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100
A CENTURY OF LEADERSHIP IN LUNG HEALTH

worldlunghealth.org

THE 51ST UNION WORLD CONFERENCE ON LUNG HEALTH

ADVANCING PREVENTION

20—24 OCTOBER 2020
VIRTUAL EVENT

CONFLICT OF INTEREST DISCLOSURE

√ I have the following Conflict of Interest(s) to report:

Please tick the type of affiliation / financial interest and specify the name of the organisation:

√ Receipt of grants/research supports: __IMI as detailed in last slide__

☐ Receipt of honoraria or consultation fees: _____

☐ Participation in a company sponsored speaker's bureau: _____

☐ Tobacco-industry and tobacco corporate affiliate: _____

√ Stock shareholder: __GlaxoSmithKline Pharmaceuticals__

☐ Spouse/partner: _____

☐ Other: _____

IMI AMR Accelerator

Structure and Strategy

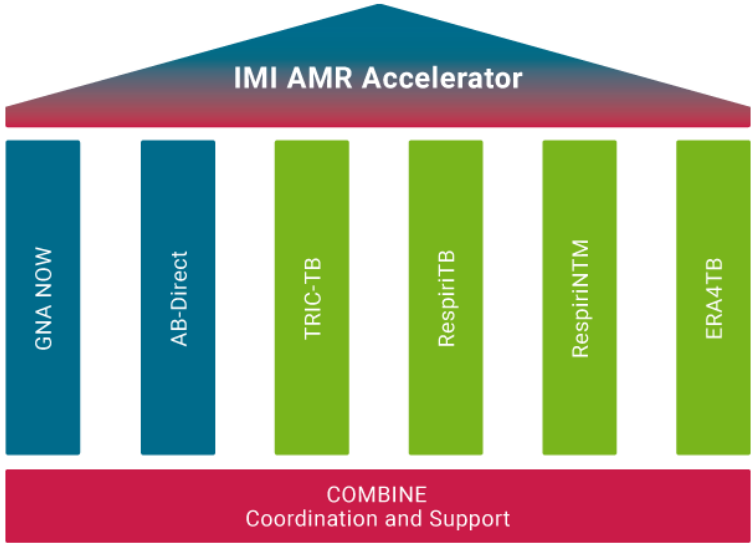
Karen O'Dwyer

GlaxoSmithKline Pharmaceuticals, COMBINE Project Leader

22 October 2020

IMI's Antimicrobial Resistance (AMR) Accelerator Program

comprises several projects with the shared goal of progressing the development of new medicines to treat or even prevent resistant bacterial infections in Europe and worldwide.



The AMR Accelerator

Currently 58 participants, >295 M€ budget

Current Goals : by 2025

10 new preclinical candidates

Up to 5 Phase II-ready compounds

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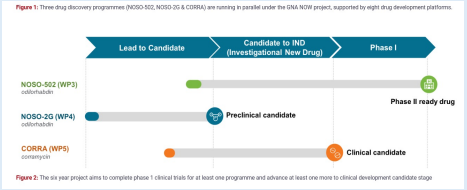
AMR Accelerator Projects (www.amr-accelerator.eu)

ERA4TB

ERA4TB is expected to revolutionize the way in which tuberculosis treatments are developed thanks to its parallelized, multi-entry pipeline structure, analogue to a production line. This structure will enable to systematically investigate the efficacy of several drug candidates and combinations simultaneously while allowing new molecules to enter the project pipeline at the research stage corresponding to the degree of knowledge on said candidate drugs gathered before the project.

With this approach, the ERA4TB consortium expects to reduce the time required for the development of new tuberculosis treatment regimens by up to a quarter.

