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
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.

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

- **ERA4TB**
- **COMBINE**
- **GNA NOW**
- **TRIC-TB**
- **RespiriNTM**
- **RespiriTB**
- **AB-Direct**

**GNA NOW**

- **RespiriNTM**
- **RespiriTB**
- **AB-Direct**
- **TRIC-TB**
- **COMBINE**

**Depositor is a novel antibiotic currently under development. The objective of the project is to explore a potential new option for the treatment of photoreactive bacterial infections by demonstrating adequate penetration of a novel antibiotic in targetable prostate tissues.**

- Conducting in-vivo studies to predict human exposures of photodegradation in healthy and infected prostate.
- Monitoring photodegradation in healthy and prostate tissues following single oral dose of photodegradation in targetable prostate tissues or photoreactive.
- Building a photodegradation pharmacokinetic/pharmacodynamic (PK/PD) model based on the generated clinical data to describe photodegradation penetration into human prostate and prostate tissue.

- Developing a pharmacokinetic pharmacodynamics (PK/PD) model that relates the photodegradation exposure (E) with the effect (P).
- Screening the probability for targeted antagonism for subjects in prostate cancer and non-tumor based on data from the healthy volunteer study to support the evaluation of dosing regimen for disease.
- Building the predictive clinical and clinical data, evaluating and contributing to the current understanding of transitions across species.

Ultimately, the data generated by AB-DIRECT will contribute to a decision on whether or not to use clinical trials of photodegradation as a treatment for severe infections caused by A. photovarable or photodegradation caused by E. coli. AB-DIRECT is part of the AMR Accelerator program.

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 II (BAD) and MAH 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 ETB/PTH doses will deliver a better tolerated and more potent drug combination than standard doses of ETB alone, and this can massively impact the current TB treatment armamentarium and significantly improve both patient experience and treatment outcomes.
## AMR Accelerator Project Portfolio

**September 2020**

<table>
<thead>
<tr>
<th>AMR Accelerator Project</th>
<th>Asset Owner</th>
<th>Programme</th>
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<th>Development Stage</th>
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</table>

**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.

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**The Union**
AMR Accelerator Projects: currently under development

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

Mono drug studies (preclinical & clinical)
(mAb) relevant safety pharmacology/toxicology
Preclinical or clinical (EBM) proof of efficacy

Preclinical combo studies
Studies in mice and others

Phase Ila combo studies
One-month studies to explore the safety, drug-drug interactions, efficacy in combination, and dosing of individual components

Phase IIc combo studies
Studies with the intended duration of the regimen with a 12-month follow-up after treatment initiation

Phase III combo studies
Studies with the intended duration of the regimen with a 12-month follow-up after treatment initiation

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
The COMBINE Project

A coordination role and a scientific mission around capability building

- WP1 Coordination & Support
- WP2 IT Infrastructure & Data Management
- WP3 Communication & Networking
- WP4 Improve Clinical Trial Design and Analysis
- WP5 Standardize Animal Infection Models

Define data requirements

Inform planning of new trials & experiments in AMR Accelerator projects; uptake of learnings

Refine

PREDICTION of human efficacy and trial design for higher success rate

Preclinical and clinical data sets

Non-clinical data with predictive value

Data access
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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