Incentivising Antibacterial R&D

Issue

There is an urgent need for new antibacterial agents. The spread of resistance to antibacterials has become a global threat to public health, reducing the options available to healthcare providers to manage life-threatening infections. As well as managing traditional sources of infection, many modern medical interventions such as chemotherapy, acute cardiac interventions, elective surgery, transplantation and care of neonates require effective antibacterials.

Three key challenges have caused a number of pharmaceutical companies to discontinue R&D investment in this area and have contributed to a lack of new antibacterials in development:

1. Unique scientific challenges associated with antibacterial discovery research
2. Evolving, uncertain and regionally divergent regulatory requirements
3. A relatively low prospect of a reasonable return on investment

The growing threat of resistance and the complexities of this area increasingly demand a collaborative response, moving beyond the scientific community to include policy makers, healthcare funders and other stakeholders. This document summarises GSK's ongoing commitment to antibacterial R&D and our position on how the above challenges could be addressed by different stakeholders.

GSK's Position

- Despite the challenging scientific, regulatory and commercial environment, GSK is committed to delivering new antibacterials to help address the growing threat of antibacterial resistance. This commitment includes:
  - a dedicated R&D team focussed on antibacterials for serious and life-threatening infections.
  - proportionate promotional activities that support the appropriate use of antibacterials, aiming to reduce resistance by ensuring that the right drug is prescribed at the right dose, for the right duration (antibacterial stewardship).
  - ongoing efforts to engage with scientific and medical communities and share the experience we gain in our R&D work, to contribute to the progress of medical science.
  - in an effort to further support antibacterial stewardship initiatives, a commitment to provide data[1] on the volume of our new antibacterials sold to healthcare institutions and support for research into the possible link between antibiotics in the environment and resistance.
  - recognising that high levels of antibacterial use in farming has the potential to cause resistance, we commit not to license our new antibacterials for agricultural use.

- Tackling the threat of antibacterial resistance however demands a collaborative response. The private and public sectors comprising R&D companies, biotechs, academia, governments, regulators and healthcare professionals need to work together. A good example of this is the Innovative Medicines Initiative (IMI) New Drugs for Bad Bugs (ND4BB) programme[2]. ND4BB is aimed at supporting and expediting the R&D of new antibacterial treatments by collaborative working on the scientific challenges. It has brought together the EU, industry and academia and has a total budget of nearly €224m. GSK is a committed partner.

[1] providing there are no legal constraints preventing us from doing so
[2] ND4BB was launched in May 2012 as part of the 6th IMI Call and covers 2 topics: "Innovative Trial Design & Clinical Drug Development" and "Learning from success and failure & Getting Drugs into Bad Bugs". See http://www.imi.europa.eu/content/stage-1-4 for more details.

- GSK supports the new regulatory concepts under discussion in the US and Europe aimed at providing a streamlined registration route for new antibacterials for focussed use in well-defined high need patient populations. In addition, the regionally divergent regulatory requirements need to be aligned to enable consistent and pragmatic antibacterial development programmes.
- In countries prohibiting provision of antibacterials without a prescription, GSK supports strict implementation of these laws. Other countries should develop formal channels to ensure appropriate dispensing to patients.
- New approaches to rewarding antibacterial R&D investment are required to maintain investment from companies still active in antibacterial R&D, and to attract new entrants:
  - In the short term, the curative and life-saving value of existing and emerging antibacterials needs to be adequately reflected in pricing policies.
  - In the longer term, an economic model that encourages antibacterial R&D investment by overcoming the recognised market failures is needed. De-linking the reliance on sales volume as the key driver of economic returns could help achieve this.
- GSK stands ready to engage with policy makers in addressing these challenges and to work with them in developing a fiscal and regulatory framework that supports existing and future antibacterial R&D.

BACKGROUND

GSK's Commitment to Antibacterial R&D

GSK has, for many years, been committed to the discovery, development and marketing of innovative new antibacterials[3]. These products have not only helped to widen the range of important bacterial infections which can be successfully treated, they have also helped to combat emerging new bacterial resistances.