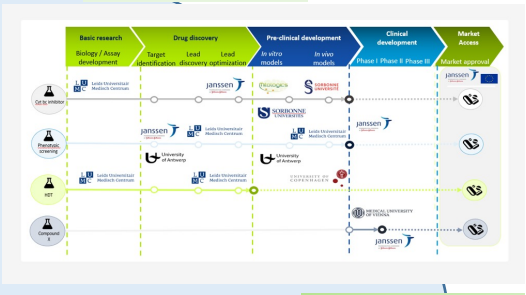
GNA NOW



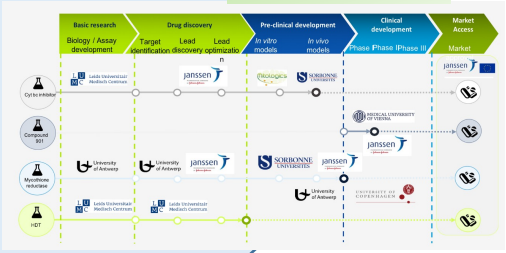
COMBINE

- **COMBINE** will coordinate the AMR Accelerator and support the delivery of projects across the Accelerator in order to progress a pipeline of potential new medicines to treat and prevent infections with resistant bacteria;
- **COMBINE** will establish an IT infrastructure for management, integration and analysis of combined data from across all Accelerator projects, perform regular data management reviews, leverage best practices, create software specifications, review existing tools;
- **COMBINE** will facilitate communication among Accelerator projects, with the AMR community and beyond as well as disseminate news and results, work in close collaboration with existing AMR drug development initiatives;
- **COMBINE** will share and analyse vaccine and antibacterial data, to improve the design and analysis of clinical trials;
- **COMBINE** will improve the understanding of animal infection model reproducibility and translation to clinical efficacy

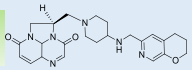
RespiriNTM



RespiriTB



AB-Direct



Gepotidacin is a novel antibiotic currently under development. The objective of the project is to explore a potential new option for the treatment of pharyngeal or prostatic bacterial infections by demonstrating adequate penetration of a novel antibiotic in tonsillar and prostate tissues.

This will be achieved in the project by:

- Conducting in vivo studies to predict human exposures of gepotidacin in healthy and infected prostate;
- Measuring gepotidacin levels in tonsillar and prostate tissue following single oral dose of gepotidacin in subjects undergoing elective tonsillectomy or prostatectomy;
- Refining the PBPK and the population pharmacokinetic (PopPK) models based on the generated clinical data to describe gepotidacin penetration into human tonsillar and prostate tissue;
- Developing a pharmacokinetic-pharmacodynamic (PKPD) model that relates the gepotidacin tissue exposure (PK) with the effect (PD)
- Determining the probability for target attainment for subjects in plasma, prostate and tonsils based on data from the healthy volunteer study to support the evaluation of dosing regimens for disease;
- Analysing the prostate non-clinical and clinical data, evaluating and contributing to the current understanding of translation across species.

Ultimately, the data generated by AB-DIRECT will contribute to a decision on whether or not to run clinical trials of gepotidacin as a treatment for throat infections caused by *N. gonorrhoeae* or prostate infections caused by *E. coli*. AB-DIRECT is part of the IMI AMR Accelerator programme.

TRIC-TB

The specific objectives of this IMI project are to deliver one Phase II ready booster molecule, having a) completed preclinical CTA enabling studies and b) completed Phase I (SAD and MAD) for safety and PK evaluation in healthy volunteers. Ultimately, the results from this project will pave the way for the booster to be integrated into new, improved regimens to treat TB including MDR-TB. A small molecule booster in combination with lower ETH/PTH doses will deliver a better tolerated and more potent drug combination than standard doses of ETH alone, and this can massively impact the current TB treatment armamentarium and significantly improve both patient experience and treatment outcomes.

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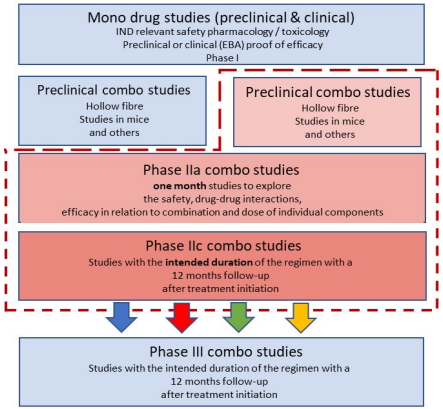
AMR Accelerator Project Portfolio

September 2020

			Novelty		Development Stage				
AMR Accelerator Project	**Asset Owner**	**Programme**	**New Class**	**New MoA**	**Discovery**	**(Pre)-Hit to Lead**	**Lead to Candidate**	**Candidate to Phase I**	**Phase I**
GNA NOW	EVOTEC	Corramycin	✓	✓			→		
	NOSOPHARM	NOSO-502	✓	✓				→	
		NOSO-2G	✓	✓			→		
TRIC-TB	BioVersys and GSK	Boosting Ethionamide		✓				→	
AB-Direct	GSK	Gepotidacin tissue distribution	✓	✓				→	
ERA4TB		ERA4TB GSK1	✓	✓			→		
		ERA4TB GSK2	✓	✓					→
	TBA	ERA4TB TBA1							→
RespiriTB & NTM	JANSSEN	65082901TBC1001						→	
		RespiriTB	✓	✓	→				
		RespiriNTM				→			
Accelerating scientific discoveries in the AMR field									
COMBINE		Providing learnings derived from shared vaccine and/or antibacterial clinical trial data and improving understanding of variability and translatability of animal models of bacterial infection.							

