New Drugs for Anti-Microbial Resistance: **Maximising the AMR Opportunity for the UK**

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The Government's 5-year AMR strategy (2013-2018) called for a new supply of safe and effective antimicrobial drugs, and this report provides a snapshot of the current industrial AMR landscape in the UK.

SMEs are at the forefront, with 23 companies progressing 47 new drug programs to address this urgent need, and for the first time, we have pulled together the UK's pipeline of new drugs to treat AMR.

Whilst this shows exciting potential, the UK's current translational capability is under invested, and not yet adequately powered to provide a sustainable pipeline of life-saving medicines to treat AMR.

This report recommends three actions:

1 **An effective work group should be formed across SMEs, government departments, investors, philanthropy and academia to build funding initiatives across the AMR drug development pipeline, using focused government interventions to maximise private sector leverage.**

2 **The Government's next 5-year AMR strategy should acknowledge the importance of SMEs as well as the strengths and gaps in the UK's AMR drug development capability and recommend cross-departmental support for focused "PUSH" investments in AMR.**

3 **The Government should make rapid progress in implementing market "PULL" reward mechanisms for the UK, to address the broken antibiot ics reimbursement model and re-incentivising innovators and private sector finance to deliver new antibiotics for patients with life-threat ening drug-resistant infections.**

Executive Summary

If the world fails to act on antimicrobial resistance, 10 million people will die each year by 2050 at a cost to the global economy of over $100 trillion (Lord O'Neill's Review on AMR).

The case for action on AMR has been clearly made by the UK both nationally and internationally, and accepted by policymakers at the highest level, culminating in the UK's UN General Assembly resolution on AMR in October 2016.

International agencies such as the EU, WHO and BARDA (US Government) are providing £100s of millions in grants to support AMR drug development, so-called "PUSH" funding mechanisms. Global health systems, such as the NHS, are also considering the introduction of new market "PULL" incentives, to reward drug innovators in an uncertain market environment.

In the UK, the life sciences industry represents one of the dominant economic sectors, generating £64 billion of turnover, and employing more than 233,000 scientists and staff. The UK is home to some of the world's top research institutes and universities working to tackle AMR, but only a handful of global pharma companies are still active in R&D to tackle AMR, and little of their work is conducted here in the UK.

The majority of the international research effort is being undertaken by SMEs, and the UK is home to over 20 such companies striving to deliver over 40 novel AMR new drug programs. Whilst this represents a great opportunity, other early-stage programs are not transitioning effectively from academia into new biotech start-ups or existing SMEs.

The snapshot of the UK's AMR drug development landscape presented here shows exciting innovation and potential, but that our pipeline is not yet adequately powered to provide a sustainable supply of life-saving medicines for critically-ill patients.

There is widespread under investment in the UK's industrial AMR opportunity and private investors are uncertain about the market potential in AMR, but are willing to follow where governments lead. Evidence from the USA suggests that companies successful in receiving PUSH grant awards can leverage up to seven times private sector investment.

This report, co-authored by the UK's leading industrial experts in AMR, calls for coordinated action across SMEs, government, investors, philanthropy and academia to significantly increase investment in the translation of new AMR programs, providing up to £500m across the next five years in particular to target the WHO's "critical priority" superbugs.

This level of investment, supporting the UK's industrial ambition, can:

- **treble the number of companies working on AMR**
- **accelerate at least 5 new programs to achieve proof-of-concept in patients in clinical trials**
- **grow the sector's value to the UK from £440m to over £3bn by 2023.**

1 The Need for New Drugs for AMR

Drug-resistant organisms are responsible for an estimated 5,000 deaths a year in the UK and 25,000 deaths a year in Europe, with a similar number in North America, increasing year on year as resistance becomes more widespread. The situation is far worse in many other less-developed areas of the world. With some of these drug resistant infections there are few or no treatment options available.

Without new antibiotics, cancer chemotherapy and many surgical procedures, from caesarean sections and hip replacements to heart transplants, will become life threatening.

The strategic case for action on Antimicrobial Resistance (AMR) has been clearly made by the UK both nationally and internationally, and accepted by policymakers at the highest level, culminating in the UK's UN General Assembly resolution on AMR in October 2016.

1.1 UK Five-Year AMR Strategy

Spearheaded by Professor Dame Sally Davies's leadership, the "UK Five Year Antimicrobial Resistance Strategy: 2013 to 2018" specifically recognises that new therapeutic options are urgently required:

"We need to get to a point where there is a sustainable supply of new, effective antimicrobials."

The integrated strategy was developed by the Department of Health in collaboration with the Veterinary Medicines Directorate (VMD) of the Department for Environment, Food and Rural Affairs (Defra), the Northern Ireland Executive, the Scottish government, the Welsh government and the UK Public Health agencies. It also reflects significant input from other government departments including the Department for Business Innovation and Skills (BIS) and the Ministry of Defence (MOD), as well as Government Agencies including the Food Standards Agency (FSA) and the Medicines and Healthcare products Regulatory Agency (MHRA).

