The UK's Centre of Excellence in AMR

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AMR Centre Ltd

Emerging Antimicrobials and Diagnostics in AMR – 20th November 2019

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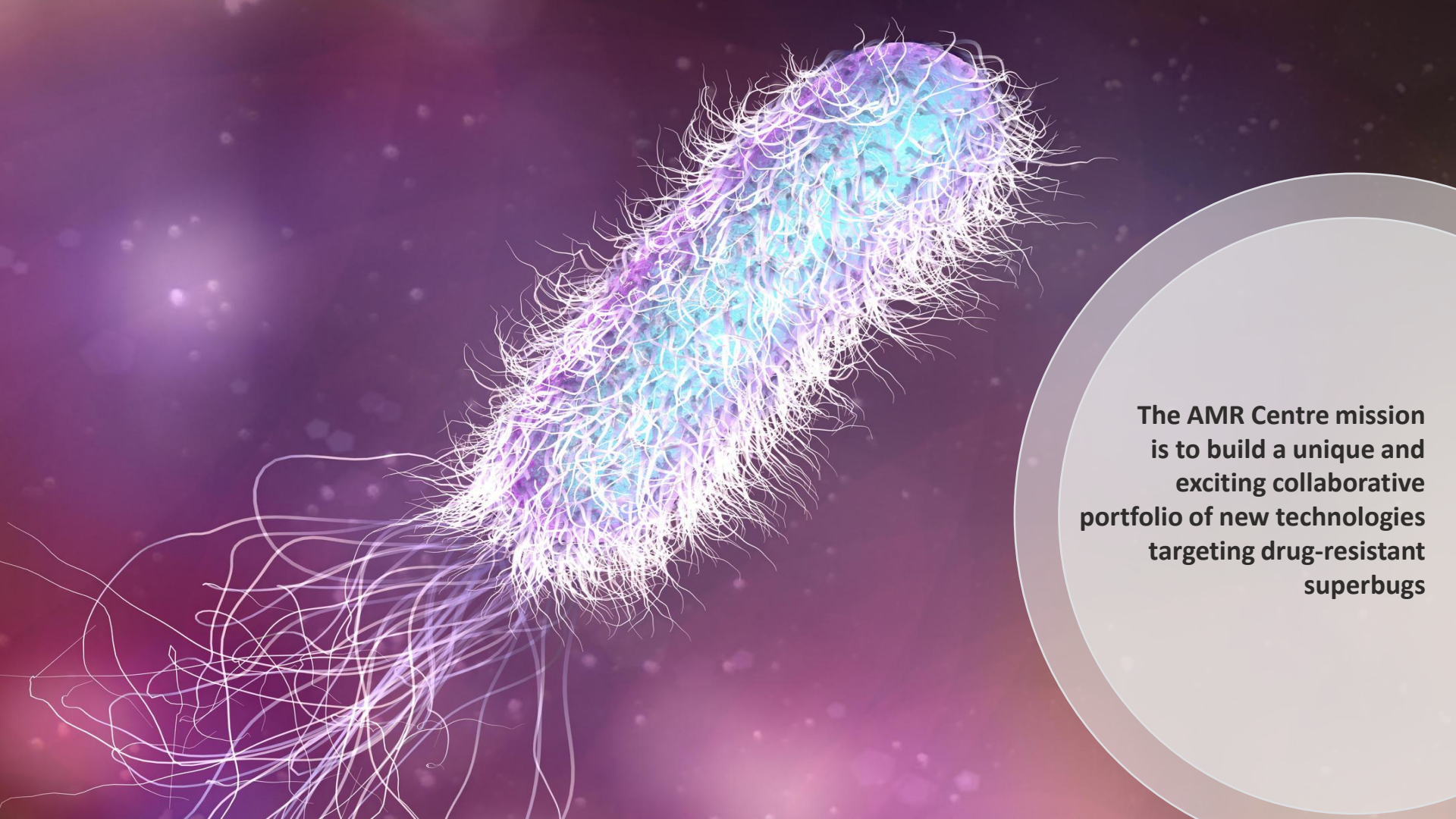


