



RSC/BTS/BSAC meeting – Tackling Antimicrobial Resistance

UK ‘State of the Nation’ in developing new drugs for AMR

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Who we are and what we do

The AMR Centre is a key part of the UK's response to the global threat from Antimicrobial Resistance. The AMR Centre is based at Alderley Park in the UK and is a for-profit public-private initiative to support and accelerate the development of new antibiotics through an integrated development capability, offering translational R&D from pre-clinical lead optimisation through to clinical proof of concept

- Established in 2017 with UK public and private investment
- Supporting the development of innovative treatments for AMR infections through flexible partnership deals
- Building new capability and leveraging UK capacity and expertise
- Translation from lead optimisation to phase 2 clinical proof of concept



Our strategic position in the R&D process

Partner with SMEs
and academia

Providing program funding, scientific expertise
and capacity to biotech and pharma partners

Licensing to 'Medium/Big Pharma' for late
stage development and commercialization

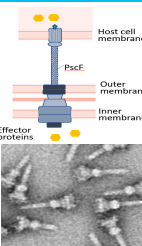


First programs target critical priority superbugs with innovative technologies

T3SS Inhibitor

MICROBIOTIX INC.

- Target Product: Prevention & Treatment of Ventilator-Associated Pneumonia caused by *P. aeruginosa***
 - Urgent unmet medical need, common infection amongst critically ill patients
 - High mortality rates: >35% for MDR strains
 - Elevated health care costs: ~\$40,000 per episode
- Mechanism:** Inhibition of type III secretion system (T3SS)
 - Needle type projection delivers toxins into host cells
 - Tissue destruction and inflammation
 - Disruption of hosts immune response
 - Prevent the establishment and dissemination of infections
 - Extra-cellular, avoid efflux and existing resistance mechanisms



Cropped image from Schrafft et al. (2020) doi:10.1073/pnas.2007054117

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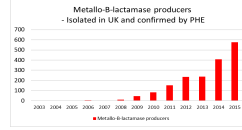
AMR CENTRE

- Co-development agreement with Microbiotix (Boston USA), supported by CARB-X
- New anti-virulence drug to block microbial T3SS systems and prevent immune response to infection
- Targeting highly-resistant strains of *P. aeruginosa*, the leading cause of deaths from pneumonia

Metallo β -Lactamase Inhibitor

MEDIVIR

- Target product:** IV combination therapy for Gram-negative infections (MBL producing) with carbapenem
 - Septicaemia, pneumonia, urinary tract infections, intra-abdominal infection etc
 - Carbapenem-resistant *P. aeruginosa*, *A. baumannii* and Enterobacteriaceae **critical** unmet medical need
- Mechanism:** Inhibition of Metallo- β -lactamases (MBL)
 - Provide resistance to all known classes of β -lactams (except monobactams)
 - Restore activity of last line of defence antibiotics - carbapenems



MBLI

Top image from Wikipedia (By GrahamColm)

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AMR CENTRE

- In-licence agreement with Medivir (Sweden)
- New MBLI to overcome resistance mechanisms emerging from India and China, e.g. NDM-1
- Targeting “critical priority” pathogens containing genetic mutations that result in resistance to most common antibiotics

Antimicrobial Peptide

eligochem
ENTER DRUGS BY DESIGN

- Target product:** Novel IV therapeutic for Gram-negative infections
 - Trauma-induced infections, septicemia, intra-abdominal and urinary tract infections
 - Carbapenem-resistant *P. aeruginosa*, *A. baumannii* and Enterobacteriaceae **critical** unmet medical need
- Mechanism:** Antimicrobial peptide that specifically disrupts bacterial cell membrane
 - AMPs are found throughout nature and have diverse structures and functions, including antimicrobial activity
 - Low likelihood for resistance and first in class therapeutic

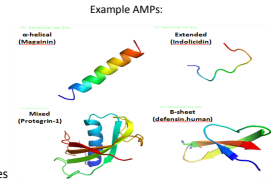


Image from Wikipedia (By Ymaho)

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AMR CENTRE

- Co-development with Eligochem (Sandwich, UK), supported by CARB-X
- New antimicrobial peptide with improved activity, selectivity and safety margins
- Targeting highly-resistant strains of *A. baumannii*, a rising cause of hospital-acquired infections worldwide

UK industrial AMR landscape

- IFPMA - AMR Industry Alliance
 - Global pharma and generics companies
- ABPI
- BIA AMR Group
 - “AMR Explainers” reports launched at UK Bioscience forum 18th October
- Industrial AMR SME group
 - “State of the Nation” report launched at UK BioInfect conference 8th November 2018
- BEAM alliance (EU)

- DHSC review on antimicrobial valuation and UK PULL incentives
- HSC select committee inquiry into 5-year AMR strategy
- Joint Industry/Government working group on AMR
 - ABPI & BIA represented
- APPG on antibiotics

UK industrial AMR landscape

- GSK
 - Antibiotic products generating approximately \$800m per year revenues
 - AMR R&D activities are principally based in the USA
 - Two new programs in clinical development for TB and Gonorrhoea
- AstraZeneca
 - Sold its commercial antibiotics business to Pfizer in 2017
 - Spun-off its small-molecule infection R&D activities into a new US-based company Entasis
 - Medimmune division has two antibody therapeutics against *P. aeruginosa* and *MRSA* in clinical development resulting from its US-based R&D
- Biotech SMEs
 - At least 23 innovative SMEs
 - At least 47 projects on new therapeutics and vaccines
 - Less than £50m total cash reserves and 11 companies have less than £1m cash
 - Many companies report having less than 12 months of cash available
 - Most companies report difficulty in recruiting
 - **There are now fewer than 150 industrial R&D researchers in the UK working on new AMR drugs**

