Evaluate Vantage

September 19, 2017

A call for help from the antibiotics makers

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A phase III success for Nabriva with lefamulin was richly rewarded by the stock market yesterday – shares jumped 30% and the drugmaker quickly moved to raise $80m on the back of the results. But, like other developers of novel antibiotics, the company is facing a commercial marketplace that feels much less exuberant.

This has nothing to do with the clinical profile of lefamulin, which has now demonstrated impressive efficacy in community-acquired bacterial pneumonia (CABP), and everything to do with rising microbial resistance rates that have left doctors increasingly unwilling to use powerful new products. Groups like Beam Alliance in Europe and AWG in the US are pushing for new mechanisms to encourage further investment in this space, but many fear that the necessary actions are far from materialising.

These lobby groups are formed of companies in the business of developing and selling novel antibiotics and will, naturally, be concerned with maximising profits. But it is also true that the need for new drugs to defeat increasingly resistant superbugs is growing – and these companies are operating in a counterintuitive market that is trying to restrict use of their innovative agents.

“Everyone wants to narrow their new antibiotics down to worse cases; this is understandable,” says Holger Schmoll, treasurer of Beam Alliance and finance director of Aicuris, a private German anti-infectives player. “But it means that business models will only work with high prices like oncology, and if you don’t want to have such high prices then you have to think about alternatives.”

Beam says these alternatives include pull and push incentives – tax breaks, revised pricing models, and funding more geared to smaller companies – and improvements to regulatory pathways.

Small steps

Governments in the US, Europe and Japan have acknowledged the problems facing this sector, and certain measures have been introduced to help. The US in particular has taken bold regulatory steps – the Generating Antibiotics Incentives Now Act (Gain) allowed the FDA to establish the Qualified Infectious Disease Product (QIDP) designation, allowing for an expedited NDA and an extra five years' marketing exclusivity.

Nabriva told EP Vantage that they also expect new anti-infective development incentives to make progress through Congress, and pointed out that the President’s Advisory Council on Antimicrobial Resistance has proposed a series of push and pull incentives to help manufacturers.

Government funding is also available – in the EU this comes largely through the Innovative Medicines Initiative, though Mr Schmoll says that for small companies the administrative burden of participating is onerous.

“But on pull factors [in Europe] there is nothing. What we need are reliable markets – pricing models, market exclusivity and a market entry reward. If governments don’t want us to sell many drugs or give us high prices then we need other alternatives,” he says.

A market entry reward was one of the key proposals that came out of the2016 Review on Antimicrobial Resistance, commissioned by the UK government. This concluded that developers of novel antimicrobials that meet certain pre-defined criteria should receive a payment of anything between $800m and $1.6bn, with certain strings attached, to encourage investment into the area.

The paper also recommended the setting up of a global innovation fund for early-stage and non-commercial R&D, endowed with $2bn over five years; notably, moves towards neither step have been made, and it is hard to see how measures with such global reach could easily be negotiated or funded.

Time for action?

Developers contend that more must be done, however, with pressures mounting from several directions, even before considering the high attrition rate from the pipeline in this field. Mr Schmoll points out that no new antibiotic launched in the past few years has commanded a price of over $300 a day in Europe, as cheap generic versions of older products continue to place a natural ceiling on the cost of novel agents.

“The ideas are now clear – the politicians now have to decide to bring money into this market,” says Mr Holger. “And it’s a question of time because medical need will become more and more important. Resistance rates will go up and up.”

Assuming that Nabriva manages to repeat its phase III results in a second pivotal study next year, the company will be heading to the regulator with a project that has proven potency against several multidrug-resistant pathogens. The company hopes that its targeted spectrum against the main bugs that cause CABP will win lefaumulin a role as an early empiric therapy - analysts reckon it could achieve sales of $300-500m a year, if all goes well.

On the surface this looks like a fitting market for a small company to address, but beneath the topline anti-infectives players enjoy considerably thinner profit margins than areas like oncology. The question for policy makers is whether tinkering with regulatory frameworks or patent lives will be enough to attract investors back into this market in sufficient numbers – or whether more radical ideas like market rewards are going to be necessary.

This story has been updated with comments from Nabriva, and to clarify comments from Mr Schmoll on pricing, which was referring only to Europe.

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