The AMR Centre mission is to build a unique and exciting collaborative portfolio of new technologies targeting drug-resistant superbugs

The UK's Northern Powerhouse: Translational Infrastructure for AMR

World-class public and private infrastructure for the development of AMR drugs

Over 50% of all UK industrial R&D employees in AMR

Innovative regional SMEs driving 35% of the UK's AMR drug pipeline

NORTHERN POWERHOUSE HM Government

The AMR Centre
Alderley Park
For-profit company with public, venture philanthropic and private investors to drive translation of new therapeutics from pre-clinical development to clinical proof of concept

Northern Health Science Alliance
Manchester
Representing the 8 leading research hospitals in the National Health Service (NHS) across the North of England with access to over 15 million patients

Centre of Excellence in Infectious Disease Research (CEIDR)
Liverpool University/Liverpool School of Tropical Medicine
University centre of excellence in translation of infectious disease programs from research to clinical trials in the UK and internationally

Centre for Antimicrobial Pharmacodynamics
University of Liverpool
University centre of excellence in PK/PD supporting translation of new international drug programs into clinical trials

Medicines Discovery Catapult
Alderley Park
Innovate UK centre of excellence in the development of new tools and networks to support the development of new drugs with AMR as one of its key themes

Evotec (UK) Ltd
Alderley Park
Largest contract research organisation in Europe focused on antimicrobial drug development, supporting SMEs and its own pipeline of new drugs for AMR

Taking Action on New Drugs for AMR

Why is the antibiotics market failing?

- Incremental development, with low levels of innovation
- Development costs are too high meaning that the risk reward balance does not incentivise investors
- SMEs are doing the majority of R&D, but are under funded and under resourced
- Clinical pathways are inflexible and invariably target non-inferiority

What actions are we taking for new AMR drugs?

- Focus on innovative strategies targeting WHO critical priority drug-resistant pathogens
- **Leveraging public, venture philanthropic and private funding with capacity and expertise to reduce the cost of development and minimise requirement for equity**
- Partner with SMEs to share developmental risks and provide capacity and expertise
- Develop innovative approaches to clinical trials with regulators to get faster to a label

AMR Centre's Acquire and Build Portfolio Strategy

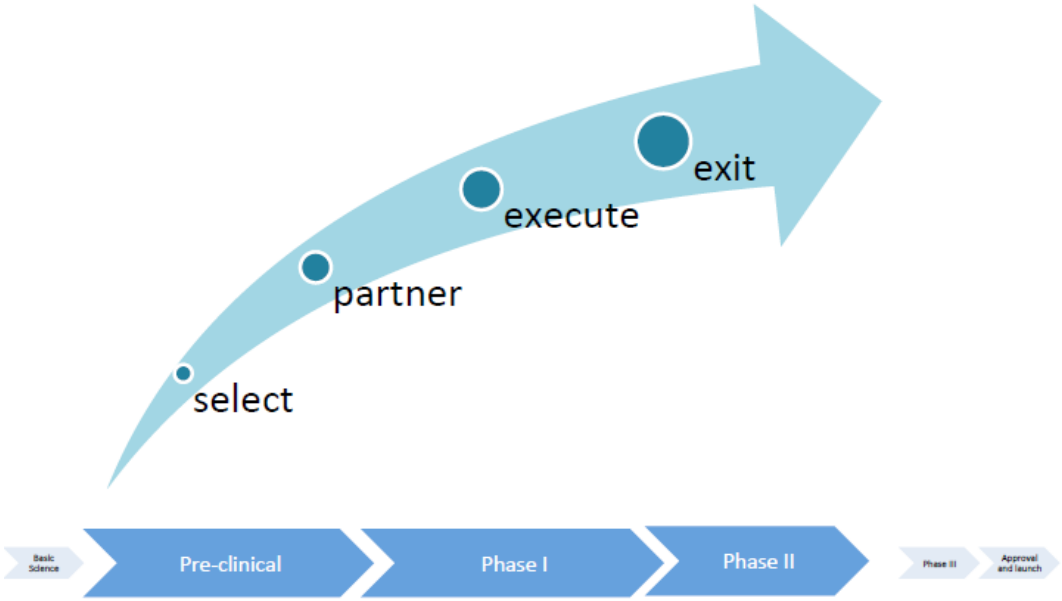
Targeting infectious diseases with high unmet need, in particular focusing on the World Health Organisation's "critical priority' pathogens

