria.

Antibiotics possess incredible power that has been taken for granted for years. This power, however, is not guaranteed. Antibiotic resistance is on the rise due to evolution, human misuse and sometimes overuse. This is a race. We need to stay ahead of the bugs and develop new antibiotics as bacteria become resistant to older ones.

Current antibiotics are no longer effective in all situations, leading to a wasteful loss of life. This is particularly the case in the three areas where we currently focus our efforts:

- Children and babies who lack antibiotic treatments tailored to their specific needs
- People affected with gonorrhoea, as this bacterium is gradually becoming resistant to all antibiotics
- Hospitalized patients who contract serious bacterial infections

With other areas of healthcare being more profitable, many investors have fled the antibiotics market. Our organization was founded to fill this gap and provide the R&D resources and infrastructure to coordinate a global response to the growing threat of antibiotic resistance.

It can take a decade and more and over US\$1.5 billion² to develop a new antibiotic treatment. In just 5 years, and with a budget of €75 million, our partnership has delivered a unique portfolio of new treatments, including one approved drug and two in phase 3 development.

To achieve success, we all need to work together. Our generation is living through a critical moment in the race against antibiotic resistance. With the right support, we can deliver new antibiotics around the world, so that all infections remain treatable, for everyone, everywhere.



OUR MISSION

The Global Antibiotic Research & Development Partnership mobilizes partners to accelerate the development and access of much-needed antibiotic treatments around the globe. Working together with governments, the private sector, academic institutions and civil society, we are driving the development of innovative solutions to antibiotic resistance.

Founded in 2016 by the World Health Organization (WHO) and the Drugs for Neglected Diseases *initiative* (DNDi), our organization brings a unique and

comprehensive approach to this global health threat:

- Development: a portfolio of rapidly available new antibiotic treatments
- Delivery: a framework to ensure all countries have access to current and new antibiotics
- Partnerships: a global network of 70 public and private partners who come together to advance our social mission

"Overall financing for antibiotic R&D is currently geared more toward early-stage development. We should significantly enhance financing towards late-stage development and access, as countries need new antibiotics now. Given the institutional experience and expertise that GARDP has built over the last five years, we hope to convince additional partners to join us and play a key role in filling this critical gap."

MANICA BALASEGARAM

GARDP EXECUTIVE DIRECTOR

ACCESS

SECURING ACCESS FOR ALL

GARDP aims to address access barriers along the entire drug-to-patient pathway and take a holistic view of access at the global, regional, national, and local levels.

GARDP maintains relationships with both innovators and generic producers to monitor the product landscape and identify opportunities to enhance drug access. At the end of 2020, GARDP signed a Memorandum of Understanding (MOU) with Dr Reddy's Laboratories and Aurigene Pharmaceutical Services Limited (APSL) to explore joint opportunities around delivering access to zoliflodacin, a new treatment for gonorrhoea, in South Africa and Thailand.

GARDP also works with innovative companies and other access organizations to accelerate access in

low- and middle-income countries. This is the aim of the MOU that GARDP signed with the Clinton Health Access Initiative (CHAI) and the pharmaceutical Shionogi & Co., Limited related to cefiderocol – an antibiotic for bacterial infections in patients with limited treatment options – in July 2021.



Another significant step forward for access was the launch of SECURE. With the support of other international organizations, GARDP and the World Health Organization (WHO) launched a collaborative initiative aiming to accelerate access to a portfolio of essential antibiotics.

SECURE's antibiotics portfolio will be adapted according to the individual country's needs. Participating countries will be able to purchase the antibiotic portfolio at affordable prices through UNICEF or alternative procurement mechanisms. SECURE will work with each country and local partners to ensure good stewardship, including guideline updates, appropriate use, improved surveillance and diagnostics, and the collection of real-time clinical data.

"Inventing and developing novel antibiotics for resistant infections is only part of the solution to the global challenge of AMR. Appropriate use of new antibiotics is vital to ensuring their durability around the world. Through our partnership with GARDP, we aim to deliver access to new antibiotics and ensure their optimal use for all patients in need."

MANOS PERROS
CEO OF ENTASIS THERAPEUTICS

PIPFLINE

GARDP'S PORTFOLIO OF ANTIBIOTIC TREATMENTS

GARDP has established a solid portfolio to tackle antibiotic resistance and achieved progress via three major research and development programmes since 2016.

CHILDREN'S ANTIBIOTICS

The primary focus is on clinical development, including the first-ever studies designed to evaluate drugs such as flomoxef and fosfomycin as alternatives in the treatment of neonatal sepsis.

