

Antimicrobial resistance (AMR) is a major and rapidly growing global public health challenge. Responsible for more than 700,000 deaths a year<sup>1</sup>, it poses a significant threat to achieving the Sustainable Development Goals (SDGs), in particular SDG 3, which aims to ensure healthy lives and promote wellbeing for all<sup>2</sup>.

The Global Antibiotic Research and Development Partnership (GARDP) is a not-for-profit research and development organization that addresses global public health needs by developing and delivering new or improved antibiotic treatments, while endeavouring to ensure their sustainable access.

Initiated by the World Health Organization (WHO) and the Drugs for Neglected Disease initiative (DNDi) in May 2016, GARDP is an important element of WHO's Global Action Plan on Antimicrobial Resistance that calls for new public-private partnerships to encourage research and development of new antimicrobial agents and diagnostics.

GARDP's programmes – sexually-transmitted infections, neonatal sepsis, paediatric antibiotics and antimicrobial memory recovery, evaluation and exploratory research – are designed to address global public health priorities. Each programme incorporates sustainable access and stewardship strategies to ensure treatments are affordable and available to all those who need them.

Partnerships are central to GARDP's model and include WHO, pharmaceutical and biotechnology companies, academia, governments, health authorities, philanthropic organisations and civil society from across the world.

# Sexually-transmitted infections

The spread of sexually-transmitted infections (STIs) is a global public health concern. In 2016, there were approximately 376 million new cases of chlamydia, gonorrhoea, syphilis and trichomoniasis<sup>3</sup>. Increasing drug-resistance is making STIs more difficult to treat.

## Gonorrhoea – a global burden

With an estimated 87 million new cases a year, gonorrhoea affects every region of the world.

In South Africa, it accounts for up to 90% of cases of urethral discharge in men<sup>4</sup>. It is the second-most frequently reported infectious disease in the USA<sup>5</sup>.

If left untreated, gonorrhoea can have serious consequences for reproductive health and fertility, particularly in women and can result in pregnancy complications such as ectopic pregnancies, spontaneous abortions and stillbirths. Gonorrhoea also significantly increases the risk of contracting and transmitting HIV in men and women.

## The rise of drug-resistant gonorrhoea

The spread of drug-resistant gonorrhoea is rapidly outpacing the development of new medicines. WHO data shows alarmingly high levels of drug-resistance to the antibiotics used to treat gonorrhoea. In a survey of 77 countries, 97% reported recorded instances of drug-resistance to commonly used treatment regimens and 66% to cephalosporins, the last options for monotherapy (treatment with a single drug).

*N. gonorrhoeae* is classified as being 'high priority' on WHO's list of pathogens representing the greatest threat to human health and most in need of new antibiotics<sup>6</sup>

## GARDP'S STI PROGRAMME

GARDP's STI programme aims to help tackle the global public health threat of drug-resistant STIs. It includes efforts to develop a new treatment for drug-resistant gonorrhoea, investigate new combinations of antibiotics to treat STIs, and ensure sustainable access strategies.



## OBJECTIVE

### By 2023

To develop and deliver at least one treatment that will most impact on public health by ensuring it meets three criteria

- works against drug-sensitive and drug-resistant gonorrhoea.
- is suitable for integration into international and national STI treatment guidelines.
- can address urogenital and extra-genital infections.

## TO DATE, GARDP HAS

- With the support of WHO and global experts, developed an R&D strategy for STIs. Published in 2017 in *PLOS Medicine*<sup>7</sup>, the peer-reviewed article outlines the strategy – starting with an R&D roadmap to accelerate the development of antibiotics to tackle drug-resistant gonorrhoea.
- Entered into a partnership with Entasis Therapeutics (started 2017) to develop a new antibiotic known as zoliflodacin, a novel, first-in-class oral antibiotic that has shown high activity against drug-resistant gonorrhoea in a phase II clinical trial published in the *New England Journal of Medicine*<sup>8</sup>.
- Initiated the clinical development plan for zoliflodacin, including completing two clinical pharmacology studies to better understand its pharmacokinetics and safety and secured advice, for a forthcoming phase III clinical trial, about how to best register the drug.
- Started pharmaceutical development activities to secure a treatment formulation for use in trial sites and patients, with a focus on affordability by reducing the cost of manufacture, while ensuring that quality is retained.

## LOOKING AHEAD

- A multi-site phase III pivotal (designed to provide evidence to be able to approve a drug) clinical trial will start in summer 2019 in the Netherlands, South Africa, Thailand and the United States. This trial will support registration of zoliflodacin for uncomplicated gonorrhoea in high burden countries.  
In parallel, GARDP will carry out non-clinical activities such as microbiology surveys to ensure the product is effective against recent and geographically diverse strains of gonorrhoea.
- The partnership agreement with Entasis Therapeutics includes a sustainable access strategy. If zoliflodacin receives regulatory approval, Entasis will grant GARDP an exclusive license with sublicensing rights in 168 low and middle-income countries, while retaining commercial rights in high-income countries.
- GARDP will continue to work on its pharmaceutical development plan through which it is committed to work on cost and affordability. If the trial is successful, it is expected that zoliflodacin will offer a significant opportunity as a pilot case study in how to introduce antibiotics into the market in a way that can assure appropriate use.

## A GLOBAL COLLABORATION

The STI programme has built strong partnerships with stakeholders including from WHO, research and industrial partners and governments across the world.

Partners include the Department of Infectious Diseases, Public Health Service Amsterdam – the Netherlands. South African Medical Research Council; Centre for HIV & STIs; National Institute for Communicable Diseases, University of KwaZulu Natal; Wits RHI, University of Witwatersrand – South Africa. WHO Collaborating Center for STIs, University Hospital Örebro – Sweden.

Bureau of AIDS, TB, and STIs, Department of Disease Control, Thai Ministry of Public Health; Thailand US CDC Collaboration, Thai Red Cross AIDS Research Center; University of Mahidol, Tropical Medicine Hospital – Thailand.

Entasis Therapeutics; National Institute of Health (NIH) and National Institute of Allergy and Infectious Diseases (NIAID); University of Birmingham, University of Florida – United States.

1 [Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations](#) The Review on Antimicrobial Resistance Chaired by Jim O'Neill, 2014

2 [Sustainable Development Goals](#) [sustainabledevelopment.un.org/SDG3](http://sustainabledevelopment.un.org/SDG3)

3 World Health Organization (WHO), [Report on globally sexually transmitted infection surveillance 2018](#)

4 Sentinel Surveillance, STI South Africa, [Communicable Disease Communiqué](#), February 2016

5 The US Centers for Disease Control and Prevention (CDC): [Sexually Transmitted Disease Surveillance](#).

6 [WHO priority pathogens list](#) for R&D of new antibiotics – February 2017

7 Alirol E, Wi TE, Bala M, Bazzo ML, et al. (2017) [Multidrug-resistant gonorrhoea: A research and development roadmap to discover new medicines](#). *PLoS Med* 14(7): e1002366.

8 Taylor, S, Marrazzo, J, Batteiger, B et al.,(2018) [Single-Dose Zoliflodacin \(ETX0914\) for Treatment of Urogenital Gonorrhoea](#), *The New England Journal of Medicine*,