GARDP
Global Antibiotic Research & Development Partnership

GARDP Sexually Transmitted Infections Program

Emilie Alirol, PhD, Project Lead, STI program

Committee on Prevention and Control of STI in the United States

7 Oct 2019

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

GARDP
Global Antibiotic Research & Development Partnership

Executive Summary

Ambition

€500 million to accelerate development and delivery of 5 new treatments that address the most urgent public health needs

Vision

All infections are treatable for everyone, everywhere

Mission

Bring together the public and private sectors to develop new treatments for bacterial infections. We ensure responsible and sustainable access, addressing the public health impact of antibiotic resistance

GARDP Strategic Pillars

1. **Research & Development:** Address global public health needs with a focus on clinical and pharmaceutical development
2. **Public health-oriented portfolio & partnerships:** Via public and private actors & networks, and through in-kind and direct contributions, build a public health oriented portfolio to deliver new and accessible treatments.
3. **Sustainable access:** Advocate for, facilitate and/or implement work related to Licensing, Public Health Policy & Use, Regulatory approvals in high-burden countries, Manufacturing & Supply, Procurement and Reimbursement models.

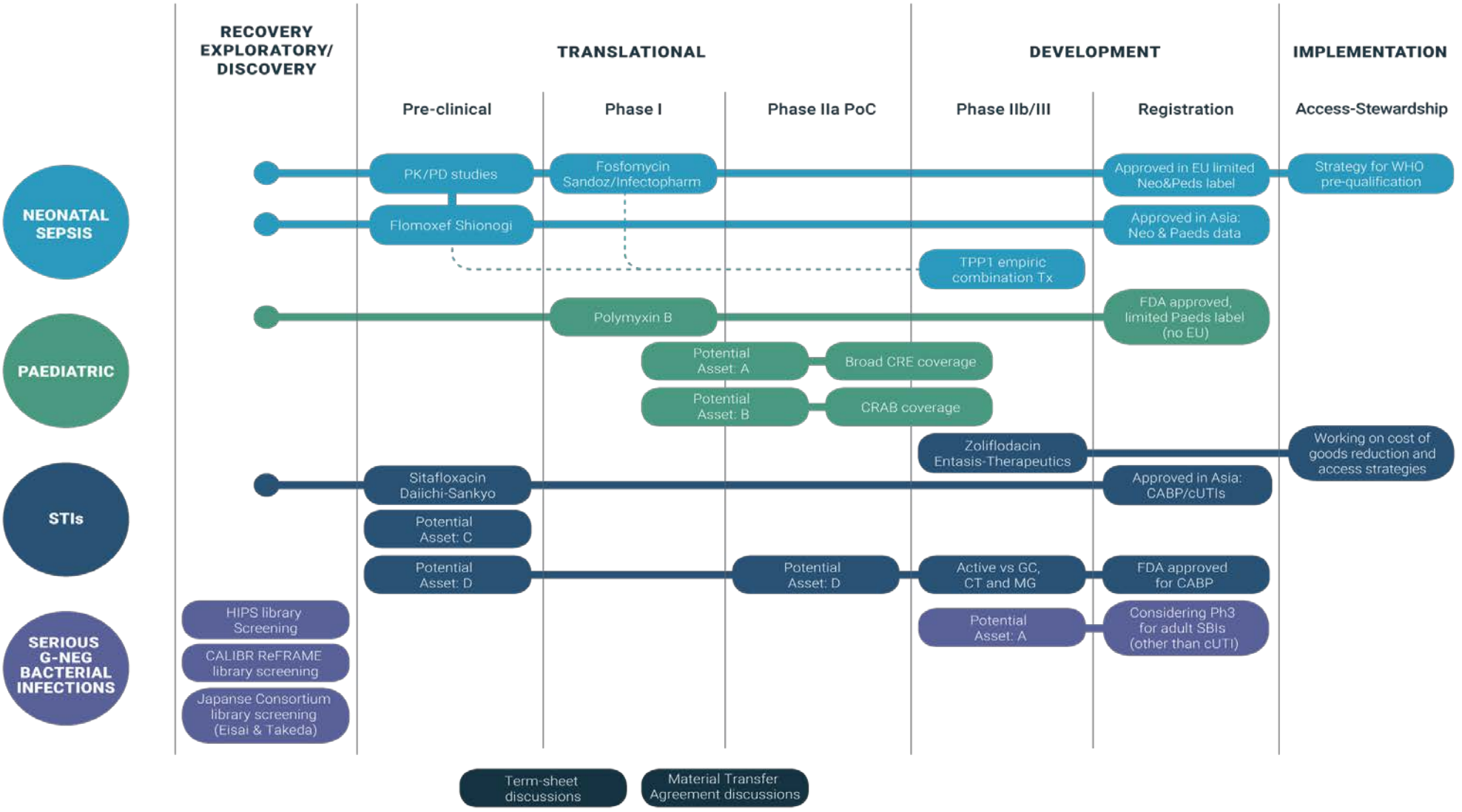
GARDP
Global Antibiotic Research & Development Partnership

