Lupin Boss On Getting Biosimilar Manufacturing Right, Albuterol Outlook

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Executive Summary

Lupin managing director tells *Scrip* that manufacturing competence will be a "big advantage" in the biosimilars space, and also believes that the US albuterol market remains "very lucrative" despite the entry of authorized generics.

LUPIN'S MANAGING DIRECTOR NILESH GUPTA

Lupin Ltd. isn't fretting about not being among the early movers in the biosimilars space and believes that those who can get the manufacturing of these products right could potentially hold a distinct edge.

In an interview with *Scrip*, the Indian company's managing director Nilesh Gupta reiterated that being early in the biosimilars sector "would not have been an advantage," noting that while products such as granulocyte colony-stimulating factor (G-CSF) became a "nice opportunity" for some, there have also been "casualties" along the way for pegylated G-CSF.

"I think now is the time to be able to do the right kind/range of products, be in time for patent expiry as well," Gupta said.

The US biosimilar market for Amgen Inc.'s short-acting neutropenia drug Neupogen (filgrastim) has seen significant uptake for Teva Pharmaceutical Industries Ltd.'s Granix (the filgrastim) and Sandoz's Zarxio (filgrastim- sndz), the first biosimilars approved under the new regulatory pathway in the US.

In July last year, Mylan NV commenced commercial US sales of Fulphila (pegfilgrastim-jmdb), the first-to-market biosimilar version of Amgen's Neulasta, co-developed with Biocon Ltd. (Also see "Cyberus Grant Up For January Udenyca Launch, Prices Biosimilar At 33% Discount To Neulasta" - Scrip, 9 Nov, 2018.)

Earlier this year Sandoz International GMBH resubmitted its application for biosimilar pegfilgrastim to the US FDA, following the complete response letter received in June 2016. Sandoz's biosimilar Ziextenzo (pegfilgrastim), however, received market authorization from the EC last November, while Lupin's pegfilgrastim is expected to complete clinical studies this year, with an anticipated filing not planned until next year in the US.

Manufacturing Advantage

Lupin, which hopes to hit the market in Japan with its biosimilar etanercept in the second half of fiscal year 2020 and is awaiting EU approval of the product, believes strength in manufacturing could be an important differentiator in the segment.

Gupta said that while "everyone talked of a big glut in capacity" for biosimilars, in reality there isn't one and Lupin was hard pressed to find partners for etanercept.

"When we looked around for partners, there were very few that we felt were the right people to engage with for even partnering on additional etanercept manufacturing for example. The ability to develop products of the right quality and manufacture them responsibly is going to be a big advantage in the biosimilars space and that's something we've already got," the Lupin icon asserted.

The Indian company is currently implementing a significant expansion – about six times its current capacity – for etanercept at its Indian site. In March this year, Lupin received an EU GMP certificate for its mammalian facility in Pune, where biosimilar etanercept is to be manufactured. The biosimilar drug substance facility has also been inspected by Japan's regulator, the PMDA, with a successful outcome.

'US Biosimilar Market Will Open Up'

Lupin has a partnership with Mylan under which the US firm will commercialize the Mumbai-based company's biosimilar version to Amgen/Pfizer's Enbrel (etanercept) in Europe, Australia, New Zealand, Latin America, Africa and most markets throughout Asia. In March this year, YL Biologics Limited, a Japanese joint venture between Lupin's subsidiary Lupin Atlantis Holdings SA, local generics firm Yoshindo Inc. and Lupin (through its Japanese subsidiary, Kyowa Pharmaceutical Industry Co Ltd), received approval to manufacture and sell biosimilar etanercept in Japan.

On whether Mylan would likely be the partner of choice for the US as well, Gupta maintained that etanercept was "something that we felt we will try to keep for ourselves for the US," so the firm partnered for many of the other markets.

"We are doing studies right now. We have another three products in development. The intent would be to partner with who we consider as the right partner and in that Mylan would certainly be among those we could consider but there could be others as well," he said, also referring to "a lot of maturity and understanding" of biosimilars at Mylan.

