

**AMR  
CENTRE**

**RSC/BTS/BSAC meeting - Tackling Antimicrobial Resistance**

**UK 'State of the Nation'  
in developing new drugs for AMR**

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The AMR Centre

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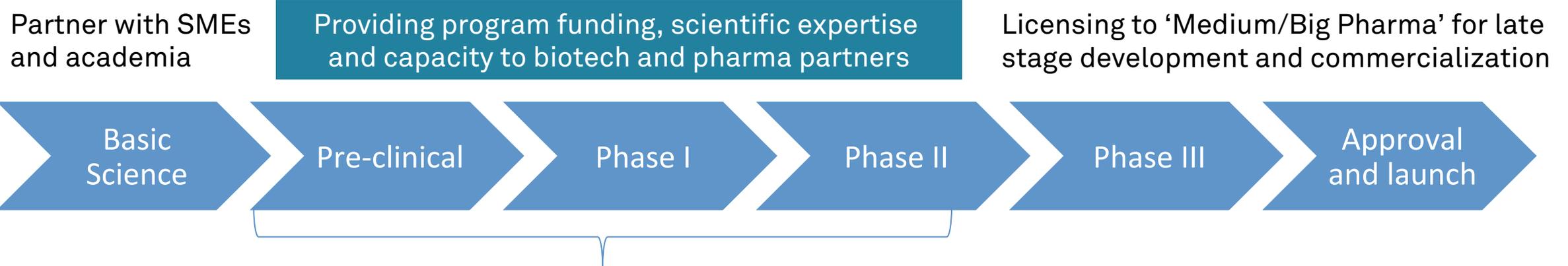
# Who we are and what we do

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

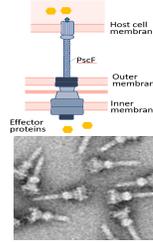


# First programs target critical priority superbugs with innovative technologies

## T3SS Inhibitor



- 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:10.1371/journal.pone.0200924

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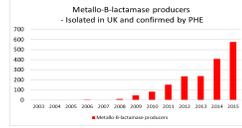


- Co-development agreement with Microbiotix (Boston USA), supported by CARB-X
- New anti-virulence drug to block microbial T3SS systems and prevent immune response to infection
- Targeting highly-resistant strains of *P. aeruginosa*, the leading cause of deaths from pneumonia

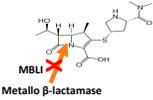
## Metallo $\beta$ -Lactamase Inhibitor



- 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- $\beta$ -lactamases (MBL)**
  - Provide resistance to all known classes of  $\beta$ -lactams (except monobactams)
  - Restore activity of last line of defence antibiotics - carbapenems



Year	Number of Producers
2003	0
2004	0
2005	0
2006	0
2007	0
2008	0
2009	0
2010	0
2011	0
2012	0
2013	0
2014	0
2015	0
2016	0
2017	0
2018	0
2019	0
2020	0
2021	0
2022	0
2023	0



**Metallo  $\beta$ -lactamase**

Top image from Wikipedia (By GrahamColm)

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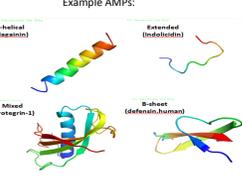


- In-licence agreement with Medivir (Sweden)
- New MBLI to overcome resistance mechanisms emerging from India and China, e.g. NDM-1
- Targeting “critical priority” pathogens containing genetic mutations that result in resistance to most common antibiotics

## Antimicrobial Peptide



- 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



**Example AMPs:**

Image from Wikipedia (By Ymahu)

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- 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 18<sup>th</sup> October
- Industrial AMR SME group
  - “State of the Nation” report launched at UK BioInfect conference 8<sup>th</sup> 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

