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Interview – Europe endorses Prosonix's respiratory fix

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In a respiratory market dominated by big names it should come as a surprise that it is a private UK group – Prosonix – that thinks it can get the first approval for a generically equivalent suspension-based metered-dose inhaler. Amazingly, this might lead to the first fully substitutable version of GlaxoSmithKline's Advair.

The key lies in last week's acceptance of Prosonix's EU filing for generic fluticasone, which shows that the company has overcome a huge barrier to entry, its chief executive, David Hipkiss, tells *EP Vantage*. Its secret? "Fix it before you mix it."

This might sound flippant, but it neatly sums up Prosonix's focus on particle engineering. In a sense particle engineering goes back to basics, looking at designing the API rather than, for instance, developing a solution for a metered-dose inhaler (MDI) and then trying to convert this into a suspension or dry powder.

"We're not a discovery company," says Mr Hipkiss. "Spending $5-6bn on discovering a new drug might not be the way forward in this therapy area. But we're not a device company either. We don't need to be; there are ten a penny."

He sees the UK MHRA's acceptance of the filing for Prosonix's generic fluticasone (PSX1001) as a major endorsement – the regulator "wouldn't have validated the dossier if something was missing". This, he insists, is as important as the deal the group struck in April with Mylan for this project and its US version.

Non-clinical pathway

The central issue here is the EU pathway that was followed in the MHRA application, with PSX1001 being filed on *in vitro* data alone. An approval on this basis would imply that the generic API is precisely the same as the brand's – key to allowing true substitutability.

This is a holy grail in the respiratory space, where for instance full generic competition to Glaxo's blockbuster Advair is still up in the air (*Glaxo scores a win and a loss as respiratory future takes shape, December 9, 2013*).

"I suspect [others] have tried [the EU *in vitro* pathway] and failed. To the best of our knowledge there has not been an approval of a suspension-based MDI via the *in vitro* route to date," says Mr Hipkiss.

Recent EU approvals of Advair copies include Cipla's Serroflin and AirFluSal Forspiro from Novartis's Sandoz division. "Well done to Cipla," says Mr Hipkiss. "But their product is for two of three strengths only ... with a dissimilar label. Sandoz's is the same story; it's technically not directly substitutable."

Interestingly, Mr Hipkiss believes that the EU hurdle here is tougher than in the US, so Mylan will be paying close attention in seeking ANDA equivalence for fluticasone in the US. Although the FDA does require pharmacokinetic and pharmacodynamic studies, demonstrating an "*in vitro* match" in the EU would count for a lot.

To square the circle, Prosonix's next project is generic salmeterol, which in Advair is the LABA counterpart to the steroid fluticasone. This project is coded PX1439, and is partnered with an undisclosed European company, as is PX1442, a version of Boehringer Ingelheim's Spiriva.

The goal for Prosonix is to use the EU *in vitro* pathway – which will hopefully have been "litmus-tested" by PSX1001– for all three monotherapies, and then for the Advair copy.

"It's a big technical challenge," admits the chief exec. "But we've done it with fluticasone, which everyone knows is difficult, and we're doing it with salmeterol. People are going to assume, rightly, that we can do it with Advair."

Triple

Meanwhile, Prosonix is developing the LAMA glycopyrronium as a branded generic, for which a phase IIa trial

has been completed. The main reason for this is to provide an off-patent LAMA to which the company can reference data in a future filing for a triple steroid/LABA/LAMA combo.

AstraZeneca and Glaxo are pursuing such triple combinations, and Mr Hipkiss agrees that there is an important patient set in which these will be applicable. Where opinions diverge is pricing, and Mr Hipkiss insists that a product pitted directly against an incumbent has to be discounted.

Indeed, this fits into a developing equation in which regulators are raising the bar for generics on the one hand, and austerity and global prescribing guidelines are hitting pricing on the other. Seeing the extreme pressure that Glaxo has come under in the US, maybe Mr Hipkiss has a point.

And the end game? “We’re very well backed by our VC companies, but they’ve got to make a return,” he says. “They’re not charities.” Regulatory action on the fluticasone filing will be one trigger to watch.

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