1.2 Review on Antimicrobial Resistance

During 2014, the Prime Minister asked Lord O'Neill to establish an independent review of the AMR threat.

The Review on AMR was supported in its work by the UK Department of Health, HM Treasury, and the Foreign and Commonwealth Office, as well as the Wellcome Trust.

The Review published a series of eight papers highlighting the broken antibiotics market model, the clear human and economic case for action on AMR, and proposed a new paradigm for the incentivisation of research and development of new antibiotics, vaccines and diagnostics, providing $2bn of new grant funding to support R&D (PUSH incentives) and proposing new market models for reward and reimbursement (PULL incentives).

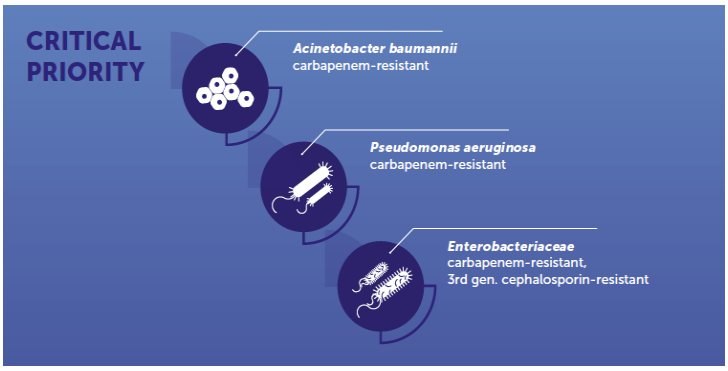
According to the Review, unless new treatment options for AMR are developed, drug resistant infections could kill over 10m people each year and wipe over $100trillion from the world economy by 2050.

2 The International Response to AMR

In response to the UN resolution and subsequent calls to action, new global initiatives have been initiated to identify the most important drug-resistant organisms, understand the gaps in the global R&D effort and to address both PUSH and PULL incentivisation.

2.1 World Health Organisation Priority List

The World Health Organisation (WHO) has published an expert ranking of priority pathogens and diseases to be addressed by international R&D efforts.



Of "critical" importance are drug resistant, so-called Gram-negative "KAPE" pathogens, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* and *Escherichia coli*, as well as tuberculosis.

Few of the drugs in clinical development tackle these particular pathogens. Much of the current pipeline is composed of analogues of existing drugs: **new classes of drug and new therapeutic targets are required.** The WHO has also urged renewed funding initiatives to address the lack of new products in the pipeline to address such "critical" priority pathogens.

2.2 DRIVE-AB Pipeline Evaluation

Funded by the EU's Innovative Medicines Initiative, the DRIVE-AB initiative's final report highlights that there are substantial gaps in the global pipeline versus the WHO priority pathogens. In some key disease areas, there are no new options in clinical trials, and the number of new projects in pre-clinical research is inadequate to generate a sustainable pipeline of new drugs to treat AMR.

DRIVE-AB called for an extra $250m per year of new global PUSH funding to incentivise participation on development of a new pipeline of antibiotics.

2.3 European Union PUSH Funding

The IMI initiative has established two grant-awarding programs, "ENABLE" to support pre-clinical projects and COMBACTE to support clinical trials.

ENABLE has a total budget of €89m from 2014 to 2020, €59m from the EU and €30m from the members of EFPIA, the pharma industry representative body in Europe. COMBACTE has total funding of €504m to 2020, with €208m from the EU and €296 from EFPIA members and other sources.

ENABLE has awarded €5.9m to 7 UK universities and research institutes to build capacity but only €0.98m to two UK SMEs (Redx and Helperby) to support their development programs.

COMBACTE is supporting a number of clinical trial programs from the UK-headquartered international pharma companies AstraZeneca/Medimmune and GlaxoSmithKline, though no SME programs have been supported to date.

The EU has an additional AMR instrument as part of the EIB's Innovfin mechanism, designed to support clinical research projects with repayable debt finance. No awards have been made to date to UK companies.

It is unclear whether UK companies will be able to access these EU-funded initiatives until the detailed provisions of BREXIT are understood.

2.4 US PUSH funding

The US government has similar clinical and pre-clinical support programs via BARDA (Biomedical Advanced R&D Authority), the principal biodefense agency for the USA.

BARDA has deployed directly $100s of millions in support of advanced clinical trials undertaken in the USA, and $62m was awarded in 2017 to the UK's Summit Pharma PLC to progress their *C. difficile* product Ridinilazole in Phase 3 clinical trials.

Support for pre-clinical R&D projects is provided via the CARB-X consortium, with $450m of funding over 5 years, including $250m from BARDA, $150m from the Wellcome Trust,

$25m from the Bill and Melinda Gates Foundation, and $25m from the UK's GAMRIF fund (DfID).

To date, 28 projects have been awarded grants, totaling up to $155m. From this, four UK programs have been funded, to a value of $6.0m in total, 4% of the CARB-X grants awarded.