AMR Accelerator Projects : currently under development

UNITE4TB
(Stage 2 negotiation Call 20)
~200 M€ budget



Modelling the Impact of mAbs and vaccines on the reduction of AMR
(Call 23)

- Evaluate burden of disease
- Develop a model to estimate the cost and benefits of mAbs and vaccines in AMR

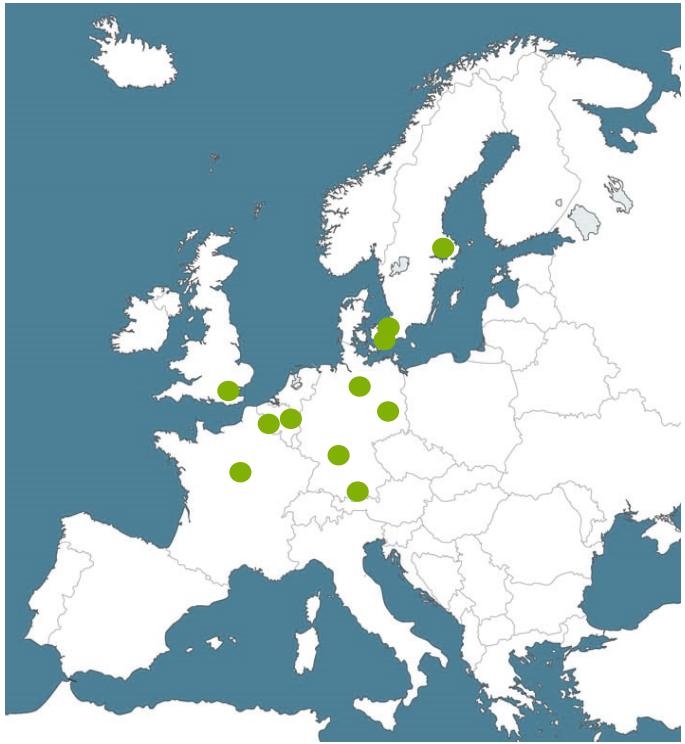
The AMR Accelerator: what's in it for me?

Perspective from an Industry (EFPIA) Partner

- **Benefits of this Public Private Partnership Model:**
  - ✓ **Sharing of cost and risk for capability building and portfolio building**
  - ✓ **Diversity of thought seeding quality and innovation**
  - ✓ **External validation and large network for expert advice**
- **Challenges include no direct funding to EFPIA partner, and complexity of reaching agreement across multiple partners.**

Keys to Success: Collaboration – Transparency - Flexibility

COMBINE – Coordination and Support of AMR Accelerator



Universities, research organisations, public bodies, non-profit groups:

- Uppsala University (UU) Sweden Coordinator
- Paul-Ehrlich-Institut (PEI) Germany
- Fraunhofer Gesellschaft (FRAUNHOFER) Germany
- Statens Serum Institut (SSI) Denmark
- BEAM Alliance (BA) France

Small and medium-sized enterprises (SMEs) and mid-sized companies (<€500 m turnover):

- Asclepia (AC) Belgium
- GRIT42 (G42) Denmark
- BIOCOM (BC) Germany

EFPIA companies:

- GlaxoSmithKline (GSK) United Kingdom Project Lead
- Evotec (EVT) Germany
- Janssen (JNJ) Belgium

