

Helperby Therapeutics Group Ltd.

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HELPERBY

Breaking resistance one antibiotic at a time

Helperby's antibiotic-resistance breakers are a powerful tool serving to prolong and boost antibiotic efficacy and should help counter the growing global crisis of antibiotic resistance.

Bacteria have been around for more than three billion years. During this time they have evolved sophisticated defense mechanisms against fellow bacteria, including the ability to produce compounds that kill other bacteria (so-called antibiotics) and ways to fend off other bacteria's attacks (so-called antibiotic-resistance mechanisms).

About 70 years ago, scientists started harnessing antibiotics for human use against infectious diseases and rapidly amassed an armamentarium consisting of 20 different compound classes and over 200 subclasses capable of keeping a broad spectrum of bacteria at bay. However, the initial burst of antibiotic discovery soon fizzled out, and in the past 40 years only two new classes of antibiotics have been commercialized.

During this period of antibiotic use, however, bacteria have been given an opportunity to evolve new defenses; widespread global use of antibiotics by millions of individuals and physicians has therefore propagated many new antibiotic-resistance mechanisms.

As a result, bacteria now have accumulated multiple-drug-resistance (MDR) mechanisms, meaning that the existing antibiotics are no longer sufficient to control a number of infections, creating a global health crisis. Given that modern medicine is largely built on the availability of powerful antibiotics to thwart infection following surgery, transplantation and cancer treatments, this state of affairs does not bode well for the future.

According to a review on antimicrobial resistance¹ commissioned by the UK government in 2014, if resistance continues to increase at the current rate, by 2050 it could lead to a rise in the number of those who die each year from 700,000 per year worldwide now to 10 million, a reduction of 2%–3.5% in the

gross domestic product and a global cost of up to \$100 trillion.

Multiple solutions have been implemented, including tighter management of antibiotic use both by humans and in livestock and the introduction of economic and regulatory incentives to expedite the development of novel antibiotics. But given that the current antibiotic pipeline is woefully inadequate to meet the necessity for the large numbers of new antibiotic molecules needed by 2050 to counter the rampant antibiotic-resistance crisis, new strategies have to be developed.

As the UK government report¹ points out, "There could be profound health and macroeconomic consequences for the world, especially in emerging economies, if antimicrobial resistance (AMR) is not tackled."

The Helperby solution

Against this backdrop, London-based Helperby Therapeutics has developed a new tool to help avert this crisis, antibiotic-resistance breakers (ARBs). ARBs are small molecules identified using a proprietary approach to screen for antibiotic efficacy-boosting properties. ARBs rejuvenate existing antibiotics that might have lost their efficacy against certain resistant bacteria by interfering with the cells' MDR mechanisms. The advantages of this approach, besides the extension of the effective lifetime of an antibiotic, are the reduction of toxicity (as lower doses of the antibiotic can be used), acceleration of the antibiotic's activity and avoidance of resistance emergence.

Helperby has a number of ARBs in development, many of which have the capacity to rejuvenate at least one antibiotic class (Fig. 1). ARBs, when used in combination with old antibiotics, can target both systemic and topical bacterial and fungal infections.

Because of the versatility of ARBs, Helperby is involved in studies to expedite their introduction for use against an array of diseases around the world. Lead compound HT61, a topical ARB, is in phase 2 testing for treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) in the United Kingdom. Another ARB entered phase 1 studies in 2016 for carbapenem-resistant *Escherichia coli* (CRE) in complicated urinary tract infections. Three other ARB combinations are in preclinical testing for other infections. Helperby also has one ARB that recently completed human testing for Gram-negative anaerobic bacteria in the mouth associated with halitosis. This program is partnered with Cadila Pharmaceuticals and is slated for further partnering in Europe and elsewhere in 2016.

The Helperby opportunity

The antibiotic market is currently valued at approximately \$44 billion and is expected to increase in value by approximately fivefold with the advent of much needed new solutions to the ever-growing MDR problem.

Rejuvenated antibiotics such as the ones enabled by Helperby's ARBs are highly valued. One needs to look no further than Merck's acquisition of Cubist for \$9.5 billion, which was largely driven by Cubicin (daptomycin) and other improved versions of older or existing antibiotic classes that target resistant bacteria through, for example, the addition of a β -lactamase inhibitor to an existing cephalosporin.

Helperby's global strategy is two-pronged: the company intends to grow opportunities by balancing the development of new solutions for high-margin product opportunities in developed countries while also creating affordable options for developing countries. The company already has active programs in Asia and North America, and it is looking to expand into other territories.

According to Anthony Coates, CSO at Helperby Therapeutics, "The main partnership goal of Helperby Therapeutics is to develop the company's pipeline of ARBs in combination with old or existing antibiotics in developed high-margin countries, and in developing countries as affordable medicines."

1. Review on Antimicrobial Resistance. *Antimicrobial Resistance: Tackling a Crisis for the Health and Wealth of Nations* http://amr-review.org/sites/default/files/RARJ2810_Review_Launch_Paper_09.12.14_WEB_OUTLINED.pdf

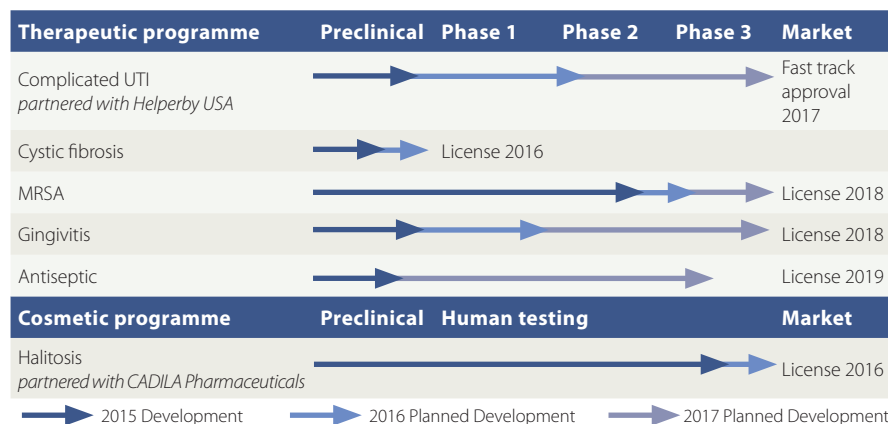


Figure 1: Helperby's ARB pipeline covers a broad range of infectious agents.

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