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Interview – Nabriva comes out fighting

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Working in the world of antibiotics means having to work that little bit harder. Just ask Nabriva: a successful pivotal trial of its lead candidate, lefamulin, a novel antibiotic belonging to entirely new class, barely caused a flicker in its share price last month.

True, the company managed to raise around $70m on the back of the results, but this had to be done at a discount to its 2015 IPO price. Concerns about the economic potential of new antibiotics have depressed valuations in this space, but Colin Broom, the group's chief executive, believes that lefamulin is a different case. "Don't look at other antibiotic launches in last 10 years; they haven't had a good position. Hospitals will want this stocked," he tells *EP Vantage*.

Mr Broom's optimism is based on a belief that lefamulin will be positioned as a first-line option for community-acquired bacterial pneumonia (CABP), an infection that ranks as a leading cause of hospitalisation but that has seen no truly novel treatment emerge for 15 years. Belonging to a class called the pleuromutilins – which have been used in animals for many years – lefamulin represents a new mechanism of action with which to fight bacteria that are becoming increasingly resistant.

The propensity for resistance looks to be low with the pleuromutilins; lefamulin binds to the bacterial ribosome, a well-conserved area, and resistance has been very hard to generate in the lab, Mr Broom says. Meanwhile, lefamulin is available both orally and intravenously, a feature that should bestow advantages in the hospital setting and allow expansion into the community.

On the shelf

Currently, a patient admitted to hospital with CABP will be typically treated with either a combination of two antibiotic classes – a β-lactam like ceftriaxone and a macrolide like azithromycin – or moxifloxacin, which is a fluoroquinolone.

But both approaches have drawbacks. The former involves antibiotics that are only available intravenously, so patients must switch to a different oral option when they are discharged, while resistance is a growing problem with macrolides. And though the fluoroquinolones are highly effective Mr Broom describes them as a "blunderbuss" – they are very broad, and off-target effects are a big issue, in particular the potential to trigger *Clostridium difficile* infections.

"Clinicians want to put fluoroquinolones back on the shelf," he says. "We see lefamulin as a partial replacement for moxifloxacin, and on the other hand a better treatment than the combinations. So it's very well positioned to get in between those two and push them both to the side."

He also maintains that lefamulin ticks several boxes for hospital antibiotic stewardship committees – those tasked with ensuring appropriate antibiotic usage.

"Lefamulin's targeted spectrum, relatively short duration and effectiveness in this population makes it a very strong candidate to be used as empiric monotherapy," he says.

Off the shelf

The Leap 1 data unveiled last month went part of the way to support these claims. Lefamulin proved to be non-inferior to moxifloxacin in patients with moderate to severe CABP, with no obvious safety concerns and a more tolerable gastrointestinal profile.

Leap 2 will read out early next year, and another win is crucial for regulatory success and the asset's broader commercial potential – the trial tests the oral form in less severe patients, against oral moxifloxacin.

Sellside estimates for peak US revenues sit at around $400m, but Needham analysts believe that blockbuster status is in reach if the company can drive adoption in the outpatient setting. Mr Broom concedes that this would probably require the help of a partner.

"In the US with a targeted sales force we can see all the institutions that see a lot of pneumonia – we're not talking about hundreds of reps – and I think we can have a relatively rapid ramp-up. Down the road we may want to partner if we see more use in the community." Negotiations are already under way over ex-US rights to the project, he adds.

Still, persuading doctors to take lefamulin off the shelf in the first place represents perhaps the biggest challenge

facing Nabriva, and Mr Broom admits that it will have to be priced appropriately to encourage first-line use. He also acknowledges that substantial medical education will be needed in the coming months.

“From a medical perspective lefumulin is very compelling, but most clinicians don’t know about it. Our job over the next 18 months is to let them know there’s another antibiotic coming along that is going to be very useful to have,” he says.

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