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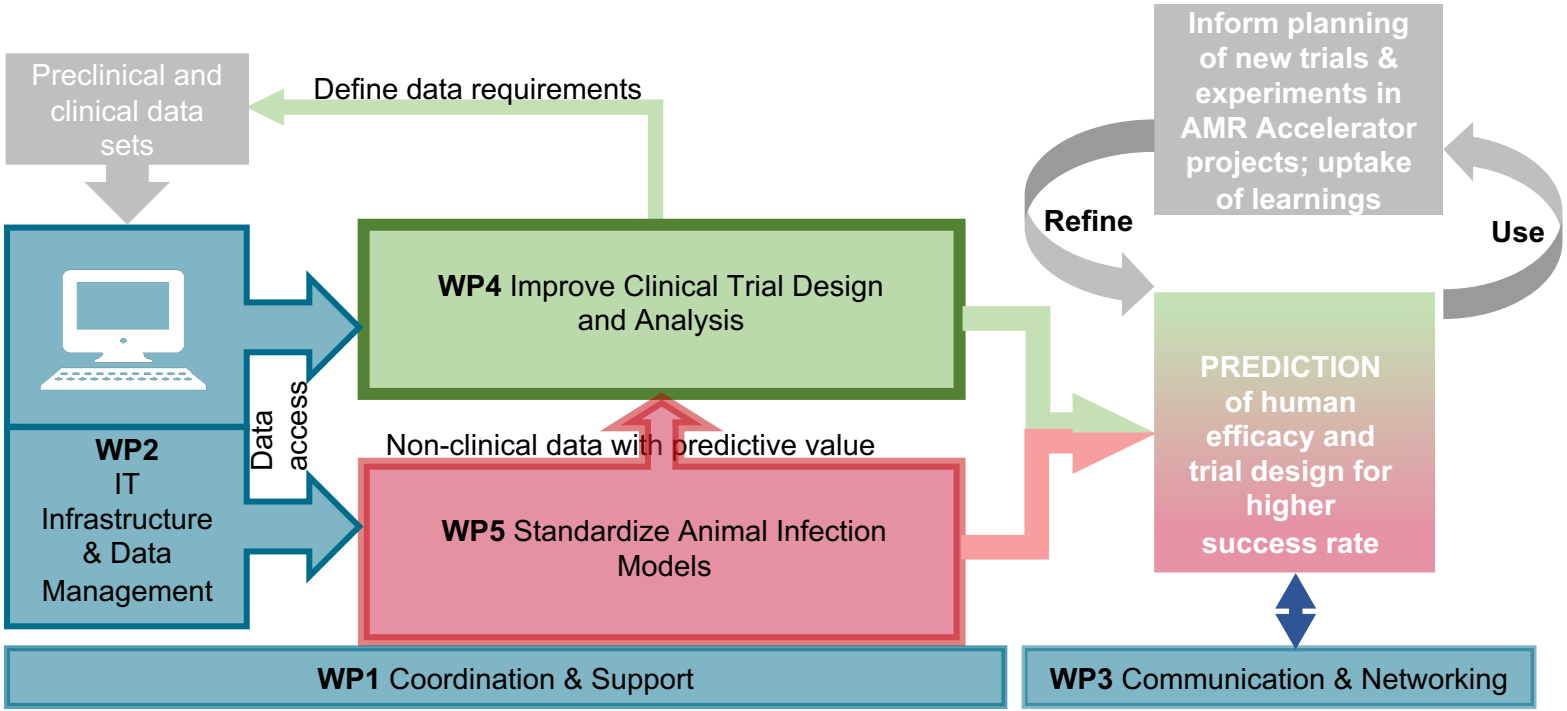
The COMBINE Project

A coordination role and a scientific mission around capability building



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You Can Help! - Open Call for Data

Call for non-clinical (preclinical) and clinical data sets from the study of prevention or treatment of bacterial infections

Antibiotics, vaccines, monoclonal antibodies, pathoblockers and phages

We are specifically looking for
1) Matched pairs of preclinical toxicology data and Phase 1 studies
2) Matched pairs of preclinical PK/PD analysis and clinical PK/PD studies
3) Matched pairs of preclinical efficacy in challenge models and data from efficacy trials
4) Data from clinical trials for prevention or treatment of bacterial infections

What pathogens?
- ESCAPE pathogens: *Enterococcus faecium, Staphylococcus aureus, Clostridioides difficile, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacteriaceae*
- *Neisseria gonorrhoeae*
- *Mycobacterium tuberculosis*

Submit your Expression of Interest:
AMR-data-technical.COMBINE@grit42.com
Deadline extended to October 2020

Acknowledgements

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https://www.imi.europa.eu/

imi innovative medicines initiative

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