Acquiring a portfolio of innovative technologies with at least *in-vivo* efficacy demonstrated to fast track towards clinical proof of concept

Developing novel therapeutic approaches for critical priority diseases by:

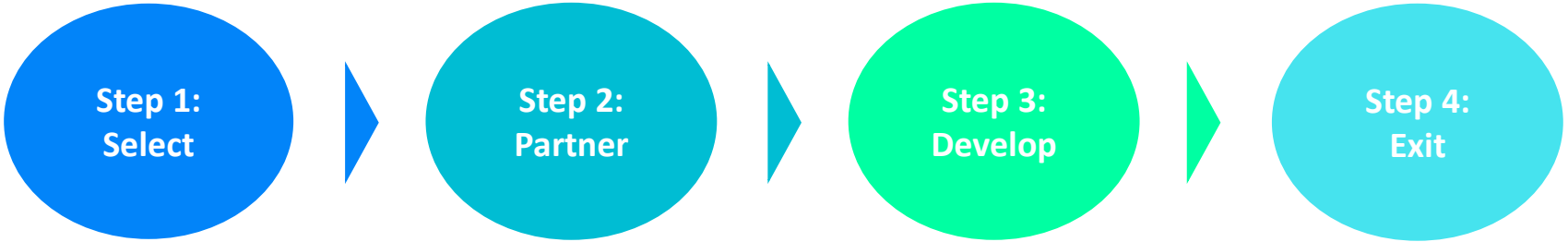
• In-licensing - with AMRC responsible for development to clinical proof of concept with the option to back-license to partner or out license to third party

• Co-development - with a fully integrated, collaborative partnership managed by a joint steering team responsible for marketing or licensing to third party



UK Network in Action: AMR Centre – Shionogi collaboration

AMR Centre Business Model



Initial meeting in Japan in 2017 supported by UK Department for International Trade

Extensive AMRC due diligence and Scientific Advisory Board review

AMRC re-design of clinical program and new Target Product Profile developed

Shionogi license to AMRC in 2019

AMRC responsible for Phase 1 and Phase 2 trials using established clinical and patient networks

Regular joint steering committee meetings through the project

Led by AMRC clinical project team with NHS clinicians

Phase 1a/b to be conducted in NHS clinical trial facilities at Liverpool

Supply chain and CMC outsourced to partner CMO

Shionogi commercialisation option after Phase 2

Reward for AMRC to re-invest in programs and return value to our public, philanthropic and private investors

