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Roche Reviewing Next Steps For Lebrikizumab After Mixed Phase III Data

By Jessica Merrill

ONE OF TWO IDENTICAL PHASE III trials testing the IL-13 blocker in severe asthma patients met its primary endpoint, while the other failed.

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The fate of **Roche**'s late-stage respiratory drug lebrikizumab appears uncertain after mixed results in Phase III testing. The company announced Feb. 29 that only one of two identical studies testing the interleukin-13 blocker in patients with severe asthma turned in positive results while the other failed.

The news is a disappointment for Roche, which has been looking to bolster its portfolio in a competitive market for asthma. Lebrikizumab is a biologic targeted to select patients with severe asthma who aren't controlled on existing medications, including corticosteroids, but even the severe asthma segment is already being courted by several other big pharmas.

Competing effectively in the therapy area, amid increasing competition and pressure from payers, will require stellar data.

GlaxoSmithKline PLC's *Nucala* (mepolizumab) was approved by FDA in November as a first-in-class IL-5 inhibitor for severe eosinophilic asthma. Several other IL-5 and IL-13 inhibitors are in late-stage development, including candidates by **Teva Pharmaceutical Industries Ltd.**, **Sanofi/Regeneron Pharmaceuticals Inc.** and **AstraZeneca PLC** *(Also see "On The Respiratory Horizon: A Wave Of Biologics For Asthma" - Pink Sheet, 15 Jul, 2013.)*. Teva's IL-5 blocker *Cinqair* (reslizumab) is pending at FDA following a positive FDA advisory committee review in December *(Also see "Teva's Reslizumab Gets Panel Nod For Adult Asthma, Unanimous 'No' For Adolescents" - Pink Sheet, 9 Dec, 2015.)*.

"We have talked to a number of payers, and it is going to be quite challenging," said Roger Longman, CEO of the reimbursement intelligence firm Real Endpoints, of the severe asthma drug market.

"It's not quite clear just how these drugs are going to be able to demonstrate significant incremental value over each other," he said.

A competitive market and payer concern over the high cost of biologics could result in a situation where drugs are pitted against each other on formularies so that payers can secure big rebates. The high wholesale acquisition cost of Nucala, about $32,500 per year, has already drawn criticism. The Institute for Clinical and Economic Review determined in a draft report in December that the product needs to be significantly discounted to make it cost effective *(Also see "GSK's Nucala Is Significantly Overpriced, ICER Draft Report Finds" - Pink Sheet, 30 Dec, 2015.)*.

Roche, along with its ex-US marketing partner **Novartis AG**, has had the only biologic on the market approved for moderate-to-severe asthma not controlled by corticosteroids. *Xolair* (omalizumab), a human immunoglobulin E (IgE) blocker, has been on the US market since 2003 and generated sales of CHF1.28bn ($1.28bn) for Roche in the US in 2015.

Much of the advances around IL-5 and IL-13 in asthma stems from learnings around the development of Xolair. Cells known as Th2 that play a role in the production of IgE also produce cytokines IL-5 and IL-13. The pathways are closely related and it

still remains uncertain which approach may ultimately be the most effective. Roche had also been developing a drug, quilizumab, in Phase II testing that works upstream from Xolair and targets the M1 prime segment of IgE, but decided not to progress it further in late 2014.

As for the Phase III results for lebrikizumab, Roche said in a statement, "These data require further interpretation and analyses are ongoing to better understand the results and determine next steps."

The LAVOLTA I and II studies were identical, double-blind, randomized, multi-center, placebo-controlled trials testing lebrikizumab in patients with severe asthma uncontrolled on a corticosteroid and a second medication. The trials enrolled all-comers but analyzed patients for levels of serum periostin or blood eosinophils, two biomarkers of airway inflammation. The studies enrolled more than 2,100 patients.

The company released only the top-line results from the two studies, but said LAVOLTA I met the primary endpoint, showing a significant reduction in the rate of asthma exacerbations at 52 weeks in people with higher levels of serum periostin or blood eosinophils. It also demonstrated a significant improvement in lung function as measured by forced expiratory volume in one second (FEV1). The observed effect in the primary and secondary endpoints, however, was less than seen in Phase II testing.

In LAVOLTA II, the exacerbation reduction results did not meet statistical significance, the firm reported. No new safety signals were observed in either study.

Roche is also testing lebrikizumab in a range of additional trials, according to clinicaltrials.gov, including in patients with chronic obstructive pulmonary disease and mild-to-moderate asthma.

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