SEXUALLY TRANSMITTED INFECTIONS

A potential new treatment for gonorrhoea, zoliflodacin, is being investigated in a pivotal phase 3 trial.

SERIOUS BACTERIAL INFECTIONS

This programme includes two antibiotics with the potential to treat infections caused by WHO priority pathogens. The first is cefepime-taniborbactam, for which we are in the recruitment stage of a crucial phase 3 clinical trial, and the second is cefiderocol, which was recently approved by the Federal Drugs Administration and European Medicines Agency. Access work activities are well underway for all these projects.

| DISCOVERY | DISEASEAREA | TRANSLATIONAL | DEVELOPMENT | | REGULATORY | IMPLEMENTATION |
|-----------------------------|--------------------------------------|---|--|-------------------------------|--|--|
| | | Pre-clinical / Early Clinical | Paediatric trials | Phase 3 | Registration Status | Registration Status |
| AMR Screening Consortium | | | | | Cerepime-taniborbactam (NCE) Venatorx Pharma** | Access strategy |
| Antibiotic potentiators | SERIOUS BACTERIAL INFECITIONS | | Cefiderocol*** Neonatal PIP/PSP | | Cefiderocol (Shionogi)*** Approved USA / EU | Access opportunity |
| Natural Products | | Potential candidate A (NCE or repurposed) | | | | |
| | NEONATAL SEPSIS | IV Fosfomycin | Treatment regimens Public health strategic efficacy and safety trials | | Approved in EU, with Neo & Paeds label | |
| TICS | | Flomoxef | | | Approved in Asia: Neo & Paeds data | |
| CHILDREN'S ANTIBIOTICS | | Amikacin | | | Approved globally: Neo & Paeds data | |
| | PAEDIATRIC DEVELOPMENT | Polymyxin B* | Regulatory paediatric plans (serious bacterial infections paediatric & neonates) | | Approved in USA, with limited Neo & Paeds label | |
| | | Paediatric cefepime- taniborbactam (NCE) Venatorx Pharmaceuticals | | | | |
| | | Potential candidate A (NCE or repurposed) | | | | |
| | | | | Zoliflodacin (NCE) Entasis | | Acces strategy including manufacturing development |
| | SEXUALLY TRANSMITED INFECTIONS | | | Therapeutics Inc. | | Surveillance / Prevalence studies |
| | | Potential candidate B (NCE) | | | Approved in USA / EU for CABP | |

^{*} Under review/on-hold

^{**}Development of cefepime-taniborbactam is sponsored by Venatorx Pharmaceuticals and has been funded in whole or in part with federal funds from NIAID/NIH/HHS and BARDA/ASPR/HHS in the United States and the Wellcame Trust in the United Kinadam

[🕶] Potential pipeline addition, MOU signed between GARDP, Shionogi and Clinton Health Access Initiative (CHAI) to explore cefiderocol access in LMIC

2021 HIGHLIGHTS

CHILDREN'S ANTIBIOTICS

Antibiotic resistance disproportionately affects children, especially newborns (babies under 28 days old). Over 560,000 neonatal deaths were linked to AMR in 2019, with over 140,000 directly attributed to AMR³.

Despite the urgent need for antibiotics that are tailored to children's specific needs, the development of new treatments and expansion of access to existing antibiotics continue to be neglected. GARDP established its children's antibiotics programme to address this crucial gap in antibiotic R&D, with a special emphasis on developing new antibiotic treatments for newborn babies who are most at risk from drug-resistant infections.

"We desperately need research and investment into new, safe, and effective antibiotics for our newborns, who have different needs than adults. The treatments, formulations, and dosages all need to be tailored to neonates."



TANUSHA RAMDIN

SENIOR NEONATALOGIST AT CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL, SOUTH AFRICA

OUR ACHIEVEMENTS IN 2021

IDENTIFIED

three potential combination treatments for neonatal sepsis

ADVANCED

the clinical development of cefepime-taniborbactam, a potential new antibiotic treatment, for children

INITIATED

collaborations to develop access to antibiotics

OUR NEXT CHALLENGE?

"In 2022, we will focus our efforts on using what we learned in our neonatal observational study to pursue clinical research around the three antibiotic combinations that show promise in treating newborns with sepsis. This will include identifying new study sites and building on the strong framework for our clinical trials. We will also continue to strengthen our collaborations around accelerating access to existing antibiotics for children."



Children's Antibiotics Project Leader, GARDP



2021 HIGHLIGHTS

SEXUALLY TRANSMITTED INFECTIONS



An estimated 374 million new cases of curable sexually transmitted infections occurred among 15- to 49-year-olds globally in 2020⁴.

