GARDP
Global Antibiotic Research & Development Partnership
A joint DNDi / WHO initiative

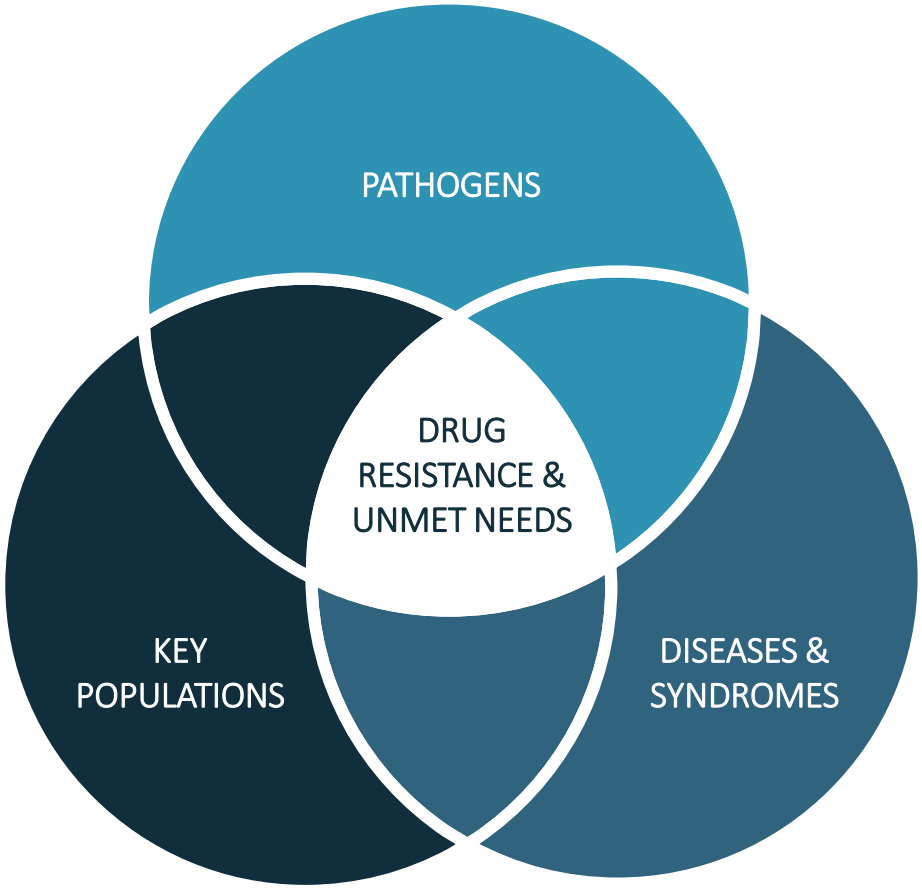
Antibiotic resistance

A threat to global health and development

Dr Manica Balasegaram, Executive Director
1 April 2019

Addressing global public health needs

GARDP is the only global R&D initiative with a focus on AMR and access



Focus and objectives:

- Drug-resistant bacterial infections on WHO priority pathogen list.
- Deliver 4 new/improved treatments by 2023 with a robust pipeline.
- Appropriate use and access.

Founding partners

- World Health Organization
- Drugs for Neglected Diseases *initiative*

Programmes:

- Neonatal sepsis.
- Paediatric antibiotics.
- Sexually-transmitted infections.
- Memory recovery and exploratory including adult serious bacterial infections.

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GARDP - an innovative model and approach

Notably, the flexible and unique model allows GARDP to

GARDP
In-house:
- public health expertise
- product development & clinical trial know-how

Work from any entry point along the R&D pipeline through to patient access.

Target important indications less likely to be developed by other actors.

Ensure access and stewardship of products developed by GARDP in contractual agreements with the private sector.

Invest funding in programmes driven and directly executed by GARDP and our partners.