Overall significant reduction in cost and time to proof of concept

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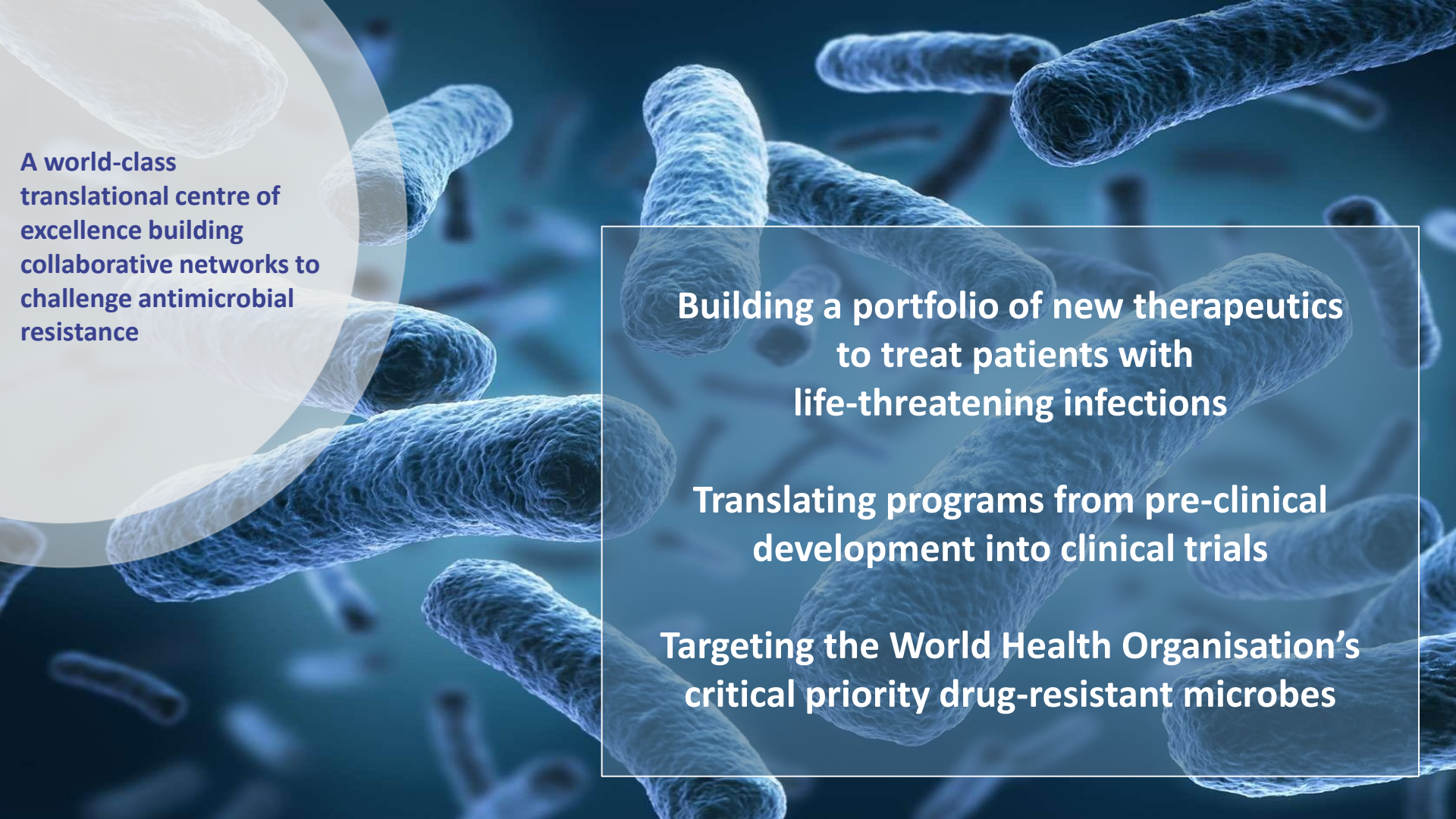