This included an ever rising 82 million cases of gonorrhoea⁵, as well as others such as chlamydia, syphilis, and trichomoniasis. Gonorrhoea is getting increasingly difficult to treat as it develops resistance to current treatment options. GARDP is working hard to ensure that gonorrhoea remains treatable for future generations to come.

"A Neisseria gonorrhoeae infection is particularly insidious, as it often lacks symptoms. However, if left untreated, gonorrhoea can have serious and permanent consequences, including infertility, ectopic pregnancies, and an increased risk of contracting HIV."

JOSEPH WOODRING

PRINCIPAL INVESTIGATOR FOR THE ZOLIFLODACIN TRIAL, SILOM COMMUNITY CLINIC; AND SENIOR MEDICAL OFFICER, CENTERS FOR DISEASE CONTROL AND PREVENTION, THAILAND

OUR ACHIEVEMENTS IN 2021

ADVANCED

R&D through several projects, including the development of an in vitro Hollow Fibre Infection Model (HFIM) to examine the effectiveness of zoliflodacin, a potential treatment for gonorrhoea

ACTIVATED

8 new trial sites, bringing the total number of sites to 14, and advanced recruitment for the phase 3 trial of zoliflodacin

LED

key initiatives that will facilitate future access to zoliflodacin

OUR NEXT CHALLENGE?

"In 2022, we will continue to progress the development of zoliflodacin by increasing the recruitment target of the phase 3 trial, initiating the final drug product manufacturing process, and further defining the public health value through regulatory and access pathways to ensure the future availability of a much-needed treatment option."



2021 HIGHLIGHTS

SERIOUS BACTERIAL INFECTIONS

Surgical procedures and chemotherapy put patients at greater risk of a bacterial infection, which is a major cause of death in hospitals and healthcare settings.

Antibiotic resistance is making matters worse. In the US, it is estimated that between 39% and 51% of bacteria that can cause surgical-site infections and 27% of bacteria capable of causing post-chemotherapy infections are now resistant to commonly used antibiotics⁶. The World Health Organization identifies

carbapenem-resistant Gram-negative bacteria as 'critical level' priority pathogens that urgently require new treatments and as being among the greatest threats to health. GARDP is continuously working with its partners to develop novel treatments for these dangerous bacterial infections.



"We, like many others, suffered last year due to COVID-19, but we're back up and running."

CHRISTOPHER BURNS

PRESIDENT AND CEO, VENATORX PHARMACEUTICALS (US)

OUR ACHIEVEMENTS IN 2021

COMPLETED

Venatorx enrolment for the pivotal phase 3 trial of cefepime-taniborbactam, a promising new antibiotic treatment

IDENTIFIED

10 sites to be part of a network in India and South Africa that will improve our understanding of how to treat drug-resistant infections in adults and children

INITIATED

an agreement to deliver access to cefiderocol, a new and recently approved antibiotic, in the countries that need it most

OUR NEXT CHALLENGE?

"We have made good progress towards the development of new treatment options for serious bacterial infections. Together with Venatorx we aim to gain regulatory approval for cefepime-taniborbactam. We are focused more than ever on completing plans to expand access for this and other much-needed treatments."

FRANÇOIS FRANCESCHI

Head of Asset Evaluation and Development and Serious Bacterial Infections Project Leader, GARDP



ADVANCING ANTIBIOTIC R&D

DISCOVERY & EXPLORATORY RESEARCH

In December, GARDP published an open-access report which found that the early discovery antibacterial pipeline remains insufficient for delivering the new antibacterial treatments we need.

GARDP's discovery and research programme aims to discover vital next-generation antibiotics and address critically underfunded and



neglected gaps in research and development.

GARDP screened 22,816 compounds and 1,280 natural product extracts in 2021. As a result, we identified two hit compounds and 36 hit extracts. Since 2020, we have screened nearly 100,000 compounds and extracts for antibacterial activity. We are now exploring three series of compounds as possible new antibiotics, and are investigating three more for their potential to enhance the effects of old ones.

PRESERVING & SHARING

GARDP's Scientific Affairs team has worked actively for three years to improve, accelerate, and streamline antibiotic discovery and R&D by facilitating learning and knowledge exchange.

In 2018, GARDP created the REVIVE website – revive.gardp.org – to capture and share new and existing knowledge and skills in antibiotic discovery and R&D, as well as to support and connect this global community. Users from 198 countries have accessed the REVIVE

website since its launch, with over 4,200 website views per month.

