Abstract

Big and Small Pharma in the Development of Infectious Disease Treatment

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The pharmaceutical industry is currently declining or dramatically reducing its antibacterial research and development. The costs and complexity of drug discovery and development have shifted investment from drugs targeting short course therapies for acute infections towards long term treatment of chronic infections or chronic diseases. Big pharmaceutical companies have either out-licensed their anti-infective research program and/or have returned rights to their originators, mainly small biotech companies. For small pharmaceutical companies, the lack of finding large Pharma partners for the clinical development leads to the risk of 'going-alone' and costs for the clinical development often blows up their financial resources.

Thus, anti-infectives have lost their attractiveness for Big and Small Pharma.

Additional reasons include a highly competitive field of widely available inexpensive generics, difficulties to discover novel classes of agents, failure of genomic approach to deliver new targets to date and high development costs for Phase III including multiple indications. The approval procedure through Mutual Recognition or centrally, reflecting the 'medical diversity' of EU countries, often leads to label restrictions further reducing the return of investment. Reimbursement and price control is another big issue, particularly in Europe, resulting in a reduction of the revenue.

Thus, such a little chance of an adequate return of investment hardly justifies the investment of 500-800 million Euros for a clinical development of an antibacterial agent, if there are other compounds for chronic treatments with much higher revenue.

It would be reasonable that small biotech companies focus on fewer therapeutic targets which require smaller markets for their products, will be the place for discovery of novel antibacterials in the future. But considering that small companies have to fulfill the same criteria to register drugs they will have a hard time moving their drug candidates through the clinical development and approval process. It could be easily become a battle of surviving. Success may well depend on big pharma companies ultimately showing an interest in the product being developed.

What is required to improve this situation?

A major issue is communication and cooperation between the involved parties. Guidance as an incentive for industry would be an important point. Considering the current incentives, the 'Fast Track Designation' (FDA) would be most appropriate for antibacterials against resistant

strains and provides close communication with the authorities including an accelerated approval process.

In the EU ‘Scientific Advice’ is an option, although not similar to Fast Track, because it is a single approach, which is non-binding. It can be repeated, but takes time. The ‘Orphan Drug Status’ is another incentive which usually does not apply for antibacterials and is not very helpful. New incentives like ‘wild-card’ market exclusivity or ‘modified wild-card’ market exclusivity (extended market exclusivity to another compound or another antibiotic of the same manufacturer) have been repeatedly brought up by different parties including IDSA and, of course, industry and would probably have the highest potential impact, but there is currently no legal prerequisite in place.

Recent initiatives of the FDA to provide continuous guidance are appreciated and would lead to more label certainty which is a crucial point in the development of new antibacterials. Such a scheme would be helpful for Europe as well considering its multiple countries’ requirements. The new Future Medicine Legislation in the EU does not include anything like continuous guidance although they encourage companies to seek for scientific advice. But despite this outlook, FDA and EU will likely extend the terms of their recently announced information-sharing agreement which may help to provide more clarity on specific dossier requirements and the label to be expected.