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Roche’s asthma stumble gives Glaxo the upper hand

Jonathan Gardner

GlaxoSmithKline’s battered respiratory pipeline got its first good bit of news in some time today. Its recently launched severe asthma injection, Nucala, will have one less immediate threat with Roche’s announcement that rival lebrikizumab failed one of its two pivotal trials.

The Swiss group will now see its filing plans set back for perhaps two years, giving Glaxo’s Nucala a better competitive position for its first couple of years on the market. With Teva’s reslizumab due an FDA decision tomorrow, it is looking like a two-horse race until at least 2018.

Roche said the Lavolta I trial met its primary endpoint, showing that lebrikizumab could significantly reduce asthma exacerbation compared with placebo over one year of treatment in patients with uncontrolled asthma and taking both corticosteroids and a second controller medication like a long acting muscarinic antagonist.

Lavolta II, on the other hand, missed the same endpoint. Roche did not disclose any secondary endpoint data for the failed trial, although it said Lavolta I also met a secondary endpoint of improvement in lung function.

Given that the trials were identical in design, the only conclusion that can be drawn is that one is a fluke. One way to demonstrate to regulators that Lavolta II is the fluke is a third identical study – which at a year to complete could only expect to have data in 2017, making lebrikizumab eligible for approval in 2018 in a best-case scenario.

Roche disclosed little about its plans, other than saying that the data would be examined further and presented at an upcoming medical meeting – the American Thoracic Society meets in May and the European Respiratory Society in September.

There is a possibility that additional analyses would reveal consistent subgroup data in both trials, allowing for regulatory filing; however, this would put lebrikizumab at a competitive disadvantage to Nucala, which won approval in patients age 12 and older with severe asthma of eosinophilic origin.

How much better?

Consensus sales forecasts are not especially high for lebrikizumab – $369m in 2020. Yet this is one of a number of interleukin-blocking antibodies set to enter the market in the next few years, representing the main growth area for asthma medications as older inhaled treatments like Glaxo’s Advair lose market exclusivity.

The asthma antibody landscape		
	Project	**Company**
Marketed		
Anti-IL-5 Mab	Nucala	GlaxoSmithKline
Filed		
Anti-IL-5 MAb	reslizumab	Teva Pharmaceutical Industries
Phase III		
Anti-IL-13 MAb	lebrikizumab	Roche/Chugai
	tralokinumab	AstraZeneca
Anti-IL-4 alpha MAb	dupilumab	Sanofi/Regeneron Pharmaceuticals
Anti-IL-5 MAb	benralizumab	AstraZeneca
Phase II		
Anti-IL-13 MAb	RPC4046	AbbVie/Celgene
Anti-IL-17A MAb	Cosentyx	Novartis
Anti-IL-23 MAb	BI 655066	Boehringer Ingelheim
Anti-IL-3, IL-5 & GM-CSF MAb	CSL311	CSL

These medications focus on eosinophilic asthma, a severe form of the disease marked by elevated white blood cell counts, which promotes inflammation of the airways. Because they are biological treatments targeting a smaller population with hard-to-control disease – which can result in hospitalisation and other expensive medical interventions – prices can be expected to be higher.

Nucala premiered at $32,500 a year in the US, which the review body the Institute for Clinical and Economic Review said was more than double what is a cost-effective price. By comparison, in asthma, Advair cost about $4,121 per patient per year in 2015, according to data from *EvaluatePharma*'s USA Sales, Volume & Price module.

Nevertheless, Nucala's forecasts climbed as it approached its FDA approval in November, and now stand at $1.4bn in 2020. But if the tug-of-war between pharma and payers in 2014-15 has taught the sector anything it is that launches of pricey biological agents in disorders with inexpensive small-molecule alternatives have underperformed.

Glaxo's fourth-quarter earnings statement showed Nucala sales of £1m ($1.4m) in just a month on the market, so it might not be until mid-2016 that its sales trends will be apparent – and indeed, this could affect forecasts across the space, which currently stand at about $3bn.

As for other potential entrants, AstraZeneca will surely be looking at the lebrikizumab data with keen interest. It has two phase III interleukin antibodies in asthma – one of them, tralokinumab, blocks IL-13 like lebrikizumab, and the other, benralizumab, blocks IL-5 like Nucala and reslizumab.

Roche's stumble gives Glaxo some additional manoeuvring room as it tries to match launch expectations. Locking up exclusive contracts in return for discounts might be a wise tactic before Teva can roll out its rival and clinical-stage projects reach key catalysts.

Trial	**ID**
Lavolta I	NCT01868061
Lavolta II	NCT01867125

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