



ANTIMICROBIAL RESISTANCE EXPLAINED

**A summarised guide  
to antimicrobial resistance**



2019

## Foreword

The 21st century is proving to be one of the most exciting and prolific periods of innovation in biosciences and healthcare, and UK bioscience companies are at the forefront of this innovation.

These companies are a key part of the UK Bioindustry Association (BIA)'s membership, and we provide a home for them through our Advisory Committees and working groups on antimicrobial resistance, cell and gene therapy, engineering biology and genomics.

We are delighted to publish this short summary of **A guide to antimicrobial resistance and how UK excellence is helping tackle this global challenge** as an accompaniment to our Explainer series, within which we describe what these four strategic technologies are all about, and showcase the important contributions being made by some of the UK bioscience firms who make up our dynamic and innovative membership. You can access the full versions of these Explainer documents on our website, or get in touch with us if you would like some hard copies.

We hope you enjoy reading them.



**Steve Bates OBE CEO,**  
**UK Bioindustry Association**

## What is antimicrobial resistance?

Antibiotics are a triumph of modern medicine, but the success of penicillin and many other antibiotics developed since has created an entirely new healthcare challenge, that of antimicrobial resistance (AMR). Some harmful bacteria have evolved to resist the effects of antibiotics. Bacteria reproduce and evolve rapidly and can share helpful DNA easily among each other, not just with their offspring, fostering the spread of this resistance. Genes that encode antibiotic resistance are passed around far and fast. The surge of AMR means routine surgical procedures, like appendectomies or caesarian sections, may become life-threatening. Over 700,000 people are estimated to die each year due to drug-resistant infections such as methicillin-resistant *Staphylococcus aureus* (MRSA). These so-called 'superbugs' are responsible for increasing outbreaks of hospital-acquired infections.

Without new, effective medicines, the annual death toll from resistant bugs could reach over 10 million by 2050, according to some estimates. As first-line antibiotics lose their efficacy, physicians are forced to select from a dwindling range of more expensive, and often more toxic antibiotics. The result: longer recovery times, reduced quality-of-life, and higher costs and risks. Many large drug companies have cut or discontinued antimicrobial drug R&D due to diminishing returns and the number and novelty of antibiotics approved over the past 30 years has fallen sharply.

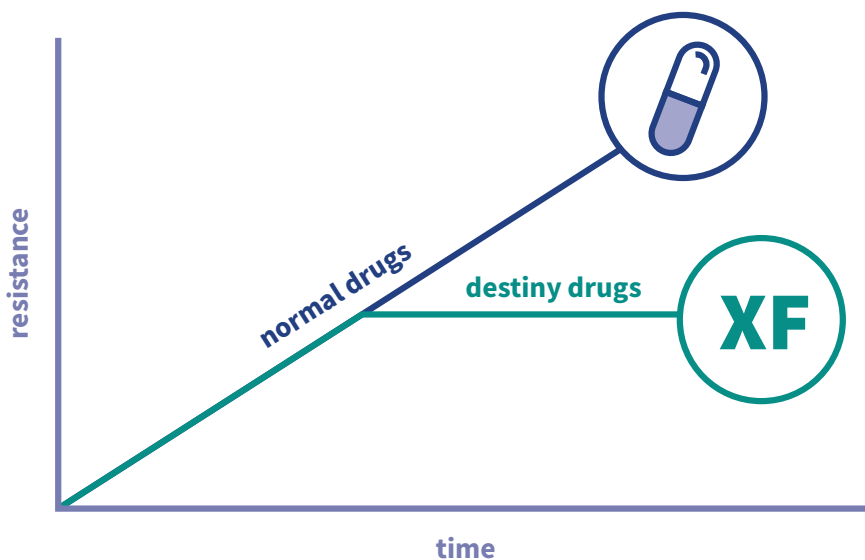
# Destiny pharma

Destiny Pharma's drug candidates attach to and kill harmful bacteria in a different way to existing antibiotics, generating no resistance to date. The Sussex-based company has developed anti-bacterial drug candidates that work very differently to existing antibiotics. Destiny Pharma's lead compound, exeporfinium chloride, (codenamed XF-73), is a molecule that binds rapidly to the bacteria's outer membrane and makes it leaky, causing the loss of compounds critical to the superbug's survival. XF-73 is administered as an intra-nasal gel.

It has already been shown to be safe and effective in reducing nasal bacteria that cause post-surgical infections in studies involving over 200 subjects. XF-73 has been granted Qualified

Infectious Disease Product (QIDP) status by the US regulatory authorities (FDA) expediting approval and increasing the duration of market exclusivity. Destiny Pharma's technology has already attracted a range of international investors and partners. Early research was part-funded by the European Union and the opening US clinical trial by the US National Institutes of Health.