2.5 WHO/DNDi PUSH Funding

The WHO has teamed up with the Swiss DNDi (Drugs for Neglected Diseases Initiative) organization to create GARDP (Global Antibiotic R&D Partnership).

With an initial budget of €56m (€51m provided by the German Government and up to £1m from the UK's GAMRIF (DfID). GARDP priorities are the development of paediatric applications, establishment of expert networks and new drugs for sexually transmitted diseases including Gonorrhoea.

There have been no GARDP awards to UK companies to date.

2.6 Novo Foundation REPAIR Fund

The Novo Foundation, a charitable foundation based in Denmark, has announced a DKK1 billion (£120m) AMR fund – the "REPAIR fund" - to provide investment into international companies focused on WHO "critical priority" targets, as convertible loans or via royalty-based structure.

The first round has been launched for European companies and a second round is planned for later in 2018 for companies in the US and Canada.

Novo has also announced the start-up of an early stage translational "accelerator" in Copenhagen, the Bio-Innovation Institute, which will have AMR as one of its themes, established with DKK500m (£60m) funding allocated over the next three years.

2.7 International PULL Funding Initiatives

With no new classes of antibiotic introduced for over 30 years, we need innovation, but new antibiotics will need to be used sparingly to guard against evolving new drug-resistant microbes. That translates to poor sales on drugs that are currently reimbursed

at low price levels due to historical generic competition. So companies with responsibilities to shareholders focus instead on drugs that do sell well, targeting therapies for conditions such as cancer or diabetes where medicines attract premium valuations or may be taken over a patient's lifetime.

At the same time, the clinical effectiveness and the relatively low cost of traditional antibiotics have combined in a perfect storm of overuse, accelerating the development of antibiotic resistance to all major classes of antibiotics.

In recognition of this broken market model, there is international recognition that market "PULL" incentives need to be introduced to reward new drug developers that might never otherwise be able to recoup their investment from regular sales.

In the USA, the Re-Valuing Antimicrobial Products (REVAMP) Act of 2018 is progressing through Congress. If this law is passed, a company with a new antibiotic that addresses a priority medical need could receive a certificate for up to 12 months additional market exclusivity. It can transfer or sell this to another company to use on any other high-value drug: potentially worth billions of dollars to recoup their R&D investment in antimicrobial development.

Lord Jim O'Neill, who led the UK government's influential review on AMR, has called for a new international taxes on overall drug sales - citing the industry's continued inactivity and dependence of the whole sector on effective antibiotics as a justification for introducing a levy on sales of other drugs to fund AMR market "PULL" rewards worth up to $1.2bn.

In the UK, NICE and the Department of Health have commissioned research on new models to value antibiotics, and are now considering the introduction of a pilot scheme for PULL incentives in the NHS.

Whilst the focus of this report is to support UK SMEs with PUSH incentives and leveraged private capital, the timely introduction of PULL incentives in the UK and around the world is also critical to re-invigorate the antibiotics market and provide adequate incentivisation for pharma companies to bring life-saving AMR medicines to the market.

3 UK PUSH Incentives

The UK has a number of specific vehicles to support the development of new biomedical products and technologies, including for AMR.

3.1 Biomedical Catalyst

Since 2012, the Innovate UK/MRC biomedical catalyst (BMC) has awarded over £250m to over 300 projects across the UK.

According to data provided by Innovate UK, 28 AMR programs have been supported to date with a total grant value of £21.3m over the past 6 years, covering diagnostics, therapeutics and vaccines across all microbial infections.

Innovate UK support for UK projects targeting WHO G- critical pathogens							
Grant support £m		2012-13	2013-14	2014-15	2015-16	2016-17	2017-18
Discuva	Cambridge	1.62				1.05	
Blueberry	Cheshire	0.15					
Cantab	Cambridge	2.32				0.8	
Phico	Welwyn		0.97				
Bactevo	Cambridge					1.05	
	Total	4.09	0.97	0.00	0.00	2.90	0.00

For the WHO "critical priority" pathogens, the BMC has supported five programs over six years (two programs have received two awards each) with a total of £8.0m granted, £3.7m for new discovery platforms and £4.3m into pre-clinical development of new AMR therapeutics.

3.2 Innovate UK AMR Capital Grants

In December 2016, IUK ran a competition on behalf of the Department of Health to distribute £4m in small capital awards to build capacity in AMR R&D. The recipients have not been announced yet, but are understood to be a number of public bodies, universities and private companies.

3.3 Global AMR Innovation Fund, GAMRIF

Announced in 2017, GAMRIF is a £50m initiative across DFID and DH to support innovation in AMR.

The first GAMRIF project announced is a £10m UK/China initiative to encourage collaborative R&D between UK SMEs, UK academia and Chinese partners, with a further £10m pledged by the Chinese Government in matched funding. This covers a wide range of AMR activities, including traditional Chinese medicine and veterinary applications, and includes the development of novel therapeutics and diagnostics. UK companies can apply to receive up to £750k per program, with successful applicants awarded in 2019.