GARDP programme objectives

SERIOUS BACTERIAL INFECTIONS (SBI)		• Accelerate development of new antibiotics to deliver at least one **new treatment** addressing serious infections in **hospitalised** adults caused by **WHO priority pathogens**
CHILDREN	Neonatal sepsis	• Develop an **alternative first-line treatment for clinically diagnosed cases of sepsis** and a new treatment for confirmed **multidrug resistant pathogens**
	Paediatrics	• **Repurpose and optimize use** of **old antibiotics** and **accelerate** development of **new antibiotics** for at least one new and **improved treatment** for children
SEXUALLY TRANSMITTED INFECTIONS (STIs)		• **Accelerate** development of **new antibiotics** and **develop at least one** new **treatment** for difficult to treat and drug resistant infections
EXPLORATORY & DISCOVERY		• **Assess new antibiotics**, 'recovered' drugs and combinations for inclusion in GARDP priority programs • **Identify novel antibiotics** for new and under-exploited targets to translate into treatments for drug-resistant infections

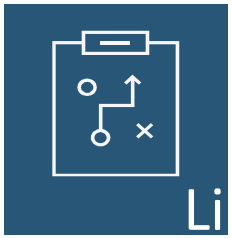
GARDP
Global Antibiotic Research & Development Partnership

GARDP pipeline



GARDP
Global Antibiotic Research & Development Partnership

GARDP Access framework for public health impact



Licensing

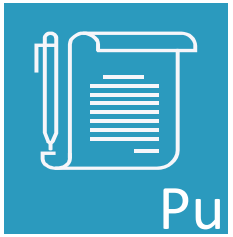
In & out-licensing supporting:

- Quality manufacturing
- Early access across high-burden countries
- Appropriate marketing

Regulatory

Collaborating with WHO & national regulators for:

- Public health evidence (need and use)
- Global registration
- Label extension



Public Health Policy & Use

- Early Access programmes
- Guidelines to ensure appropriate access
- Surveillance for resistance emergence
- Diagnostics for stewardship

Outsourcing Strategies

- Cost of goods focus
- Defining best practice in manufacturing
- Maintaining a core network of partners

Procurement

- Better understanding national needs in key high-burden countries
- Facilitating cost-saving procurement mechanisms to support demand

Reimbursement Models

- Non-volume based sustainable reimbursement models

GARDP's intensity of engagement will vary for each of these interventions and will include:

Advocating | Facilitating | Implementing

GARDP
Global Antibiotic Research & Development Partnership

Short-term Target Product Profile for uncomplicated GC

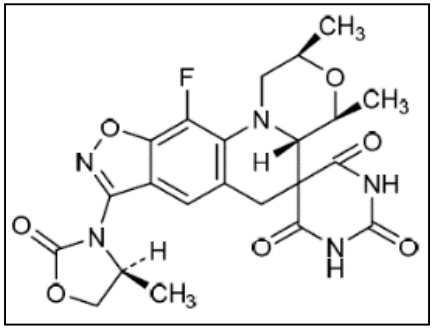
	IDEAL	MINIMUM
Activity against co-infecting STI pathogens	*Chlamydia trachomatis* *Mycoplasma genitalium*	*Chlamydia trachomatis*
Patient population	Adults and adolescents	Adults and adolescents
Clinical efficacy (Urogenital infections)	97% (95% CI, 95-100)	95% (95% CI, 90-100)
Clinical efficacy (Extra-genital infections)	Equivalent to current treatment regimens	Equivalent to current treatment regimens
Mechanism of action	Bactericidal	Bactericidal
	Intracellular activity	-
Activity against resistant strains	Activity against ESC and macrolide-resistant NG strains	Activity against ESC and macrolide-resistant NG strains
	No cross resistance with other Ab	Limited cross-resistance with other Ab
Safety and tolerability	Safe in pregnancy and lactation	-
	No patient monitoring required	Minimal outpatient monitoring required
Contra-indications	None	Pregnancy and lactation
Drug-Drug Interaction profile	None	Minimal
Route of Administration / formulation	Oral	Oral
Dosing Schedule	Single dose	Single dose
Treatment duration	One day	One day
Stability	Heat stable, 3-year shelf-life in region 4b	Heat stable, 2-year shelf-life in CRT
Time to patient availability	5 years	7 years