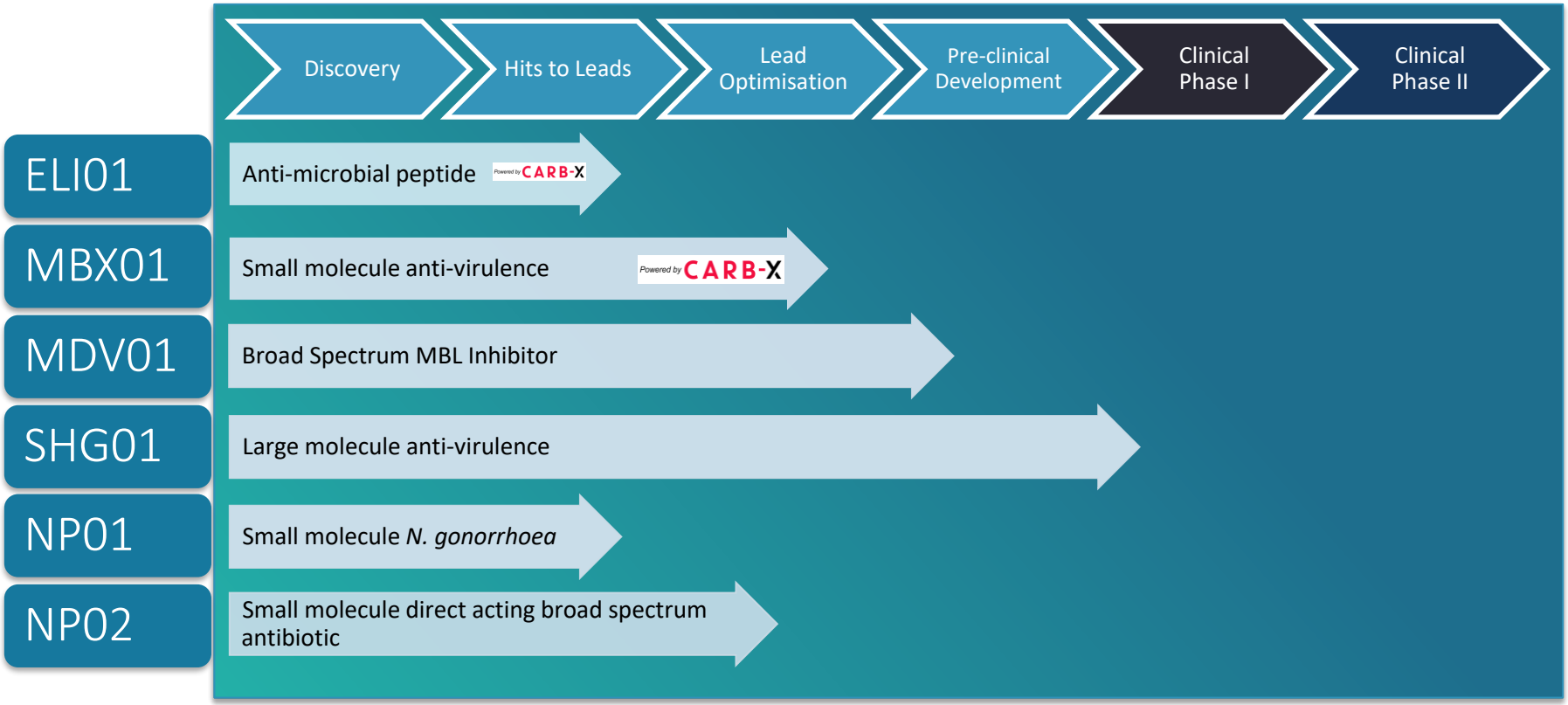
A world-class translational centre of excellence building collaborative networks to challenge antimicrobial resistance

Building a portfolio of new therapeutics to treat patients with life-threatening infections

Translating programs from pre-clinical development into clinical trials

Targeting the World Health Organisation's critical priority drug-resistant microbes

AMRC Portfolio & Pipeline



Case Study

MDV01 – Development of a Broad Spectrum Metallo-β-Lactamase Inhibitor

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AMR Undermining Modern Medicine

World Health Organization
Model List of Essential Medicines

21st List
2019

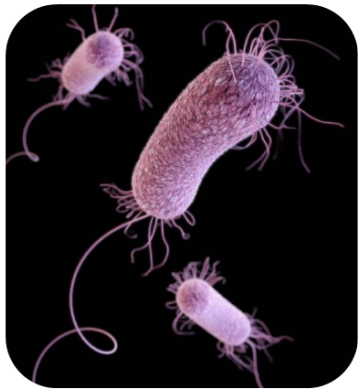
Bloomberg Businessweek

5 September 2019, 05:01 BST

Superbugs Deadlier Than Cancer Put Chemotherapy Into Question

● In India, patients and their families face a heart-wrenching choice: forgo lifesaving treatment or run the risk of a killer infection.

By Jason Gale



"Yes, your cancer will be controlled, but then you may die of infection"