In May 2018, in addition to the £1m already pledged to GARDP, GAMRIF announced an award of £20m to the US-based CARB-X initiative, to support new therapeutics targeting WHO "critical priority" pathogens with a particular emphasis on treatments to be made available for patients in less developed countries.

GAMRIF has also invested £5m in FIND, an international effort on diagnostics for poverty-related diseases, and £10m into veterinary collaborations in Canada and Argentina.

3.4

The MRC has also put funding directly into AMR research, however further funding is required to address translation from academic drug discovery into early pre-clinical development. The recent MRC call for collaboration with China excluded "proposals focused solely on developing or evaluating new targets, therapeutics, diagnostics or interventions to control or treat infections," and the MRC decided not to participate in a recent EU Joint Program Initiative on AMR (JPIAMR) call on new targets.

4 The UK Industrial AMR Landscape

The UK industrial AMR therapeutics landscape comprises two major pharma companies, 23 SMEs, the AMR Centre, the Medicines Discovery Catapult, mid-size pharma company and contract research organisation Evotec, a number of academic-based industrial 'accelerators' and major charities such as the Wellcome Trust and LifeArc.

4.1 Pharma Companies

GlaxoSmithKline is the UK's only major pharma company with antibiotic products on the market, generating approximately $800m per year revenues. GSK's R&D activities are based in the USA, and the company has two new small-molecule products in clinical development for TB and Gonorrhoea.

AstraZeneca has sold its commercial antibiotics business to Pfizer in 2017 and has additionally spun-off its small-molecule infection R&D activities into a new US-based company Entasis Therapeutics. AZ's biopharma division Medimmune has two antibody therapeutics against Gram-negative *P.aeruginosa* and Gram-positive MRSA in clinical development, resulting from its US-based R&D facilities in Maryland.

4.2 SMEs

The UK has 23 innovative SMEs working on 47 projects on new therapeutics and vaccines to address AMR.

16 of these programs are targeting WHO "critical priority" Gram-negative pathogens, 16 are focused on Gram-positive pathogens, such as MRSA and *C. difficile*, and a further 15 are early stage with the potential to treat both types of pathogen.

As shown in section 5, the UK SME AMR pipeline has the potential to make a global contribution but is significantly under invested.

According to Companies House financial records, SMEs have a total of £47.2m cash reserves on their balance sheets, with one company having over £28m of this. Eleven companies have significantly less than £1m in cash, and most companies report having less than 12 months of cash available to support programs.

All reporting companies stated that existing programs have been delayed and new projects not started due to the lack of funding.

Importantly, companies report that in some cases they do not have sufficient cash reserves to meet matched funding commitments, preventing or delaying successful applications for international PUSH funding mechanisms.

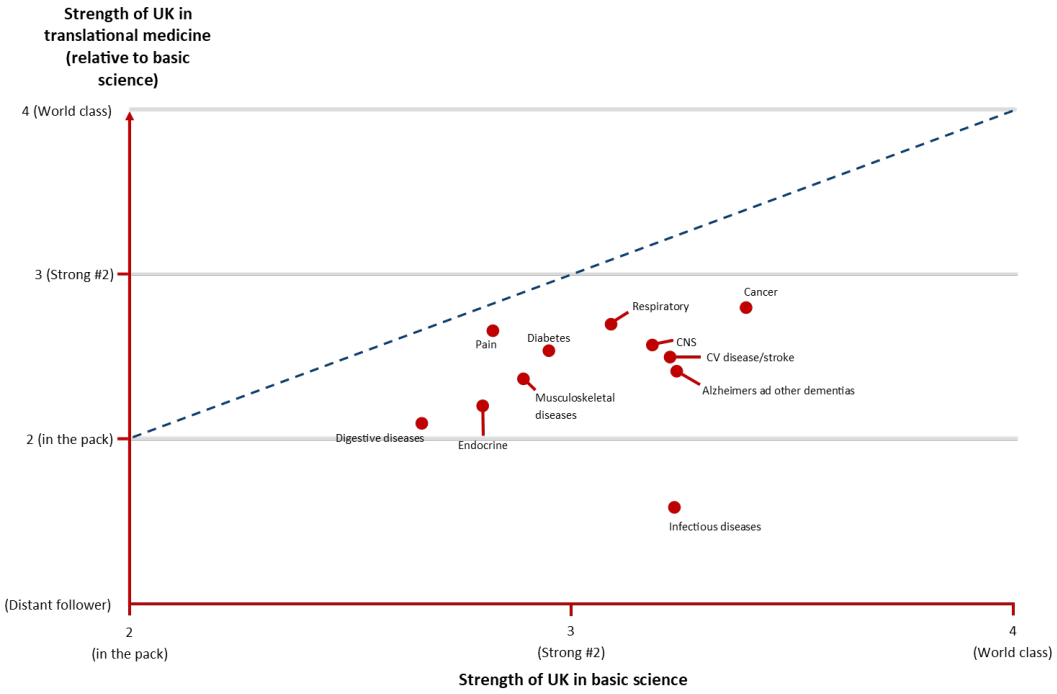
Companies also report the availability of skilled and experienced staff is an issue, particularly in microbiology.