Our Scientific Affairs team has built relationships with over 70 scientific societies and partner organizations globally, which work with us to help disseminate GARDP's educational content among the international antimicrobial R&D community. Six new societies joined our network in 2021, including the Australian Research Council (ARC) Research Hub to Combat AMR, the Federation of European Microbiological Societies (FEMS), and Students against Superbugs Africa.

OUR ACHIEVEMENTS IN 2021

WELCOMED

46 new experts into our REVIVE community, which now includes 148 members

POSTED

10 new Antimicrobial
Viewpoint articles
with readers from 149
different countries

HOSTED

the Antimicrobial
Chemotherapy
Conference (ACC) 2021
in collaboration with
the British Society of
Antimicrobial Chemotherapy
(BSAC), along
with 626 live participants
from 63 countries

ORGANIZED

13 webinars with an average of 210 participants per webinar from 108 countries

ADDED

99 new terms and two expert videos to the Antimicrobial Encyclopaedia, which now contains over 170 terms and 14 expert videos

OUR NEXT CHALLENGE?

"In 2022, we will screen new chemical libraries identified by computational chemistry analysis and continue our hit expansion activities. The current horizon-scanning projects for antibacterialdiscovery research targets will identify opportunities for new discovery projects, partnerships, and collaborations.

Another exciting event will be the launch of the Antibiotic Discovery & Development Roadmap, which will be hosted on REVIVE. This will provide people working on different stages of the antibiotic R&D pipeline with critical information about the entire product development pathway."



PARTNERS

COLLABORATIVE INVESTMENT TO COUNTER DRUG RESISTANCE

Our work could not be done without the investment and support of our funding partners, each of whom has a deep understanding of the urgent need to address drug resistance. Our extended gratitude goes to every one of them.

We would also like to acknowledge the ongoing recognition that the G7 and G20 give to AMR as a crucial global health issue.

GARDP is critical to delivering on the commitments made by Member States under the Global Action Plan (GAP) on AMR and the UN High Level Declaration on AMR, and it has been consistently recognized by both the G7 and G20 as a crucial actor of the global

response. G7 countries have recognized the challenge of AMR and are dedicated to addressing the problem. This included, in 2021, statements by the G7 Health Ministers and the G7 Finance Ministers, both of which called for greater investments and attention to address AMR as a silent pandemic of drug-resistant infections. The health ministers highlighted GARDP's role to "support the development and approval of much-needed innovative antimicrobial therapeutics.

THE PARTNERSHIPS WITH GOVERNMENTS, ACADEMIA, RESEARCH CENTRES, AND THE PHARMACEUTICAL INDUSTRY ARE AT THE HEART OF GARDP'S WORK. WITHOUT THEIR SUPPORT, GARDP'S ACHIEVEMENTS TO DATE WOULD NOT HAVE BEEN POSSIBLE.

BILL&MELINDA GATES foundation









































In 2021, the Swiss government recognized our mission to develop new treatments for drugresistant infections by granting a privileged status to GARDP.



"Since 2001, Geneva has devoted a significant part of its budget to international cooperation and humanitarian aid projects. We are proud to continue contributing to GARDP's efforts by funding a clinical study in Thailand aimed at developing a new treatment for forms of gonorrhoea resistant to current treatments."

> NATHALIE FONTANET **GENEVA STATE COUNCILLOR**

FINANCE

INCOME

GARDP has secured in excess of EUR 100M in funding since its inception in 2016. Despite the unpredictable nature of 2021, GARDP was able to successfully secure further funding from several partners, including:

- An increase of £4.5M in financial support from the UK's Department of Health and Social Care (DHSC)
- An increase of CHF 100k from the Federal Office of Public Health of Switzerland
- An additional \$50k contribution from the Leo Model Foundation
- A new funding of \$1.8M from the Japanese Ministry of Health, Labour and Welfare, with a further pledge of \$5.4M over the next three years

The funding environment remains volatile given the ongoing pandemic, the war in Ukraine and competing priorities across global health organizations.

- A contribution of CHF 540k made by the Canton of Geneva
- A new funding of A\$300,000 from the Australian government
- A pledge of a further EUR 400k from 2022-24 by the Principality of Monaco

Further multi-year funding support will be required in 2022 and beyond, including key renewals from core funders and new funding commitments from non-current funders.