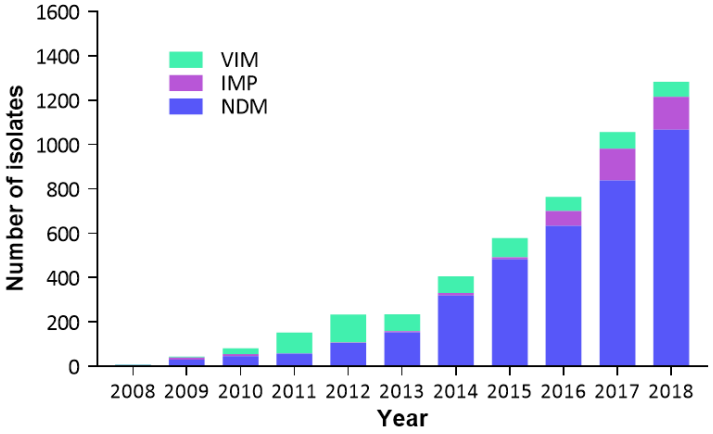
- Carbapenems are a key antibiotic on the WHO Essential Medicines List
- Antibiotics underpin all modern medicine and are essential in the immunocompromised:
  - Cancer patients
  - Surgical procedures
  - Transplant patients
- Untreatable infections on the rise
- β-lactam + β-lactamase inhibitor combinations well validated in clinic
  - β-lactams are the most commonly used antibiotics
  - β-lactamase inhibitors have preserved β-lactams since 1981 (e.g. Augmentin – amoxacillin+clavulanate)

Metallo-β-Lactamases (MBLs): A Global Threat

- Rapidly growing form of carbapenem resistance – WHO critical pathogens
- Endemic in many countries – India, China, Bangladesh
- Increasing prevalence in many western countries
- Geographical variance of MBL subtypes ie. NDM, VIM & IMP - **crucial to tackle all**

UK

Confirmed CPE isolates referred to Public Health England



ENDEMICITY & GEOGRAPHICAL VARIANCE

NDM
China
India

VIM
Greece

IMP
Japan

US

Cases of MBL-CRE reported in every state; CDC – 2017

NDM = 379
VIM = 57
IMP = 36

GLOBAL OUTBREAKS

- Italy – 350 cases NDM (2018-2019)
- Poland – 470 (2015) to 1780 cases (2016) NDM

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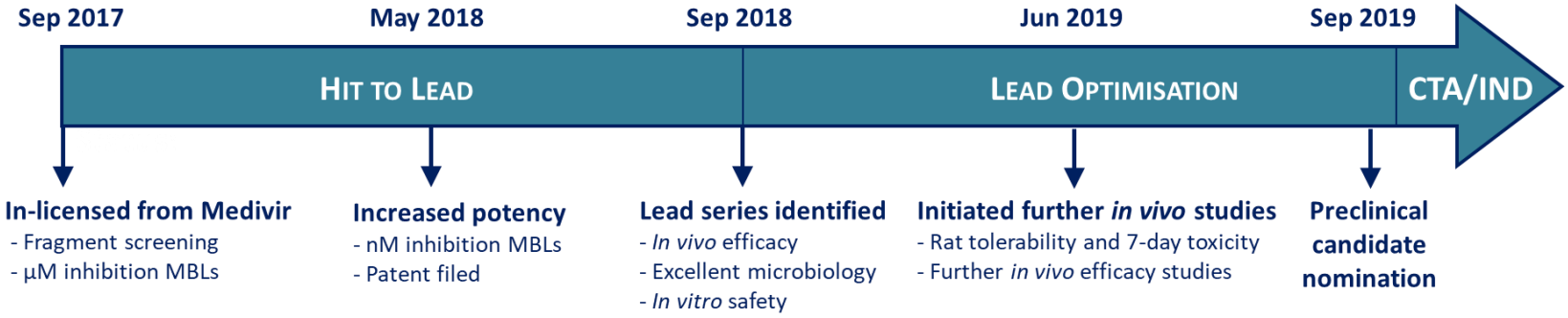
MDV01: Rapid Progression

Challenge: Metallo-β-lactamase	• Rapidly growing form of carbapenem resistance • High unmet medical need	**Endemic:** India, China, Japan, Greece **Prevalent:** Europe, UK, USA
Target:	• Prolong the utility and lifespan of carbapenems • Broad spectrum MBL inhibition **(NDM, VIM & IMP classes)** • Combination therapy versus Enterobacteriaceae • No clinical projects with this approach hit this spectrum	