It is reported that there are now fewer than 150 AMR researchers in total across all UK SMEs.

4.3 Medicines Discovery Catapult

The MDC, based at Alderley Park, is an Innovate UK-funded catapult centre, focused on developing networks and new technologies to facilitate R&D on new treatments and diagnostics with applications across all therapeutic categories.

The MDC has recognised AMR as a key area for technological development, and has further highlighted that the UK has a general weakness in infectious disease translational R&D.



Ranked on 1 to 5 scale of: 1 = Distant follower 2 = In the pack 3 = Strong #2 4 = World class 5 = Best in world

In January, a MDC joint academic/industry workshop on AMR identified further priority areas for MDC investment, and indicated that some key academic capabilities were under-resourced, for example Prof William Hope's expert DMPK facility at the University of Liverpool has less than 12 months' funding visibility.

4.4 AMR Centre

The AMR Centre (AMRC), based at Alderley Park, is an AMR-focused translational company, in-licensing programs and partnering with SMEs to provide operational support and funding to co-develop new therapeutics targeting WHO “critical” propriety pathogens. AMRC has received both private and regional public funding and has recruited over 25 staff to date expert in development of antibiotics, to build additional industrial R&D capability for AMR.

Since operational launch in August 2017, AMRC has supported three SME programs, one from the UK and two international (USA and Sweden), with two of these also leveraging CARB-X funding, and has a pipeline of UK and international projects to take forward.

4.5 Evotec UK

Evotec is a German-headquartered international life sciences company, building its own portfolio of developmental drugs as well as providing comprehensive pre-clinical R&D services to industry.

Evotec UK has a specialist 30-strong microbiology group based at Alderley Park, and additional 30 staff in its wider network supporting international AMR projects here in the UK.

Evotec has recently completed a partnership deal with major pharma company Sanofi to acquire 100 staff in France and co-develop a pipeline of infectious disease products. It is expected that this development will drive additional AMR activity into Evotec’s UK facilities.

4.6 The Wellcome Trust

The Wellcome Trust is a multi-£billion independent global research charity, with substantial investments in the development of new therapeutics. Wellcome is a major provider of funding to the US-based CARB-X initiative, having pledged $150m over a five year period. In addition, Wellcome has international initiatives in diagnostics, surveillance, access and stewardship under its global drug resistant infection strategy.

4.7 LifeArc

LifeArc is a UK based lifescience charity who undertake research at their own risk within their laboratories in Stevenage. LifeArc are actively working with the Defence Science and Technology Laboratory (dstl) and a group in Canada, The Centre for Drug Research and Development (CDRD), to identify novel, essential and druggable targets from the genomes of ESKAPE and related pathogens. They expect this work to readout in the first half of 2018 after which a number of collaborative target based projects will be initiated based on the findings.

4.8 Early Stage Accelerators

Academic research into AMR has been supported via cross-council funding initiatives and collaborative funding such as the EU’s JPIAMR program. This has led to the identification of new biology in bacteria. However, there is very little funding to see if this new biology can be translated into drug discovery projects and, frustratingly, there are a large number of potential projects stalled due to the lack of public and private funding for translation into pre-clinical development and the creation of new SMEs.

Translational expertise in AMR is available within academic centres, and new initiatives have been established or are in the pipeline.

Liverpool University and Liverpool School of Tropical Medicine are collaborating to create a centre of excellence in infectious disease research (CEIDR). Its primary aim is the development of therapeutic agents and implementation of other strategies to minimise the impact of resistance on human health, with well-established relationships with industrial partners and international bodies such as the WHO.

Dundee University already has an operational drug discovery translational capability in its Drug Discovery Unit, and is planning a new Antibacterial Drug Development Accelerator (ADDA) to provide translational services from targets to leads, if suitable funding can be secured.

At the moment, these important new initiatives are underfunded, leaving a substantial gap in early translation of AMR projects from academia to SMEs.

4.9 AMR Investors

Most investment into UK AMR companies has come from regional development funds with non-specific focus, in particular to support business creation and location at former pharma sites at Sandwich in Kent, Stevenage in Hertfordshire and Alderley Park in Cheshire.

SMEs have also taken advantage of early stage tax relief investment incentives SEIS and EIS to bring in capital from angel networks and high net worth individuals. The Government's R&D tax credit schemes are also a valuable contribution to early stage company cashflows.

A small number of companies have successfully floated on the AIM market and have raised funds to support the development of clinical-stage assets.

Whilst there is new evidence of private investors returning to the AMR sector in the USA, private investors and in particular specialist healthcare funds are largely absent in the funding of AMR companies in the UK. This is primarily driven by the significant uncertainties around the future reimbursement and reward for new antibiotics, given the broken market model described by Lord O'Neill's AMR Review. The VC attitude to AMR is generally "we understand the need but how can we value an asset?"

