Destiny Pharma advances strategy against bacteria

Assuming that all plans come to fruition, Destiny Pharma Plc could oversee the start of Phase 3 programmes in 2024 aimed at tackling two bacterial pathogens that represent a significant risk to public health. The small British company, located in the coastal city of Brighton, is raising money, speaking to regulatory authorities, and lining up partnerships to advance products for the treatment of *Staphylococcus aureus* and *Clostridioides difficile*. The Phase 3 development programmes are global projects, which would be challenging for a company of any size. So is it for Destiny, which has a small workforce and had cash and cash equivalents of £4.9 million as of 31 December 2022. But the company has significant advantages as well. These include continuity of management and an internally developed lead product.

Destiny's in-house product is an antibacterial for the prevention of post-surgical infections arising from the *S. aureus* bacterium. The second is an in-licensed live biotherapeutic intended to reduce the presence of toxic strains of *C. difficile* in the gut.

In an interview, Neil Clark, the company's chief executive, and William Love, founder and chief scientific officer, discussed progress with the products. Both have recently been reviewed in scientific journals, and one, to prevent *C. difficile*, has secured a partnership with Sebela Pharmaceuticals Inc of the US.

Destiny is now holding talks with potential partners for its wholly owned antibacterial, a nasal gel which is called exeporfinium chloride (XF-73). This follows feedback from both the US Food and Drug Administration and the European Medicines Agency on the planned Phase 3 programmes. Mr Clark said the two regulators had different approaches but both views can be accommodated.

A Phase 2 study of XF-73 completed in 2021 and the results were recently published in the journal *Infection Control & Hospital Epidemiology*. The lead author Julie Mangino is professor of infectious disease at The Ohio State University, US, and was a member of the study's Data Safety Monitoring Committee.

The placebo-controlled study enrolled 83 cardiac-surgery patients in nine centres in the country of Georgia, two centres in Serbia and two in the US. The patients all had *S. aureus* carriage. The primary endpoint of the study was to measure the change in bacteria presence in the nasal passage from baseline to one hour before surgery. The results showed that XF-73 achieved a 99.5% decrease in *S. aureus* nasal carriage. "Administration of XF-73 nasal gel <24 hours prior to surgery rapidly and significantly reduced nasal *S. aureus* burden preoperatively," the authors write.

Why is this? In the interview, Dr Love explained that as an antibacterial, XF-73 binds to the outer membrane, largely of gram-positive bacteria, causing the membrane to become leaky at a microscopic level. This allows low molecular weight intracellular components to rush out, killing the bacteria very rapidly, within minutes. "It's that loss of vital intracellular components within minutes, whether the bacteria are active or not active, that kills the bacteria," Dr Love said.

This is a different mechanism of action from many commonly used antibacterials which act on DNA or RNA replication or inhibit protein synthesis. The traditional drugs act on an active metabolism of the bacteria. This is not the case for XF-73 which can have an effect against bacteria that are moribund and even within a biofilm setting. Moreover, the fact that XF-73 can kill a bacterium quickly means the pathogen doesn't have time to mutate and throw up resistant strains. This robustness has been tested in a laboratory setting where the company tried to drive resistance from methicillin-resistant *S. aureus* (MRSA). "MRSA was not, within that test system, able to mutate and throw up strains that were resistant to XF action," Dr Love commented.

There is still some distance to go before XF-73 is reviewed by regulators for a possible market launch. The upcoming global Phase 3 programme is expected to enrol approximately 2,000 people and be spread across two trials. One will be conducted in patients who have undergone breast reconstruction after mastectomy and the other for emergency orthopaedic operations. The goal is to deliver the fullest label for XF-73. "This means it could be used before all significant surgeries to prevent post-surgical infections caused by *staph aureus*," Mr Clark said.

In 2024, Destiny is also looking to start a Phase 3 programme for its live biotherapeutic NTCD-M3 (non-toxigenic *Clostridioides difficile* strain M3) which was in-licensed in 2020 from a company owned by the developer, Dale Gerding. With a partnership with Sebela in place, Destiny has started to scale up manufacturing of the product, which is an oral formulation of NTCD-M3 spores. The concept is to use a non-toxigenic strain of *C. difficile*, which lacks the genes that can express toxic strains of the bacterium, to cover the colon of a patient after that patient has been treated with an antibiotic. This then enables the gut microbiome to return to normal.

"The non-toxigenic *C. difficile* strain occupies the ecological niche within the gut that the toxigenic strain could have, or would have occupied, had our strain not been administered," Dr Love said. "Then, over the next 20 odd weeks when the gut would normally come back into balance and the normal status of the microbiome in the gut is restored, then as that happens naturally, the temporary carriage of the non-toxigenic strain is lost," he added.

A Phase 2 study of NTCD-M3 recently reported that patients suffering from *C. difficile* infection who received the live biotherapeutic experienced a significant reduction in *C difficile* recurrence.

This article was prepared by the *MedNous* editor on the basis of a literature search and an interview with Neil Clark, CEO, and William Love, CSO of Destiny Pharma Plc.