Lupin's aim in the biosimilars segment is to be in the first wave of products, launch with a "compelling package" and then partner with the right party, geography by geography. "We are going product-by-product at this point of time," Gupta added.

On whether recent tactics, such as contracting by reference product makers that threaten loss of rebates on other products if the biosimilar is placed on a formulary, could derail the plans of companies like Lupin, Gupta said that the bundle/formulary hurdle can be used as a challenge for some period of time. But he emphasized that there is a "very clear intent" of the US government machinery to bring biosimilars to the market as well. (Also see "Biosimilars Need Better Reimbursement, Not 'Kabuki' Coverage, Gottlieb Tells Insurers" - Pink Sheet, 7 Mar, 2018.)

"Eventually the market will open up," he predicted.

Inhalation Products

Meanwhile, the first US approval of a generic dry powder inhaler (DPI) – Mylan's generic Advair (fluticasone propionate and salmeterol) – appears to have enthused firms like Lupin, which is pinning for a significant play in the inhalation space.

Lupin's filing for albuterol metered dose inhaler (MDI), a generic version of Teva's *ProAir*, is under FDA review and it anticipates a launch in the second half of fiscal 2020. The company has filed for a generic version of *Breo*vana (arformoterol tartrate) in the US and also believes that it holds a first-to-file position for its tiotropium DPI (generic Spiriva) filing.

Lupin had at the time of its fourth-quarter results indicated that the FDA approval for Mylan's Advair DPI and the "good level of substitution" seen for the product bodes well for players like itself. Mylan's Wixela Inhub (fluticasone propionate/salmeterol) was approved by the FDA with patient instructions for use that are noticeably different from the reference product, GlaxoSmithKline PLC's *Advair Diskus*, indicating the agency's willingness to accept certain device design and labeling differences in the complex generics space. (Also see "Generic Advair's Labeling Variation Stems From Permissible Design Differences, US FDA Says" - Pink Sheet, 11 Feb, 2019.)

"It's very heartening to see the FDA actually approved a DPI. It gives us the confidence that our pipeline of MDI and DPI products is approvable in the future and will help us build our complex generic business going forward," Lupin's CEO Vinita Gupta, Nilesh Gupta's sister, said at the time of the fourth-quarter results. (Also see "Lupin Results Fail To Cheer But Signal Stabilization Of US Generic Market" - Generics Bulletin, 22 May, 2019.)

Nilesh Gupta observed that for complex generics, the FDA has been "very happy to engage and have conversations" around the product, formulation, device, clinical trials and seek inputs "much more than what you would generally see with regular generics."

"The ability to converse is much more on some of these platforms. I don't think that naturally translates into a reduction in the standard that would be expected for these filings," Gupta said.

Timing, Pricing

He is optimistic that a second half launch of generic Proair remains possible, even if the FDA were to come up with some "small questions", which he hopes Lupin will be able to address "quickly and comprehensively."

"A lot of credit should be given to Mylan for pulling through with Advair. Getting the first DPI approval is significant as will getting the first [generic] MDI approval. Our product is intended to be a pure generic and hopefully the first generic to the market," he said, adding that the challenge with being the first is that there could be "vagaries that show up."

Albuterol sulfate authorized generic versions of GSK's Ventolin HFA inhalation aerosol and Teva's Proair HFA became available in January this year, while in April, Par Pharmaceutical said that it had begun shipping an authorized generic of Merck & Co. Inc.'s Proventil HFA (salbutamol) inhalation aerosol.

While Gupta declined to comment on Lupin's pricing approach for its generic albuterol, he explained that the market for the product is still "very lucrative" despite the entry of authorized generics. "The entry of a 'true' generic would be very welcome in the market. We would also have very strong cost of goods," he noted.

Peer Cipla has said that it believes it has the cost competitiveness on prices "significantly lower" than its competition, and that it would take a "fair share" of the albuterol market amid the arrival of authorized generics. (Also see "Cipla Claims Pricing Advantage For Albuterol In US" - Scrip, 23 May, 2019.)