Investing in the Development & Conservation of New Antibiotic Treatments

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Global Antibiotic R&D Partnership

Introduction

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GARDP incubation: Only just beginning

- **2014**
  - DNDi consultations Business Plan scope – AMR suggested
  - 8-9 Dec. 2014 WHO-DNDi meeting to explore PDP for antibiotics

- **2015**
  - May 2015 WHA adopts GAP-AMR + resolution
  - Oct. 2015 G7 Declaration: explore PDP for AMR

- **2016**
  - 13 Nov. 2015 DNDi-WHO consultation support for PDP
  - 1 Dec. 2015 Board approves incubation
  - 29 Feb. 2016 1st Scientific consultation Institut Pasteur

- **2017**
  - 24 May 2016 GARD Launch
  - GARD independent entity

EUR 2.5 million of the required EUR 3 million seed funding committed to date:
- Federal Ministry of Health of Germany
- The Netherlands’ Ministry of Health Welfare and Sports
- South African Medical Research Council
- United Kingdom Department for International Development
- Swiss Federal Office of Public Health
- Médecins Sans Frontières
GARD – DNDi and WHO complementary roles

WHO
- provides support in priority setting, target product profiles, stewardship, and access
- reports to member states
- secures close collaboration with AMR Secretariat, relevant WHO departments, the Essential Medicines List team, and the Global Health R&D Observatory

DNDi
- Hosts the incubation (and de facto governance) of GARD and development of business plan
- Seeks seed funding and initial project funding
- Guides scientific strategy and project development
- Builds pipeline with partners
- Sets up scientific working group and steering committee
In cooperation with the public and private sectors:

- develop new antibiotic treatments addressing AMR
- promote their responsible use for sustainable access

by setting up a not-for-profit product development partnership that will focus on global health needs, and ensuring any new product is adapted to resource-limited settings.
Guiding Principles

1. R&D should focus on the **significant bacterial infections** with an emphasis on global needs (patient-needs driven; WHO priority setting)

2. **Scientific relevance** shall guide choices

3. Antibiotic development should be financed partly through a global funding mechanism and should experiment new models for conservation and access (delinkage)

4. Sustainable **investment should be coordinated** at country and international levels (coordination and monitoring)

5. New antibiotics must be **affordable** for all and subject to a global conservation agenda (sustainable access)

Most importantly, ensure complementarity to other initiatives, fill gaps where industry may not go alone.
Next steps: build a project portfolio with member states and key partners

Short-term incubation goals:
- with WHO, determine disease priorities, up to level of TPPs
- key partnerships in place
- governance structure
- two projects end 2016, two more by end 2017 that link incentives to conservation

Potential projects in the short-term:
- Disease specific: e.g. neonatal sepsis, gonorrhea, typhoid – others to be explored
- Transversal: e.g. platform for combinations and improving usage and understanding of old antibiotics; antibiotic memory recovery initiative

Longer-term projects
- Determine upstream ‘bluesky’ research opportunities
From incubation to launch: WE ARE ON TRACK

Seed funding of 3+ million USD is required for:

Within 2 years, to become an independent organization focused on providing tools to fight AMR

### START-UP PHASE

**People and Projects**

- **2 Yrs**
- **3-5 Yrs**

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| Team        | 1 FTE DNDi (=BD, Coord., Fundraising) TOR for Core team | Recruitment process Director | 2 FTEs for core team on board | 1 additional FTE core team on board |
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| Budget / FR | DNDi core funds | Secure seed donors | Progress with key countries and funding mechanisms |
|            |                |                   | |

| Governance  | Hosted by DNDi | + External steering committee | +Scientific working group | Board and Scientific Advisory Committee |
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Scoping Short-Term Projects

Essential criteria for project selection

1. address global health need, with clear relevance for developing countries
2. fill a gap left by existing partners
3. potential for short-term fruition
4. potential to test access and conservation
5. R&D opportunity partnership/technology

Diagnostics and delinkage will be tested but are not selection criteria
Potential Pilot Projects

- NeoAMR:
  - Addressing the unmet needs and resistance issues of neonatal infections (2016)

- AMRi:
  - Recovering the knowledge of antibiotic drug developers and microbiologists (2016)

- Combinations:
  - A new paradigm in bacterial diseases treatment? (2017)

- Gonorrhea:
  - “Neglected” infection in need of new treatments (2017)
Neonatal sepsis

- Pathogens include *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and non-typhoidal Salmonellae (NTS).
- Multi-drug resistant gram-negative (MDRGN) severe bacterial infections (SBI) affect low, middle, and high income countries.
- Associated with very high mortality rates
- Treatment (at least initially) mainly empirical, and especially problematic/inadequate in areas of high resistance
Neonatal sepsis - project

AIM: develop one to two new evidence-based empiric antibiotic treatment regimens and one to two new treatments for MDR pathogens.