UK industrial AMR landscape

- Evotec UK
 - Subsidiary of German-headquartered life sciences company with portfolio of AMR drugs acquired from Sanofi
 - Provides pre-clinical R&D services to industry via specialist 30-strong microbiology group & supporting departments
- Medicines Discovery Catapult (MDC)
 - focus on developing networks and new technologies with applications across all disease areas.
 - AMR as a key theme but highlighted serious weaknesses in UK infectious disease translational R&D
- AMR Centre
 - supports SMEs with operational capability and funding to co-develop new therapeutics into clinical trials
 - targeting WHO critical priority Gram-negative pathogens
- LifeArc
 - Charity that undertakes research across multiple therapeutic areas
 - working with the Defence Science and Technology Laboratory and the Canadian Centre for Drug Research and Development to identify new drug targets for AMR
- Academic accelerators
 - University of Liverpool & LSTM Centre of Excellence in Infectious Disease Research (CEIDR)
 - Dundee University Antibacterial Drug Development Accelerator (ADDA)

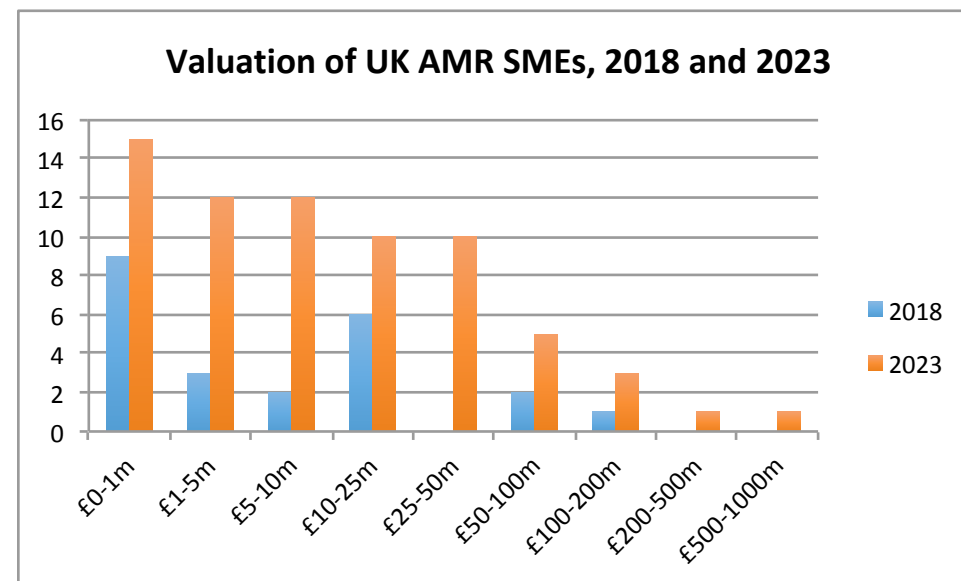
UK AMR drug pipeline

- 47 projects on new therapeutics and vaccines
 - 16 of these programs are targeting WHO “critical priority” Gram-negative pathogens ■
 - 16 are focused on Gram-positives ■
 - 15 are early stage with the potential to treat both ■
- Gram-positive drugs are more advanced given the strategic priority to address these infections in the UK over the past 10 years
- Given the inherent developmental risk and likely attrition rates, the UK pipeline has the potential to deliver one new therapeutic for Gram-positive infections
- UK industry is significantly under powered to deliver new drugs against the WHO “critical priority” Gram-negative targets
- The early stage pipeline is very weak, reflecting the lack of new projects transitioning from academia to pre-clinical development



The industrial AMR opportunity

- Developing the UK's AMR drug pipeline
 - Capitalise on our underpinning scientific strengths
 - Grow the number of SMEs
 - Translate more discovery programs into pre-clinical
 - Requires investment of £100's of millions
- Growing value for the UK
 - 23 AMR SMEs have a total market capitalisation of £440m
 - Only three companies having valuations above £50m
 - Support needed for existing SMEs to grow through equity and grant funding to translate programs through the development pipeline
 - Creation of more new entrants by translating stalled opportunities from academia into new start-ups



Can we grow a £3bn AMR industry by 2023?

Summary

- The UK's current 5-year AMR strategy called for a new supply of safe and effective antimicrobial drugs, and UK SMEs are at the forefront, with 23 companies progressing 47 new drug programs to address this urgent need
- Nevertheless, the UK's current translational capability is weak, and not yet adequately resourced to provide a sustainable pipeline of life-saving medicines to treat AMR
- Most of the SMEs in the AMR sector are significantly under capitalised and private investors do not yet see antibiotics as a priority for their investment decisions
- With focused support from public and private investors we have the opportunity to make a significant contribution to the global pipeline and growing the sector's value to UK plc

Actions

- Increase PUSH funding for translation of new drugs from discovery to clinical trials here in the UK
- Introduce PULL incentives to reward innovators and encourage investors to return to the antibiotics sector
- Support the creation and growth of SMEs who are at the forefront in the UK's response to AMR
- Coordinate our activities to avoid a fragmented approach to Government, in particular to influence the next UK 5-year AMR strategy
- Encourage researchers to join the mission to develop new drugs to address the rising challenge of infectious disease caused by AMR



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Thank You

www.amrcentre.com