4.10 AMR Charities

Alongside Wellcome and LifeArc, a number of smaller charities have been formed to highlight the issue of AMR and support patients, for example MRSA Action. However, the AMR charitable sector is small compared to other therapeutic areas. There is one dedicated AMR research charity, Antibiotic Research UK (ANTRUK), which has raised £100's of thousands of pounds to support development of new therapies to treat AMR. In 2017, ANTRUK initiated a research program to discover new antibiotic resistance breakers. By comparison, Cancer Research UK invested £432m in research funding in 2017.

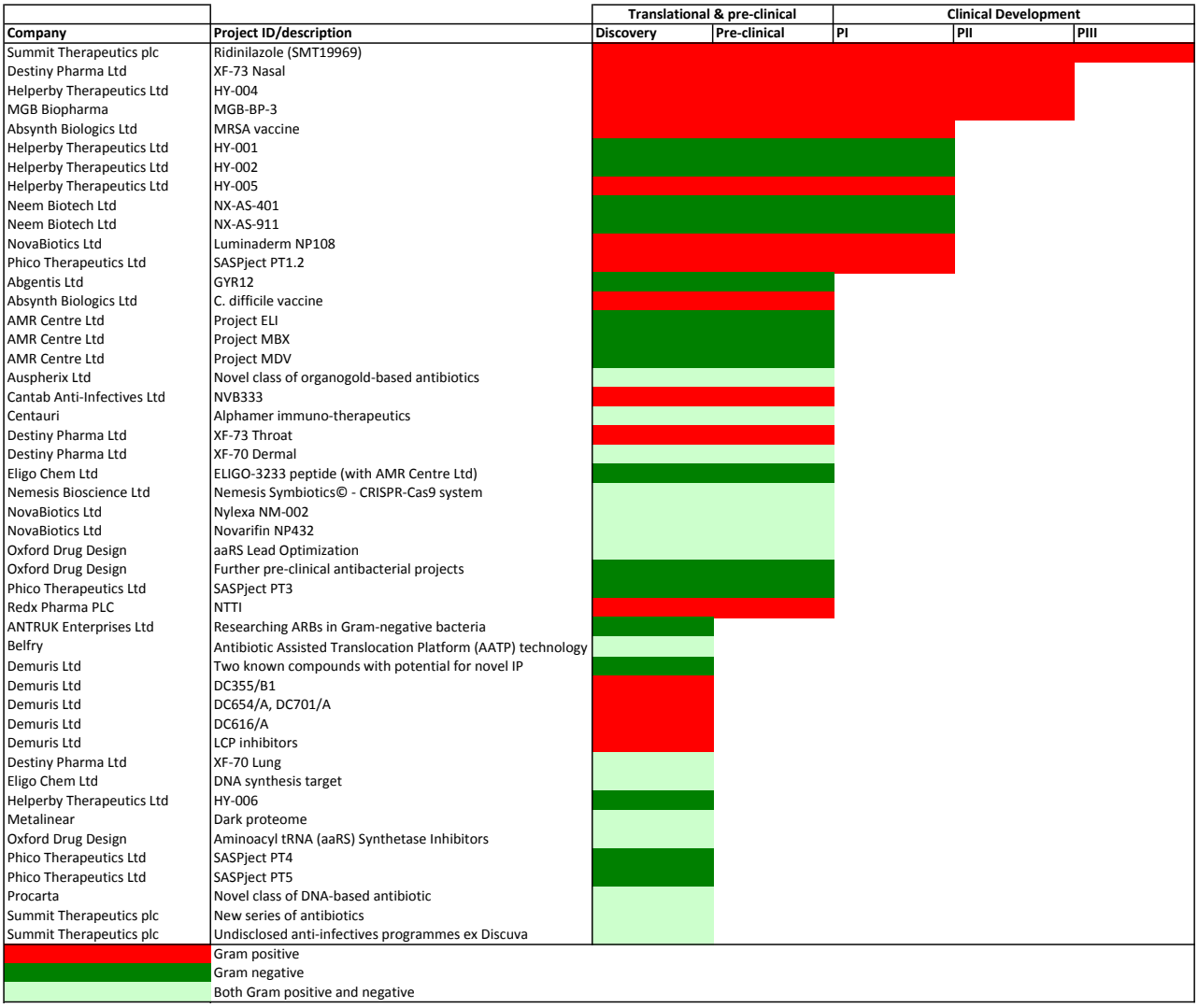
ANTRUK is seeking to bring together UK medical research charities who are impacted by AMR, such as Cancer Research UK, Cystic Fibrosis Trust, Bloodwise and Bowel Cancer UK. The aim is to establish a collaborative effort by the Third Sector which is uniquely placed through their patient facing activities to make an impact. ANTRUK wishes to see a new UK precompetitive £100 million fund created, the "Antibiotic Discovery Fund" with finance from charities, Government, pharma and social philanthropists.