• Design and conduct pharmacokinetic, observational and interventional studies in high MDR setting to determine efficacy and safety of new empiric regimens compared to existing therapies
• Develop a global network of neonatal infection centres/experts to design and conduct studies on optimal management of off patent antibiotics & other interventions in neonatal sepsis with MDR pathogens
• Determine a method for appropriate use of empiric antibiotic regimens for the management of neonatal sepsis in settings with varying prevalence of MDR pathogens (interest in a fosfoymycin-based regimen)
Globally applicable, empiric treatment regimens for the treatment of neonatal sepsis

WP1: Pre-selection of potential agents and advisory role for study conduct: expert group

WP2: Target population
   - Clinical observational study of neonatal sepsis in target settings

WP3: Bacterial epidemiology
   - Microbiological study of neonatal sepsis in target settings

WP4: Therapeutic options
   - Pharmaco-kinetic and –dynamic modelling, Hollow Fibre Model, Formulations

WP5: Clinical trial of empiric antibiotic regimens for neonatal sepsis

WP6: Project management
Gonorrhea

- Approx. 106.1 million new cases of *N. gonorrhoeae* in 2008 (21% increase from 2005)
- Causes infection of the urethra, cervix and rectum; infertility; significantly increased risk of HIV infection and transmission; ectopic pregnancy, spontaneous abortion, stillbirths, premature deliveries; and
- Severe eye infections occur in 30-50% of babies born to women with untreated gonorrhea, which can lead to blindness
- Resistance to all recommended drugs including rising resistance to injectable ceftriaxone
Gonorrhea – project current status

**AIM:** New treatment approach for areas of resistance to current treatment.

- Scoping exercise: *identify potential drug candidates* (existing, off patent, and NCEs) that correspond to the key elements in the TPPs.
- Short- to medium-term project based on, for example:
  - accelerate one or more of the NCEs in the pipeline through Phase III, registration, and Phase IV / pilot implementation;
  - development of (possibly fixed-dose) combination treatments;
  - expansion of indication to cover extra-genital sites; improved guidelines of the empiric management of STIs where drug-resistant gonorrhea is a problem)
- Develop a sustainable access pilot project for the global introduction of new treatments, including licensing, stewardship, and access.
Project: Antimicrobial Memory Recovery initiative (old/unpursued antibiotics)

AIM: recover & make available know-how and resources that led to discovery/development of antibiotics at the end of last century – stimulate the antibiotic R&D ecosystem!

- Creation of a database of individuals (available for consulting) and information that was part of any antibiotic R&D stages of old/unpursued antibiotics
  - Discovery, chemistry, formulation, PK/PD, clinical, development, regulatory
- Set up a resource centre to host available & recoverable reagents
  - Chemical libraries, bacterial strains, clinical isolates, plasmids, antibodies & other proteins, expression vectors
Project: Antimicrobial Memory Recovery initiative

CORE EXPERTS GROUP (WP 1)

- "Ask the Experts"
  - WP 2
  - Consulting
  - Advices
  - Blog

- Knowledge Legacy Program
  - WP 4
  - References
  - Docs
  - Manuals

- AMR R&D tools
  - "Repository" Program
  - WP 5
  - "AMR Box"
  - Strains
  - Plasmid, etc

- Project Recovery Program
  - WP 3
  - Information on industry projects: compounds, reports, data
  - Information on ongoing AMR projects from Users
  => Inform GARD on opportunities, landscape mapping, duplication avoidance

- PORTAL
  - Feed portal with non-confidential information

- AMRi Database
  - Project identified for further investigation by GARDP

- USERS
  - Information on User’s projects

Queries

DNDi
Drugs for Neglected Diseases initiative
Project: Drug Combination Platform

Combinations Platform

• Identify the various combinations strategies, their advantages and limitations (X nb of antibiotic against either X nb of antibiotics, or non-antibiotic compounds; ...)
• Discuss suitable properties of antibiotics and non-antibiotics that could reduce the screening space, taking into account the TPP(s) constrains (including appropriate PK/PD match, administration routes, etc.)
• Identify the technical components of the platforms:
  • Tools: robotics, readers, etc. (define possible throughput)
  • Compounds collections
  • Strains
  • Data treatment, management and sharing
• Share existing protocols to enable a complementarity between Evotec/Sanofi and IPK, and design a “standard” protocol.
• Identify suitable indications/pathogens to guide selection of compounds and pathogens in order to narrow down the workload.
• Constitute a group of experts to guide work on combinations
Sustainable access: what does it mean

- Innovation + access + conservation + stewardship (for a new Rx)
- Need to navigate wide range of contexts: LIC – HIC (Global)
- Depends on TPP / Product(s) in question:
  - New vs Old / Patented Vs Off patent
  - Need for clear guidelines at intl & national level
  - Overlap with other aspects of health care (e.g. IPC)
  - Implication on laboratory capacity required
  - What level / where in health care sector treatment will be deployed
  - Need for advocacy: e.g. to protect specific antibiotics
- Approach will need to be different to conventional PDP approach
Sustainable access: Practical steps

- Host incentive mechanism with some strings attached: need significant resources
- Focus on L&MICs, segment market: can work to ensure responsible licensing (e.g. MPP); but will require strong stewardship and access plans from HICs
- Support registration in priority countries
- Work with WHO to ensure policy change (guidelines, EML etc)
- Ensure fair and sustainable pricing: especially if phase III supported for a NCE or expanding indication of use
- Support phase IV & implementation studies
- Promote a GLC / GDF type mechanism (to ensure appropriate use, support country scale up with national plans): get GFATM support?
Sustainable access: Practical steps

- **Country level strategy** (identify key priority countries for initial implementation)
- **Focus on public or private sector?**
- **Work with MoH to update & disseminate guidelines**
- **Support laboratory capacity building**
- **Monitoring studies in key pilot countries**
- **Training of health personal**
- **Health promotion and education: link with local civil society groups..entry point?**
- **AmFM type initiative in some low resource settings with heavy dependence on private sector**
- **Appropriate packaging to assist above**
Thank you for helping GARDP