Partners

- Academia
- Civil society/ NGOs
- Research institutions
- Pharma/ biotech
- Government /international organizations

The way we work

- Prioritize public heath needs
- End to end
- Develop TPPS & scientific road maps
- Embed apropriate use & access
- In- and out-licensing, generics
- Sponsors, research studies & clinical trials

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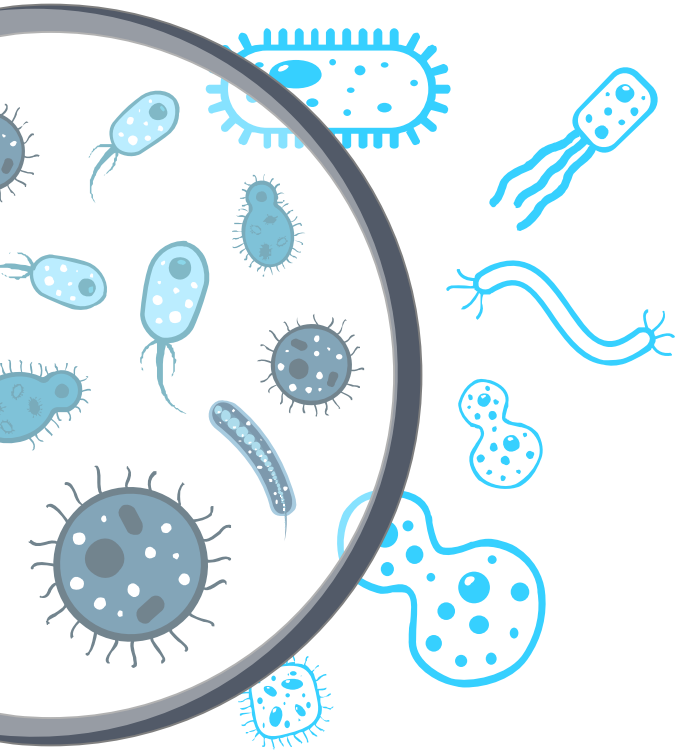
Programme highlights: status and update



Neonatal sepsis

Status

- Launched a global observational study to understand prescribing practices in Africa, Asia, EU and US.
- Completed recruitment for PK and safety study of fosfomycin.

Update

- Complete fosfomycin PK study analysis and reporting.
- Observational study: complete enrolment of 2500-3000 cases.

Paediatric antibiotics

Status

- Development programme launched for an antibiotic treatment of MDR infections.
- Agreement signed with Sandoz.
- Supported update of paediatric evidence-based guidelines.

Update

- Polymyxin B: submit plan for regulatory approval and conduct initial work required by EMA.
- Develop a global network of sites with capacity and capability.

Sexually-transmitted infections

Status

- Completed phase 1 dose evaluation study for lead antibiotic (Zoliflodacin).
- Set up activities to start phase III clinical trial in Africa, Asia, EU and USA.
- Progressing pharmaceutical development including alternative formulations.

Update

- Initiate a phase III clinical trial in Africa, Asia, EU and USA in May.
- Initiate full-scale good manufacturing practices batches of zoliflodacin.

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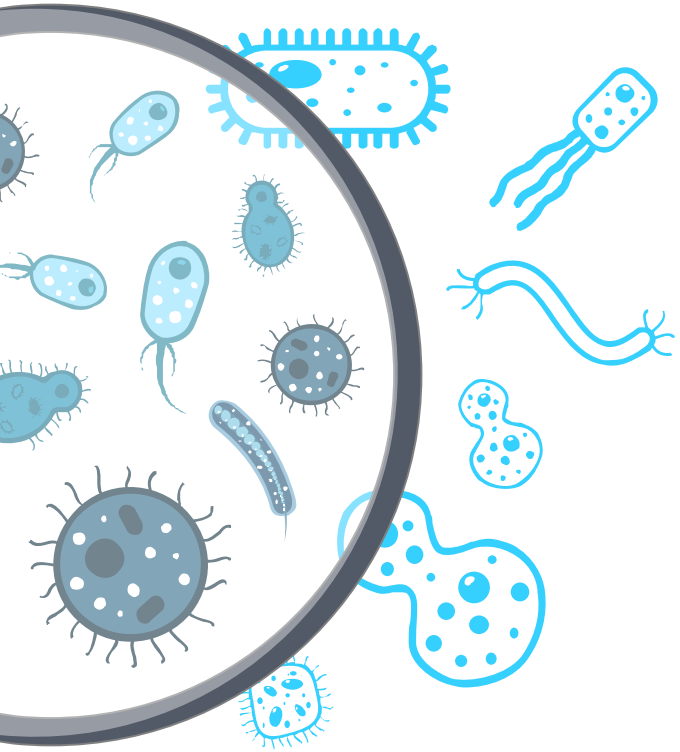
R&D highlights: status and update