Long term Target Product Profile for uncomplicated GC

	IDEAL	MINIMUM
Indication	Uncomplicated and complicated GC	Uncomplicated GC
Activity against co-infecting STI pathogens	*Chlamydia trachomatis* *Mycoplasma genitalium*	*Chlamydia trachomatis*
Patient population	Adults, children and adolescents	Adults, children and adolescents
Clinical efficacy (Urogenital infections)	97% (95% CI, 95-100)	95% (95% CI, 90-100)
Clinical efficacy (Extra-genital infections)	97% (95% CI, 95-100)	95% (95% CI, 90-100)
Mechanism of action	Unique mechanism	
	Bactericidal	Bactericidal
	Intracellular activity	-
Activity against resistant strains	Activity against ESC and macrolide-resistant NG strains	Activity against ESC and macrolide-resistant NG strains
	No cross resistance with other Ab	Limited cross-resistance with other Ab
Safety and tolerability	Safe in pregnancy and lactation	-
	No patient monitoring required	Minimal outpatient monitoring required
Contra-indications	None	Pregnancy and lactation
Drug-Drug Interaction profile	None	Minimal
Route of Administration / formulation	Oral Fixed Dose Combination	Co-packaged loose oral combination
Dosing Schedule	Single dose	Multiple dose
Treatment duration	Up to 3 days	Up to 5 days
Stability	Heat stable, 3-year shelf-life in region 4b	Heat stable, 2-year shelf-life in CRT
Time to patient availability	7 years	10 years

Zoliflodacin project

Mechanism of action
First-in-class drug (spiropyrimidinetrione)
Inhibits DNA biosynthesis by binding to topo II
Mode of Action (MoA) differs from other topo II inhibitors



Industrial partner
Entasis Therapeutics Inc

Indication: Uncomplicated gonorrhea
Formulation: granules for oral suspension in shachet
Predicted dosage: 3 g single dose

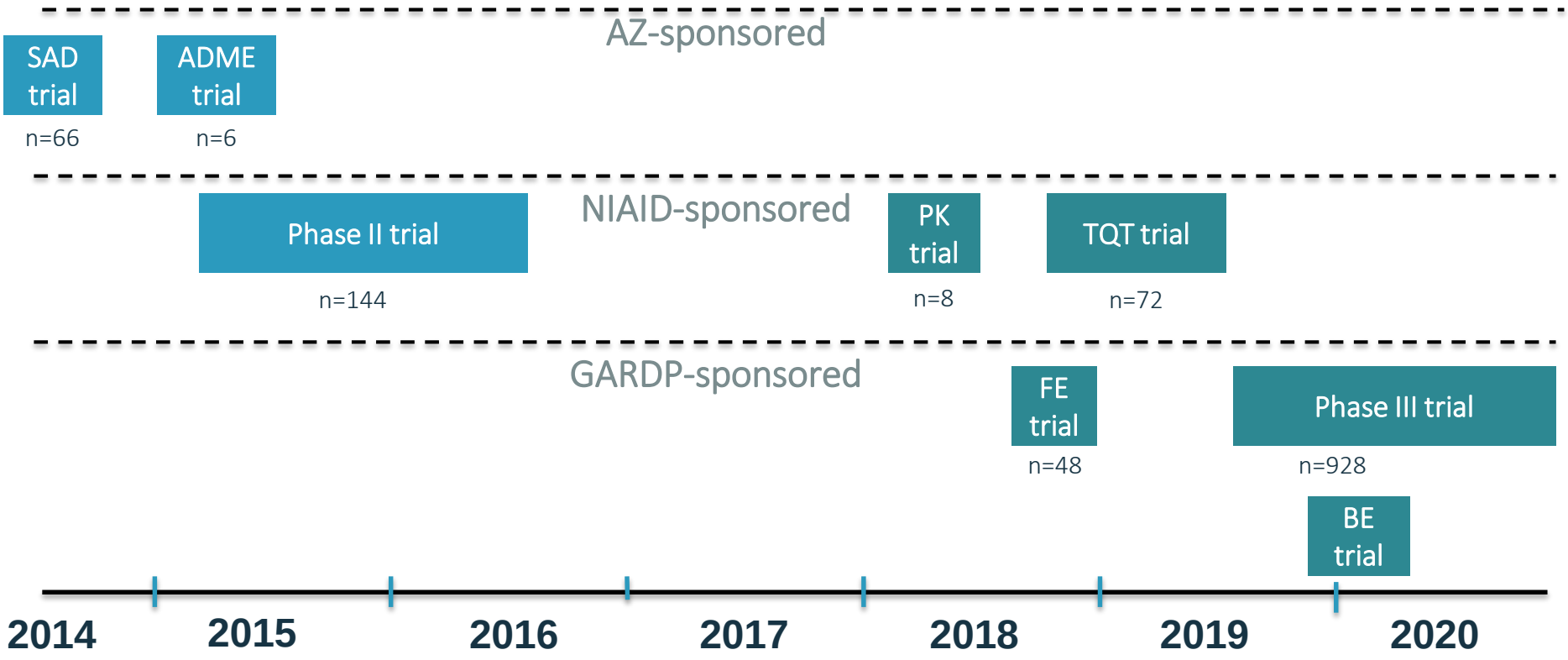
Project aim: Register, launch and roll out zoliflodacin in a selected number of high-burden countries