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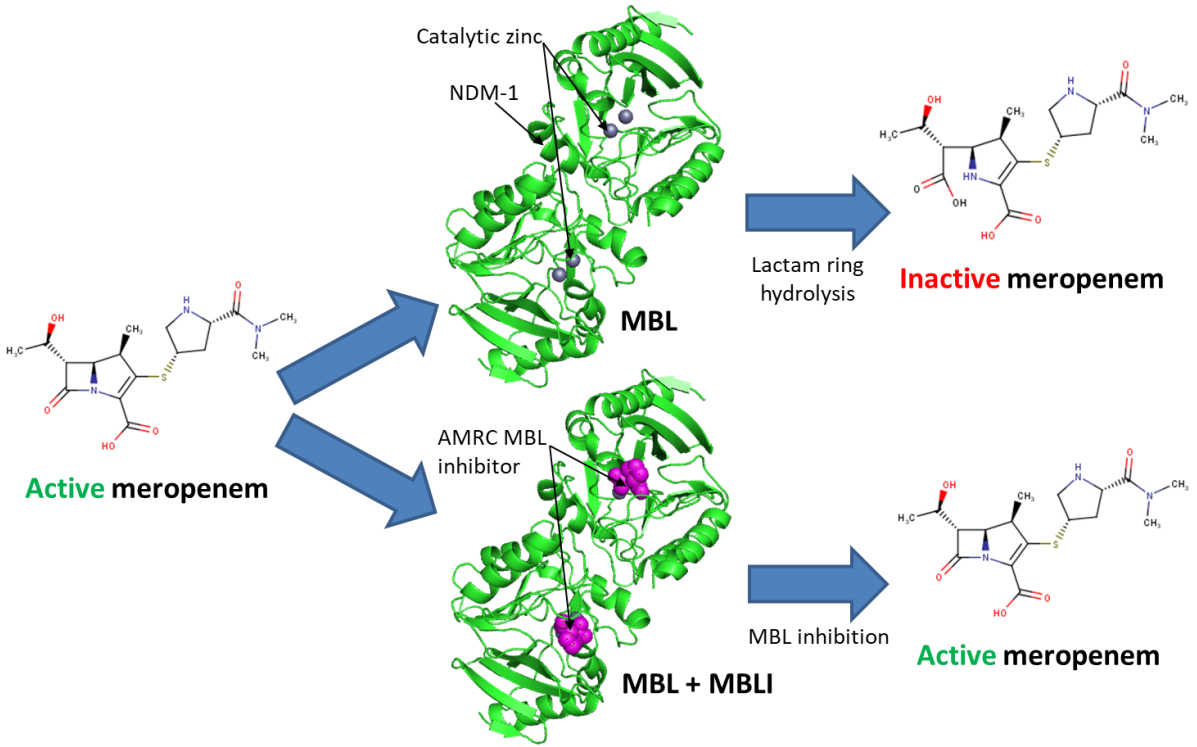
MBLs: Mechanism of Action



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MDV01: Preclinical Candidate Profile

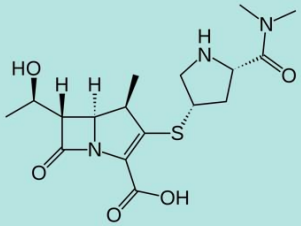
Target Product: MBL inhibitor + Meropenem for treatment of MBL-producing Enterobacteriaceae
Target Indications: Complicated urinary tract infections, lung infections, intraabdominal infection and others

Biology

- ✓ *Potent inhibition of NDM, IMP and VIM*
- ✓ *Synergistic with meropenem*
- ✓ *Efficacious in vivo*
- ✓ *Low propensity for resistance*

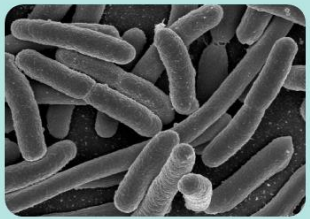
DMPK

- ✓ *Excellent in vitro and in vivo DMPK properties*
- ✓ *Supports co-dosing with Meropenem*
- ✓ *Excellent tissue distribution*



Safety

- ✓ *Excellent in vitro safety*
- ✓ *No off-target activity (MMP, Cerep, hERG)*
- ✓ *In vivo repeat-dose study*
- ✓ *Therapeutic index >50*



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Thank You

Please contact us – **info@amrcentre.com** – to find out about partnering opportunities

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