Discovery and exploratory

Status

- Established agreements to access libraries in search of new antibacterials with:
  Takeda (JP), Eisai (JP), HIPS (DE), Calibr (US).
- Agreements in place with CoADD Australia and Institute Pasteur Korea for library screening.

Update

- Library screening to commence in Q1 2019.

Memory recovery and asset evaluation

Status

- Evaluated over 50 chemical entities, between new and 'recovered' drugs.
- 2 recovered assets moving into further evaluation: Flomoxef & Sitafloxacin.
- 2 recovered assets in clinical development: fosfomycin & polymyxin B.
- Up to 6 new assets identified as potential portfolio candidates.
- Project initiated (University of Verona) to identify effective combinations to treat bacterial sepsis.

Update

- Launching serious Gram-negative infection programme.

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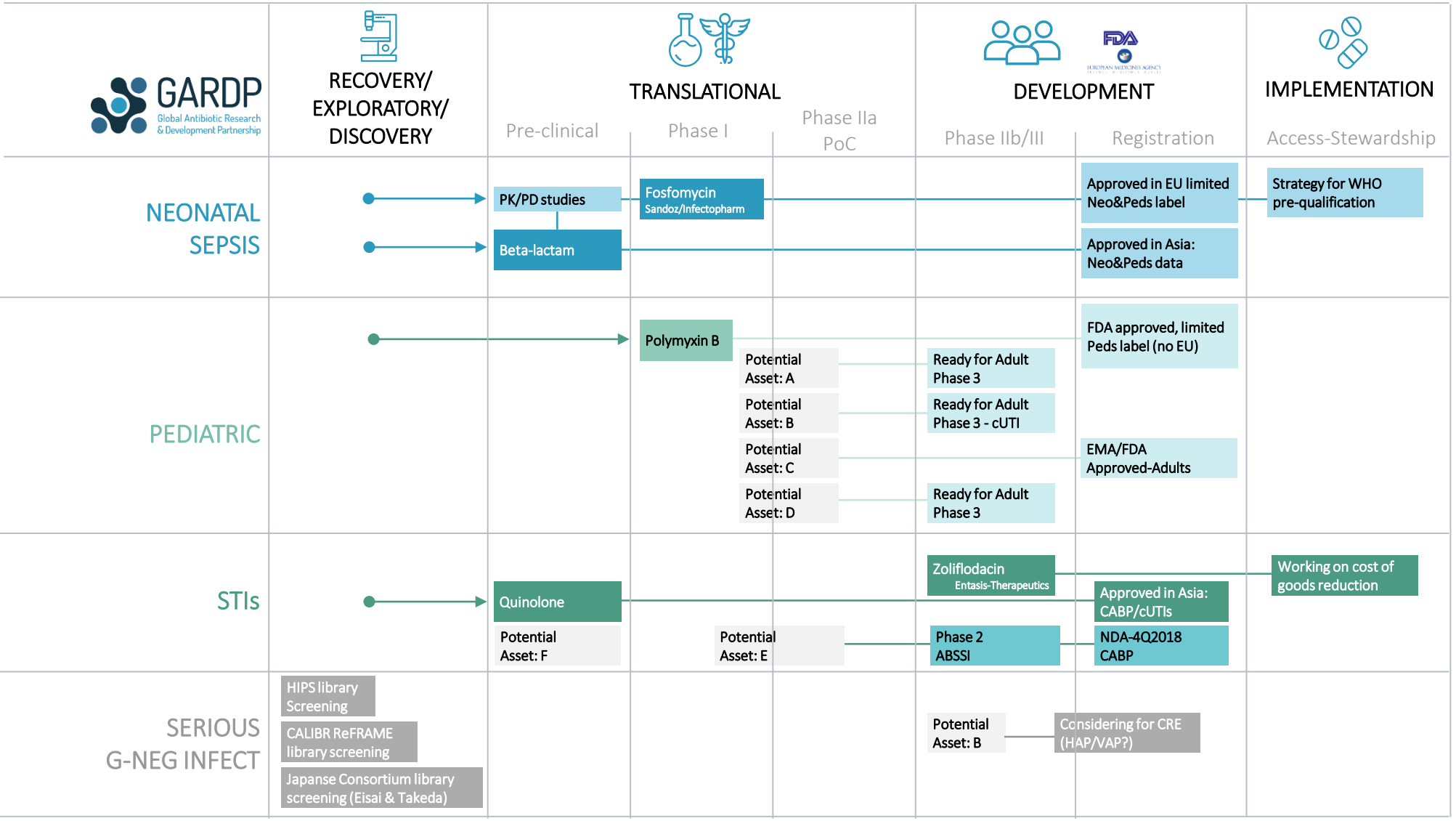
GARDP pipeline (Jan 2019)