Numbers extracted from the unaudited "2021 Finance & Performance Report". The full report, audited by Deloitte, will be available in June 2022 www.gardp.org



TOTAL FUNDING COMMITMENTS AND PLEDGES TO DATE EUR 104.7M:

| PUBLIC CONTRIBUTORS FROM 2016 - 2025 | (EUR) 101 M |
|--|--------------------|
| Germany (BMBF and BMG) | 60.1 M |
| UK (DFID, DHSC and NIHR) | 21.7 M |
| Japan (Ministry of Health, Labour and Welfare) | 7.9 M |
| The Netherlands (VWS) | 7.5 M ¹ |
| Switzerland (FOPH) | 1.3 M |
| South African Medical Research Council | 0.9 M |
| The Principality of Monaco | $0.8M^2$ |
| Canton de Genève | 0.5 M |
| Australia (Department of Health) | 0.2 M |
| Grand Duchy of Luxemburg | 0.1 M |
| PRIVATE CONTRIBUTORS FROM 2016 - 2025 | (EUR) 3.7M |
| Bill & Melinda Gates Foundation | 1.8 M |
| Wellcome Trust | 1.1 M |
| Others: Médecins Sans Frontières, Leo Model Foundation | 0.8 M |

¹ Includes pledge of EUR 4.8M ((\$5.4M) 2022 - 2025)

² Includes pledge of EUR 400k (2022 – 2024)

FINANCE

EXPENDITURE

Excluding the one-off early investment of EUR 8.9M in relation to cefepimetaniborbactam in 2020, the total expenditure increased by EUR 2.6M or 18% in 2021, reaching EUR 17.4M.

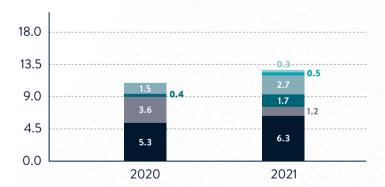
The growth of operational expenses reflects the increased activity within the Serious Bacterial Infections programme (in relation to cefepime-taniborbactam), the Sexually Transmitted Infections programme, and the continued strengthening of the R&D

structure along with, and to a much lesser extent, the setup of GARDP North America Inc.

GARDP's ratio of social mission to non-social mission spending dropped to 84% in 2021. This reduction was due to the continued impact of COVID-19 on some R&D operational activities.

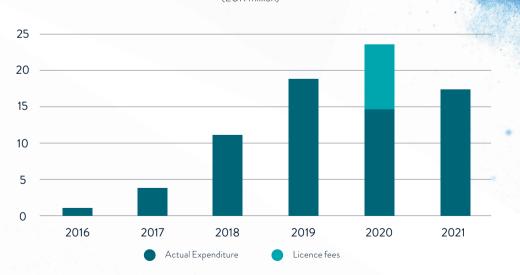
GARDP expenditure since the start of its incubation within DNDi in 2016 totals EUR 76M.

R&D expenses per programme (In million EUR)





Actual expenditure 2016 - 2021 (EUR million)



Further information on GARDP's income and expenditure will be available in GARDP's 2021 Financial & Performance Report in June 2022 on www.gardp.or



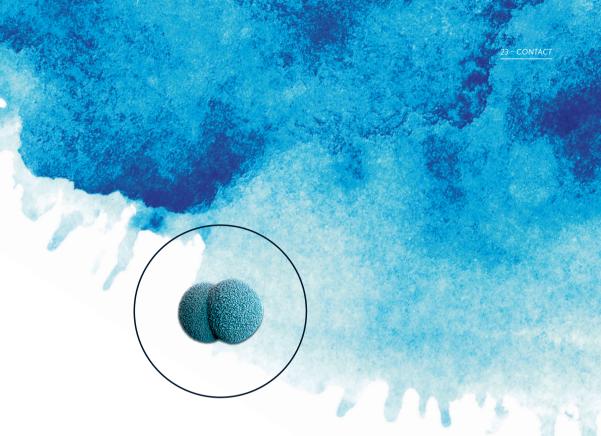
HELP US FIGHT ANTIBIOTIC RESISTANCE

To address the growing threat of antibiotic resistance, we must work together. To be part of GARDP's mission, you can:

- Become a scientific or financial partner https://gardp.org/take-action/ become-a-partner/
- Donate to GARDP
 https://gardp.org/donate-to-gardp/
- Join our Scientific Affairs activities via REVIVE

https://revive.gardp.org/about-revive/ to support and connect with the antimicrobial discovery, research, and development community.

THANK YOU FOR YOUR SUPPORT!



CONTACT

FOR MORE INFO

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Credits

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The Global Antibiotic Research and Development Partnership (GARDP) is a Swiss not-for-profit organization developing new treatments for drug-resistant infections that pose the greatest threat to health. GARDP was created by the World Health Organization (WHO) and the Drugs for Neglected Diseases initiative (DNDi) in 2016 to ensure that everyone who needs antibiotics receives effective and affordable treatment.