GSK's work in this area has meant we have developed a detailed understanding of these scientific challenges. We are committed to sharing our experiences through publications[4] and via the ND4BB IMI project.

Our strategy is to pursue antibacterial R&D and diagnostics research via collaborations and funding partnerships working with other companies, academia, and funding bodies such as the IMI, The Wellcome Trust, the Biomedical Advanced Research & Development Authority (US Government) and the Defence Threat Reduction Agency (US Government).

1) The Scientific Challenges of Antibacterial Discovery Research

Despite continued investment from GSK and other companies, only two new classes of systemic antibacterials have been launched in the last three decades. Several unique scientific challenges specific to this area provide part of the explanation for the poor record. Unlike most drugs, antibacterials have to selectively target and kill rapidly growing pathogens, while not harming the host human. To do this, they must outwit the bacteria's defence mechanisms and barriers. They also need to achieve much higher serum concentrations than many other pharmaceuticals and be safe at these higher levels. All of these factors contribute to making the discovery of new antibacterials considerably challenging.

Because of these unique challenges, specialised researchers are needed with deep expertise in antibacterial discovery and development. Over the last decades as funding (private and public) has been reduced, many such researchers have moved into other areas.

[3] including amoxycillin, methicillin, flucloxacillin, cefuroxime, carbenicillin, ticarcillin, ceftazidime, mupirocin, retapamulin and combinations such amoxycillin/clavulanic acid and ticarcillin/ clavulanic acid.
[4] For example http://vimeopro.com/pewhealth/aip-conference ; http://www.nature.com/nrd/journal/v6/n1/full/nrd2201.html

2) The need for a Supportive and Harmonised Regulatory Environment

A lack of global harmonisation, increasingly challenging statistical requirements and impractical patient inclusion criteria for antibacterial clinical trials all result in larger, longer and more expensive trials. Regulatory reform is therefore a key requirement for encouraging investment in antibacterial R&D. Specifically GSK believes that:

- The new regulatory concepts to address high unmet need that are under discussion in the US and Europe are critical for the success of antibacterial R&D. They should enable streamlined registration of new antibacterials for use in well-defined high need patient populations and we encourage expedited development of full guidance to support implementation of these innovative approaches.
- Globally aligned clinical trial guidelines are needed to ensure consistent and pragmatic statistical methodologies and study designs. Consistent labelling should then follow.
- Regulatory guidelines need to be more closely aligned with medical practice to make clinical trial enrolment more efficient and medically acceptable to clinical investigators.

3) **A New Economic Model for Antibacterials**

The above challenges have made antibacterial R&D more expensive and risky than ever before, while new antibacterials will be used very sparingly and at prices that do not reflect their true life-saving value in health care. The returns on R&D investment are therefore typically lower than for other therapy areas. This has resulted in reduced investment in this area and many companies exiting antibacterial R&D altogether.

GSK's approach is to focus R&D efforts on high patient need and serious hospital based infections and to seek R&D funding partnerships with government and non government organisations.

This work, however, needs to be supported by initiatives elsewhere. New economic models for antibacterials that both deliver commercial viability and advance public health objectives need to be considered. Policymakers need to recognise that an appropriate return on the R&D investment for antibacterials should reflect both their life-saving value today and the value they provide in protecting society against emerging and potentially unpredictable threats of the future. Furthermore, we believe that the new model should de-link or reduce the current reliance on the volume of product used to determine the economic returns received by the innovator company. We recognise the challenge of creating such a model, but believe the issue is too important to ignore.

Agreement around a model that simultaneously rewards R&D and low usage will take time. In the short term, therefore, pricing policies for new antibacterials need to reflect their true medical and societal value. There is a real danger that a failure to address the current undervaluation of antibacterials could result in the last remaining players moving investment towards other, more financially attractive, therapeutic areas. While it will not address the value issue, the GAIN Act in the US is a positive starting point to encourage R&D; however, more meaningful incentives are still needed.

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