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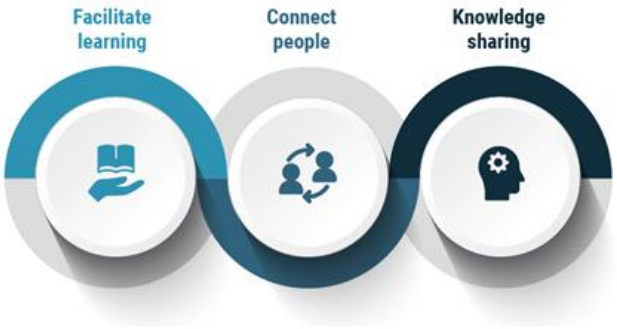
REVIVE: status and outlook



An online space to support the antimicrobial discovery, research, and development community

Facilitate learning	Connect people	Share knowledge
Status		
• 5 webinars with 1,500 registered participants. • Open access.	• Network of 120 leading experts in the field. • Sessions and networking events at key conferences.	• 6 blogs by invited authors to share knowledge and spark discussions.
Outlook		
• Develop and launch new content for webinars, and resources.	• Extend and diversify the expert network.	• Launch new blogs and implement a virtual 'AMR dictionary'.

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GARDP facts and figures

37 FTEs & 11 additional recruitments projected **in 2019.**

R&D
- 1 first in class antibiotic entering phase III clinical trial.
- 4 recovered antibiotics in different phases of development.
- 10 antibiotics under discussions with potential biotech and pharma partners.
- 4 libraries to be screened for antibiotic activity.
- 3 clinical studies completed.

Status
- Independent Swiss legal entity – in the process of seeking international organisation status.

Governance
- Scientific Advisory Committee (14 members, 4 observers).
- Board of Directors (currently 6 members, set to grow to 10).

WHO cooperation on
- Technical advice, including on stewardship and access.
- Priority setting and developing target product profiles
- Liaison with member states.

DNDi cooperation on
- Sharing specialized R&D expertise and capacity
- Leveraging regional networks
- Sharing some infrastructure to ensure value for money

Funding
- 24% of 270 million raised in support of 2017- 2023 plan and budget.
- 94.6% of funding from governments.

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KEY WHO DOCUMENTS FOR ANTIBIOTIC R&D

Priority 1: CRITICAL#

Acinetobacter baumannii, carbapenem-resistant

Pseudomonas aeruginosa, carbapenem-resistant

Enterobacteriaceae*, carbapenem-resistant, 3rd generation cephalosporin-resistant

Priority 2: HIGH

Enterococcus faecium, vancomycin-resistant

Staphylococcus aureus, methicillin-resistant, vancomycin intermediate and resistant

Helicobacter pylori, clarithromycin-resistant

Campylobacter, fluoroquinolone-resistant

Salmonella *spp.*, fluoroquinolone-resistant

Neisseria gonorrhoeae, 3rd generation cephalosporin-resistant, fluoroquinolone-resistant

Priority 3: MEDIUM

Streptococcus pneumoniae, penicillin-non-susceptible

Haemophilus influenzae, ampicillin-resistant

Shigella *spp.*, fluoroquinolone-resistant

Mycobacteria (including *Mycobacterium tuberculosis*, the cause of human tuberculosis), was not subjected to review for inclusion in this prioritization exercise as it is already a globally established priority for which innovative new treatments are urgently needed.

