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March 03, 2016

Interview: new antibacterial has a date with Destiny

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With fears over antibiotic resistance growing, pharma needs to find some answers. While many are focused on developing new antibiotics, Destiny Pharma believes that it has a potential solution with a new approach.

“It’s best described as a novel antibacterial with a rapid bacterial kill,” the group's chief executive, Bill Love, told *EP Vantage*. And it is this speed of action that could help it overcome resistance. Conventional antibiotics take hours to have an effect, but Destiny’s lead compound, XF-73, only takes a few minutes to work so the bacteria have less chance to mutate.

With typical antibiotics “you’ll be treating some bacteria that are growing; there’s the opportunity to mutate, which means the resulting offspring might by random chance be resistant to that particular mechanism,” Mr Love explained.

Rapid kill

XF-73, and other projects based on the UK company’s XF platform, comprise a porphyrin ring with two cationic arms that attack the bacterial cell membrane, giving them their fast mechanism.

“Conventional antibiotics usually act on the biochemistry of a bacterium, and often they need to be internalised to do so. That takes many hours,” said Dr Love. “But because we target the bacterial cell membrane XF drugs simply need to bind to the membrane, they don’t need to be internalised.”

Once bound they “cause the bacteria to become leaky to very low-molecular weight internal components like ATP and potassium, and that loss of those vital intracellular components kills the bacteria very rapidly”, added Dr Love.

An early indication on whether the approach works should soon be available. Results from a phase I study of XF-73, sponsored by the US National Institute of Allergy and Infectious Disease, are due in the next couple of months.

As well as looking at safety, the trial will also provide early data on whether the project, given as an intranasal gel, fulfils its goal – namely to decrease levels of staphylococci in people who carry the bacterium in their nasal cavities.

MRSA carriers

Destiny hopes that this approach could help prevent hopsital staphylococcal infections, including the dreaded meticillin-resistant *Staphylococcus aureus* (MRSA). “Around a third of the population are persistent carriers [of *S aureus*], which is fine when we’re healthy,” Dr Love said. “But if carriers go into hospital for an operation they’re at up to a nine times greater risk of post-surgical infection.”

Rather than acquiring *S aureus* from others, most healthcare-associated *S aureus* infections – over 80% – are endogenous. Tackling carriers before they undergo surgery should therefore decrease these infections; indeed, this is what was shown by a *New England Journal of Medicine* study using a decolonisation strategy with conventional antibiotics.

However, widespread use of antibiotics in this type of strategy would lead to increased resistance. If XF-73 is not linked with resistance it could be the perfect alternative for the prevention of post-surgical infection.

Another advantage with XF-73 is that it can be given once a day before surgery, whereas many antibiotics “have to be administered multiple times per day for five consecutive days prior to surgery”, Dr Love said – thus potentially introducing compliance issues.

QIDP status

Although at an early stage, XF-73 has already received a key endorsement from the FDA in the shape of

qualifying infectious disease product (QIDP) status. This allows it to be fast-tracked through registration, as well as giving it a five-year extension to its US market exclusivity.

If the phase I NIAID-sponsored study renders positive results, Destiny will move XF-73 into trials with surgical patients rather than healthy volunteers. It could be as little as two to three years until the drug reaches the market if the company partners with a larger pharma company – or a little longer if it goes it alone.

Destiny is willing to take XF-73 to approval itself, said Dr Love, but he also seemed open to the idea of a partner. He said there had been interest from potential collaborators, but noted that one reason that the sector has been so neglected in recent times was because it "hasn't been the best in terms of return on investment".

"Antbiotics are probably the most undervalued pharmaceutical on the planet considering they can save your life." He compared this with costly cancer drugs that might just extend a patient's life for a few months.

Governments are working to redress this balance with incentives for pharma companies developing new antibacterials, such as the US GAIN Act, which introduced the QIDP designation.

"At the bottom of all this there's a big need," Dr Love said. "In some cases we're down to the last antibiotic that is active against certain bacteria. And that needs to be restocked, and ideally not just restocked with traditional approaches, but also with approaches that can be more resistant to resistance."

We should soon get the first clues about whether XF-73 will help address this need.

Project	Study detail	Primary completion	Trial ID
XF-73	NIAIAD-sponsored phase I trial	May 2015	NCT01592214

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