5 Snapshot of the UK AMR Drug Pipeline

For the first time we have assembled a snapshot of the UK's AMR pipeline of new therapeutics, based on public domain information.

There are 47 programs in pre-clinical and clinical development, targeting both Gram-positive and Gram-negative pathogens and encompassing a wide variety of technological approaches to AMR.

Unsurprisingly, programs targeting Gram-positive organisms such as MRSA and *C. difficile* are more advanced given the strategic priority to address these infections in the NHS over the past 10 years.



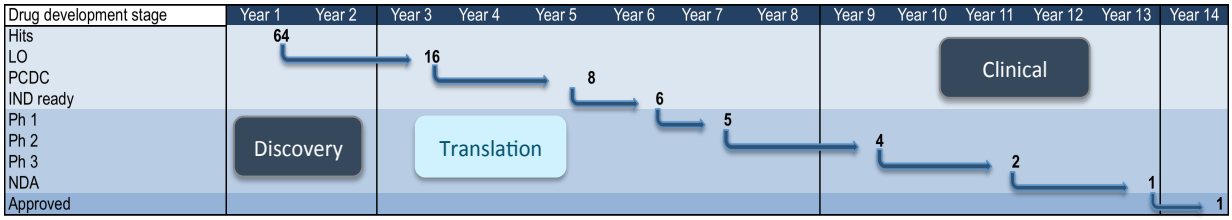
The UK pipeline has multiple products in clinical trials with the potential to deliver at least one of these new therapeutic for Gram-positive infections, but is significantly under powered to deliver a new Gram-negative drug against the WHO "critical priority" targets.

Additionally, the early stage pipeline is weak, reflecting the log-jam of new projects waiting to transition from academia to discovery and pre-clinical development.

6 Analysis of the UK AMR Pipeline Gaps and Opportunities

6.1 AMR Drug Development Costs, Risks and Timescales

Based on data published by groups expert in the development of new antibiotics, it is estimated that it costs in excess of $130m to develop a new antibiotic product, over a period of at least 14 years from discovery to approval for use in patients.



Cost per drug per stage US$m	4	4	5	1	10	25	80	1	130
Total cost per stage US$m	256	64	40	6	50	100	160	1	677

Due to the high technical risks associated with drug development, to prove that a new product is both safe and effective, it is also estimated that at least 64 discovery programs are required to achieve five programs entering clinical trials, with only one of these making it through the clinical pipeline to be approved for use commercially in patients.

Due to this attrition, when the cost of all the failures is added, the actual investment required to deliver one new antibiotic is in excess of $600m.

6.2 Funding requirement for the UK AMR Pipeline

We have used the above profile to evaluate the UK's AMR pipeline and estimate the likely funding requirement for the next 5 years, to progress the existing programs to their next major developmental milestones.

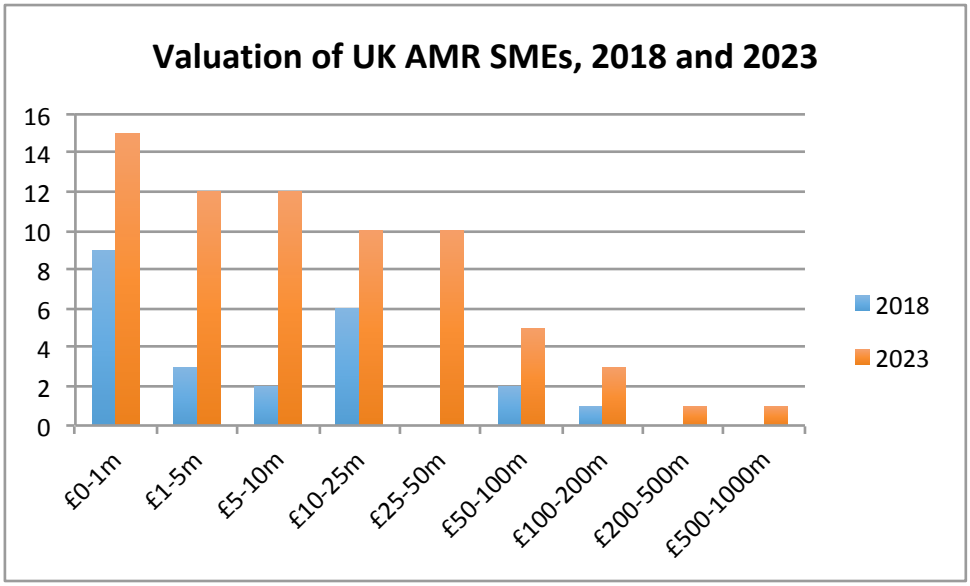
Taking into account the projected attrition rates and costs to develop new drugs, it is estimated that at least £200m will be required to progress the current UK pipeline over the next five years, substantially more than the £47m that companies currently have at their disposal on their balance sheets.