Objectives

1)To ensure the registration of zoliflodacin by delivering pivotal clinical trial(s)
2)To generate the necessary evidence to support the integration of zoliflodacin into clinical and public health guidelines;
3)To ensure sustainable and equitable access to zoliflodacin by embedding access elements in the clinical development program;
4)To support pharmaceutical development of a robust and affordable commercial product

GARDP
Global Antibiotic Research & Development Partnership

Zoliflodacin development history



SAD: Single Ascending Dose
ADME: Absorption, Distribution, Metabolism and Excretion
FE: Food Effect
PK: Pharmacokinetics
BE: Bio-equivalence

Powder for oral suspension

Granules for oral suspension

GARDP
Global Antibiotic Research & Development Partnership

Project partners

Institution	Country
• Department of Reproductive Health and Research, World Health Organisation (WHO) • Drugs for Neglected Disease *initiative* (DNDi) • Foundation for Innovative Diagnostics (FIND)	
• Entasis Therapeutics • National Institute of Allergy and Infectious Diseases (NIAID) • University of Birmingham (UAB), Alabama • ICON GPHS • Bell Flower Clinic, Indianapolis • Harborview Medical Center, Seattle • Louisiana State University, New Orleans • MetroHealth Medical Center, Cleveland • San Francisco City Clinic, San Francisco • University of Florida	USA
• Centre for HIV & STIs, National Institute for Communicable Diseases (NICD) • Wits RHI, University of Witwatersrand • University of KwaZulu Natal (UKZN) • South Africa Medical Research Council (SA-MRC)	South Africa
• Bureau of AIDS, TB, and STIs, Department of Disease Control, Thai Ministry of Public Health (MoPH) • Thailand US CDC Collaboration (TUC) • Thai Red Cross AIDS Research Center (TRCARC) • University of Mahidol – Tropical Medicine Hospital	Thailand
• WHO Collaborating Center for STI, Orebro University Hospital	Sweden
• Department of Infectious Diseases, Public Health Service Amsterdam	The Netherlands

Challenges in development new GC treatments

- Gap between regulatory requirements for uncomplicated gonorrhoea and the actual use of gonorrhoea drugs within the context of syndromic management
    - Comparator to be used in clinical development
    - Narrow non-inferiority margin
    - Differentiation of re-infections from microbiological failures
    - Activity against co-infecting pathogens
- Necessity to achieve high cure rates at pharyngeal sites
    - Single dose dogma
    - Lack of well-established *in vitro* and *in vivo* model for studying PK/PD
- Positioning of the drug (resistant infections vs clinical indication) and consequence for access and stewardship
- Clinical trials challenges
    - Inclusion of women and adolescents
    - Gathering of PK data from patients
    - Fragility of *Neisseria gonorrhoeae*
    - Differences in Standard of Care and Ethics/Regulatory requirements across countries

Thank you

Federal Ministry of Education and Research

Federal Ministry of Health

UKaid from the British people

saMRC advancinglife

LE GOUVERNEMENT DU GRAND-DUCHÉ DE LUXEMBOURG

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Ministry of Health, Welfare and Sport

icmr INDIAN COUNCIL OF MEDICAL RESEARCH

MEDECINS SANS FRONTIERES

Bill & Melinda Gates Foundation

wellcome

Leo Model Foundation