In December 2017, Destiny secured a collaboration with China Medical Systems Holdings (CMS) for XF-73 in China and certain other Asian countries. Hong Kong-listed CMS also invested £3 million in the group, supplementing the £15 million Destiny raised at its September 2017 IPO on the London Alternative Investment Market (AIM).



## Neem biotech

Neem Biotech's anti-bacterial candidates disrupt biofilms – slimy layers of bacteria associated with some of the most stubborn infections, including those found in the respiratory tract and in wounds. Bacteria in biofilms, typically stuck to a surface like skin or airways, are less sensitive to antibiotics than their free-floating counterparts.

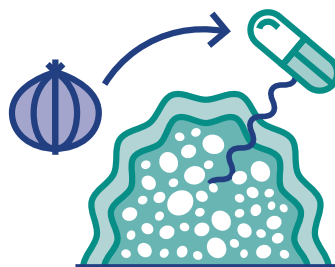
Neem's candidates interfere with the bacterial communication channels necessary to organise and build biofilms, slowing their formation and destroying them. Neem's novel approach has its roots in garlic, long known for its healing properties. Academics at the Technical University of Denmark (DTU) identified the sulphur-based compound ajoene, derived from garlic, as responsible for disrupting bacterial communication. Neem have designed synthetic, well-characterised variants of ajoene which are more stable and easier to make, with the aim of treating chronic or hard-to-heal wounds and in chronic lung infections, such as those associated with cystic fibrosis. The topically-administered candidate NX-AS-911 has been shown in the laboratory to prevent biofilm formation among *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria. Pre-clinical program NX-AS-401 is an inhaled formulation of another ajoene-inspired active ingredient. It is designed to treat chronic lung infections caused by *Pseudomonas* and *Staphylococcus* bacteria in patients with cystic fibrosis.

## Novabiotics

Aberdeen-based NovaBiotics is using some of the body's own infection fighting mechanisms as the basis for entirely novel antimicrobial medicines. The company hopes to address many of the most challenging, drug-resistant bacterial and fungal infections. With their lead compound, Lynovex, they are looking to target infections in patients with cystic fibrosis (CF).

CF is an inherited condition that causes sticky mucus to build-up in the airways and other areas, leading to recurring infection. The intensive, long-term antibiotic therapy that many CF patients need leads to high levels of resistance to the most common medicines. Lynovex is a formulation of a naturally-occurring aminothiols called cysteamine.

Cysteamine is involved in several important human cellular activities. It also cripples bacteria by switching off their ability to produce energy, disabling them. "We're boosting one aspect of what's already there in nature," sums up NovaBiotics CEO, Scientific Officer and Founder Deborah O'Neil. NovaBiotics has raised over £20 million in private investment.



# Summit Therapeutics

University of Oxford spin-out Summit Therapeutics is developing a pipeline of new antibiotics to counter the serious healthcare threat from bacterial infections. Summit is currently advancing novel antibiotics against infections caused by *Clostridium difficile* and gonorrhoea.

*Clostridium difficile* infections (CDI), which affect the colon, are often stubborn and recurrent, presenting an increasing burden on patients and healthcare systems worldwide. Summit's lead candidate, ridinilazole, has been shown in clinical trials to attack pathogenic *C. difficile* strains in a highly selective fashion. "Our strategy [with ridinilazole] is to reduce collateral damage to other gut bacteria, by building a targeted antibiotic", sums up David Powell, SVP research. "A good gut microbiome is all about diversity." Reflecting the global need for new *C. difficile* antibiotics, ridinilazole's discovery

and early development attracted funding from the UK's Wellcome Trust, while the US Biomedical Advanced Research and Development Authority (BARDA) is supporting later-stage trials. Ridinilazole has Qualified Infectious Disease Product (QIDP) status in the US, opening a faster route to approval. The company's Discuva Platform combines high-density mutagenesis with next generation sequencing capabilities to identify new drug targets and design compounds that are less likely to induce bacterial resistance.

The Discuva Platform has generated a targeted compound that kills the bug responsible for gonorrhoea, a sexually-transmitted infection designated 'urgent' by the US Centers of Disease Control and Prevention. Summit is listed on London's AIM Market and on the US NASDAQ, and has offices in Oxford, Cambridge, UK and Cambridge, MA.





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[www.bioindustry.org/policy/strategic-technologies.html](http://www.bioindustry.org/policy/strategic-technologies.html)

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