Furthermore, to capitalise on our underpinning scientific strengths and deliver an expanded UK pipeline, potentially trebling the number of SMEs and pre-clinical projects, delivering 5 new clinical assets and at least one new Gram-negative drug for patients, would require investment of over £500m from 2019 to 2023.

6.3 Opportunity for Industrial Value Growth in AMR

According to records at Companies House, the UK's 23 AMR SMEs have a total market capitalisation of £440.3 million.

As shown in the graph below, there are currently three companies with valuations above £50 million: each of these has drug programs in clinical development.



It is also clear that there is considerable scope for building value in the existing SME base, by supporting their organisational growth through increased equity support and providing grant funding to translate programs through the development pipeline, as well as creating more 'new entrants' by translating stalled opportunities from academia into new SMEs.

We believe that there is the opportunity in the UK to invest in the current pipeline and capitalise on academic strengths to create new spin-out companies, and treble the number of SMEs focused on AMR.

By doing this, we believe that the UK can grow a combined market valuation from £440m today to over £3 billion by 2023.

7 The Industrial AMR Funding Requirement

As indicated in the O'Neill Report, we believe that Government investment into the AMR opportunity will be the key to unlock private finance and enable increased access to international PUSH incentives, to build value for the UK.

We believe that this can be achieved by appropriate focus of existing funding streams for example by allocating grant funding to AMR Accelerators and into individual new drug programs from Industrial Strategy and UKR&I funding, and by supporting the creation of dedicated AMR investment funds backed by patient capital.

We anticipate that significant private capital could be leveraged by companies receiving PUSH funding from the government. To date, the mostly US companies that have received CARB-X grant funding of $155m have collectively raised over $1.1bn in equity, private sector leverage of seven times the public sector investment.

7.1 Investment in Capacity and Programs

Investment of £50m into a small number of early-stage specialist centres, for example CEIDR (Liverpool) and ADDA (Dundee), would enable up to 50 new academic technologies to be fast-tracked into pre-clinical development.

A further £100m investment into preclinical-to-clinical translation, for example at CEIDR and the AMR Centre, could support at least 10 new programs to be 'clinic ready' and bring new programs from overseas to the UK.

7.2 Equity Investment into SMEs

£30m of seed funding would enable the creation of up to 30 new AMR SMEs in the next five years.

£150m of growth funding would support up to 20 SMEs to scale-up and plan for clinical trials.

£200m of clinical investment funding would support up to 10 clinical programs with the aim of bringing at least five of these to achieve proof of concept in patients in Phase 2 clinical trials.

7.3 Funding Summary

In summary, a total investment of £500m would support the development of the UK's current AMR programs to build an expanded, sustainable AMR pipeline and support the growth of the vital SMEs at the forefront in the fight against AMR.

We believe that with this level of investment in place, combined with the UK's industrial ambition, we can treble the number of companies working on AMR, accelerate at least 5 new programs to achieve proof-of-concept in clinical trials and grow the sector's value to over £3bn by 2023.

8 Recommendations

This report makes three recommendations to maximise the AMR opportunity for the UK.

8.1 An Effective Work Group for All the Stakeholders

We need an effective mechanism for SMEs, government departments, investors, philanthropy and academia to come together in a working group to identify opportunities to build funding initiatives across the AMR drug development pipeline, using focused government interventions to maximising private sector leverage.

8.2 Support for AMR Therapeutics in the Next 5-year AMR Strategy

The Government's new 5-year AMR strategy should acknowledge the importance of SMEs as well as the strengths and gaps in the UK's AMR drug development capability and recommend cross-departmental support for dedicated investments into academia, R&D centres, SMEs and individual drug development programs.

8.3 Progress on PULL Incentives

In parallel to accelerating the AMR drug pipeline, the Government should make rapid progress in implementing market "PULL" reward mechanisms for the UK, to address the broken antibiotics reimbursement model and re-incentivising innovators and private sector finance to deliver new antibiotics for patients with significant unmet need.

Consultee organisations

Antibiotic Research UK
BioIndustries Association
Association of the British Pharmaceutical Industry
LifeArc
The AMR Centre
Medicines Discovery Catapult
Northern Health Sciences Alliance
OneNucleus
BioNow
OBN
AstraZeneca
GlaxoSmithKline
Evotec (UK)
Abgentis
Absynth biologics
Auspherix
Belfry Therapeutics
Blueberry Therapeutics
Cantab Therapeutics
Centauri Therapeutics
Demuris
Destiny Pharma
Eligochem
Helperby Therapeutics
Metalinear
MGB Biopharma
Neem Biotechnology
Nemesis Bioscience
Novabiotics
Oxford Drug Design
Phico Therapeutics
Procarta Biosystems
Redx Pharma
Summit Therapeutics
Liverpool University /Liverpool School of Tropical Medicine Centre of Excellence in Infectious Diseases Research (CEIDR)
University of Dundee Drug Discovery Unit

AMRCentre.com
Bionow.co.uk
LifeArc.org
OneNucleus.com