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Glaxo gets Advair reprieve, but HIV competition bites

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Generic versions of Glaxosmithkline's Advair have been delayed again, but doubts about the group's HIV doublets are creeping in.

The FDA has given to Glaxosmithkline with one hand and taken away with the other. A knockback for Novartis's generic version of Advair sent the UK group's shares up as much as 3% this morning, with investors no doubt hoping the entry of substitutable generics will be delayed beyond the expected mid-2018.

But it is only a matter of time before Advair falls, and Glaxo needs its new products to step in. The group talked up the prospects for its dolutegravir-based HIV doublets yesterday, but today hit Gilead with a patent infringement suit on the approval of that company's rival triplet, Biktarvy. Perhaps Glaxo has some doubts about its doublets.

Backup plan

Glaxo's move could be seen purely as an insurance policy. The UK group contends that bictegravir, the new component in Biktarvy, infringes the patent for dolutegravir, but is not asking for Biktarvy to be removed from the market; instead Glaxo seeks royalties, which could be a useful revenue stream if Gilead's product wins the HIV battle.

Berenberg analysts suggested that a 10% royalty rate on Biktarvy peak sales could add an extra £430m ($600m) to Glaxo's top line in a few years – although they added that they did not know what sort of payment Glaxo was looking for, or whether the company could win the case.

The gamble seems justifiable. Current *EvaluatePharma* sellside consensus has Biktarvy streaking ahead with 2022 sales of $5.1bn; meanwhile, Glaxo's Juluca, a doublet comprising dolutegravir and rilpivirine approved last year, is only forecast to bring in $546m – and Glaxo will have to split the revenue with Johnson & Johnson (*Glaxo scores HIV double, but bigger tests loom, November 23, 2017*).

Glaxo is developing another doublet, made up of dolutegravir and lamivudine, which is due to yield phase III data in mid-2018. This could be the bigger opportunity, chief strategy officer, David Redfern, said yesterday during the company's earnings call.

Both components are wholly owned by Glaxo's Viiv subsidiary, and the pivotal Gemini 1 and 2 trials of dolutegravir/lamivudine are targeting a larger market, having enrolled treatment-naive patients. Juluca is indicated for a smaller niche, well-controlled patients switching from a triplet regimen.

The 2022 consensus forecast for dolutegravir/lamivudine is even lower, at $323m, partly because it is further away from the market.

Still, there are doubts about whether doctors will embrace HIV doublets. Claims to be able to reduce the chronic toxicity associated with traditional three-drug regimens are important, particularly as HIV patients live longer, but infection breakthroughs remain a concern. These were reinforced last year by a case of resistance in a small, investigator-led study of dolutegravir/lamivudine; Glaxo blamed this on a “chaotically non-adherent” patient.

The general view among analysts is that physicians are still cautious about doublet therapy, and that uptake is more likely to be driven by financial constraints than clinical considerations. The former are becoming ever more important, but Glaxo has much to do to convince the market that its two-drug regimens are not just niche products.

Advair cheer

The company had reason to celebrate this morning, though, with news of a complete response letter for a generic version of Advair developed by Novartis’s Sandoz division.

It is not clear yet why Sandoz’s copycat has been rejected or whether a quick resubmission could be on the cards. But, after rebuffs for generics from Mylan and Hikma last year, Advair has clung on against the odds.

True, Teva’s Airduo Respiclick is already available, but is not directly substitutable (*Teva twin-tracks Advair competitor’s launch, April 21, 2017*).

The next big event looks likely to be an FDA decision on Mylan’s project – the company has provided a response to its complete response letter and expects to hear back in June. Hikma, meanwhile, is in dispute with the FDA, and has said it hopes to provide an update on timelines this quarter.

The chance of substitutable generic versions of Advair reaching the market by mid-2018, the base case that Glaxo put forward yesterday, now looks slimmer. But even if generics are held off until the end of the year, Glaxo still expects US Advair revenues to decline by 20-25% in 2018.

Glaxo might have dodged a bullet for now, but it still needs to fill its Advair-shaped hole. Suing Gilead could be a tacit admission that its own HIV doublets will struggle to provide a plug. Investors will have to hope that a more focused pipeline and personnel changes could usher in a more productive period of R&D at Glaxo.

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