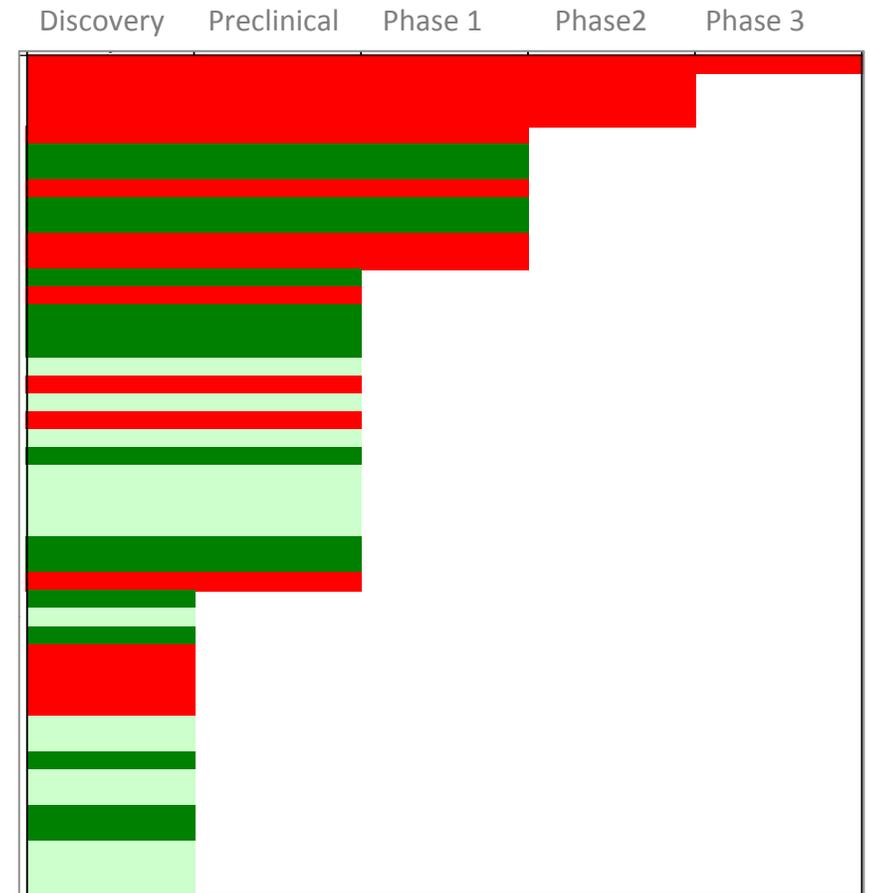
- GSK
  - Antibiotic products generating approximately \$800m per year revenues
  - AMR R&D activities are principally based in the USA
  - Two new programs in clinical development for TB and Gonorrhoea
- AstraZeneca
  - Sold its commercial antibiotics business to Pfizer in 2017
  - Spun-off its small-molecule 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)

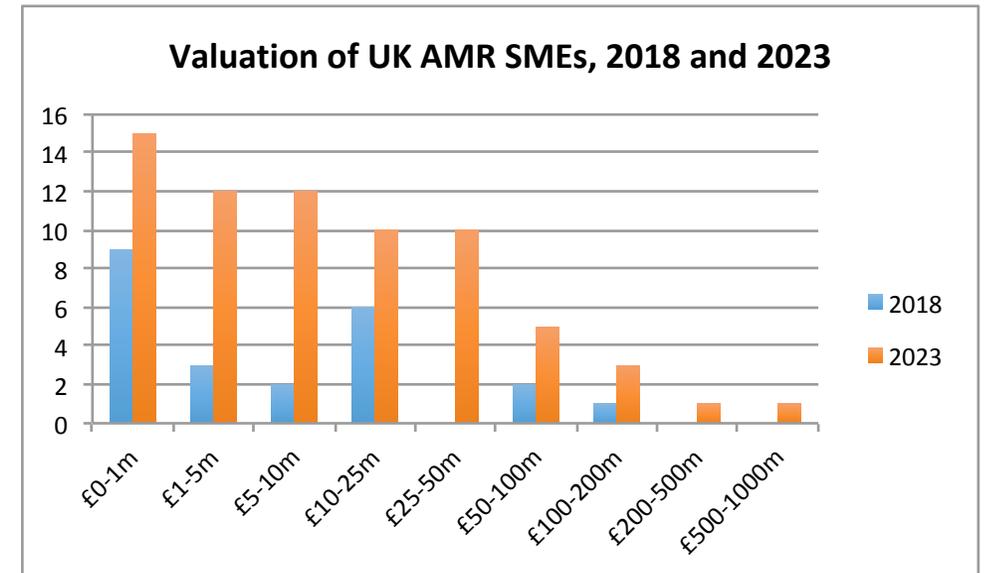
# UK AMR drug pipeline

- 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

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