* Enterobacteriaceae include: *Klebsiella pneumonia*, *Escherichia coli*, *Enterobacter* spp., *Serratia* spp., *Proteus* spp., and *Providencia* spp, *Morganella* spp.

World Health Organization

2018 Update of antibacterial agents in clinical development

EML AB 2017: syndromes considered

World Health Organization

Syndromes

1. Community acquired pneumonia
   - Children - WHO GL updates
2. Pharyngitis
3. Sinusitis
4. Otitis media
5. Hospital acquired pneumonia (HAP)
6. Ventilator associated pneumonia
7. Urinary tract infections (UTI)
8. Meningitis
9. Complicated intra-abdominal infections
10. Exacerbations of chronic obstructive pulmonary diseases (COPD)
11. Skin & soft tissue infections
12. Cellulitis
13. Surgical site infections
14. Acute infectious diarrhoea
15. Shigellosis
    - Children - WHO GL updates
16. Cholera
    - Children - WHO GL updates
17. Chlamydia - WHO GL
18. Gonorrhoea - WHO GL
19. Syphilis - WHO GL
20. Bone and joint infections
21. Febrile neutropenia
22. Severe acute malnutrition
    - Children - WHO GL updates
23. Sepsis
    - Children - WHO GL updates

ACCESS GROUP (29 antibiotics)

First and second choice antibiotics for the empiric treatment of most common/relevant infectious syndromes (21 syndromes).

First choices are usually narrow spectrum agents with positive benefit-to-risk ratios, and low resistance potential, whereas second choices are generally broader spectrum antibiotics with higher resistance potential, or less favorable benefit-to-risk ratios.

WATCH GROUP (7 antibiotic classes)

Antibiotics with higher resistance potential whose use as first and second choice treatment should be limited to a small number of syndromes or patient groups .

These medicines should be prioritized as key targets of stewardship programs and monitoring.

RESERVE GROUP (8 antibiotics or classes)

Antibiotics to be used mainly as 'last resort' treatment options that could be protected and prioritized as key targets of high-intensity stewardship programs.

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KEY ISSUES FOR DRUG DEVELOPMENT

- WHO Priority Pathogen List: priority bacteria to target.
- FDA / EMA: increased clarity on regulatory pathways; trials are relatively small and non-inferiority based; tendency is largely to develop for cUTI.
- Less clarity on what are the important syndromes and populations to consider, in relation to WHO PPL.
- Reimbursement mechanisms and future pull incentives may be linked to the ability to generate relevant evidence for efficacy against MDR pathogens, key indications / syndromes and populations.

KEY ISSUES FOR DRUG DEVELOPMENT

- Therefore GARDP is approaching drug development with two overlapping pathways:

1) **Regulatory: for market authorization**
   - Key relevant phase II and III trials, CMC/ formulation
   - Commence paediatric development as early as possible (when some adult efficacy data available)

2) **Public Health: for policy, guidelines and use**
   - Adult trials in MDR populations, specific indication studies
   - Strategic trials in paediatrics

CONSIDERATIONS FOR EML AND 'AWARE'

- Many of the new and late stage pipeline antibiotics target important MDR pathogens.
- These drugs may largely be falling by default into Reserve list (note: where do we place future important BL/ BLIs).

- What level of evidence is required to understand their relative importance within the list?

- Could some of the new antibiotics conceivably end up as ACCESS or WATCH drugs (e.g. new drug for STI).
- Certain older drugs in the Reserve List could be repurposed for certain important needs, and may be an important second line agent.

- Should there be strategic positioning of some old and new antibiotics? Guidance to developers would be useful.

Thank you

Federal Ministry of Education and Research

Federal Ministry of Health

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