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Recce nears clinic with 'master key' antibiotic to take on superbugs

By Tamra Sami, Staff Writer

PERTH, Australia – A new class of synthetic antibiotics with broad-spectrum activity is being developed by Sydney-based Recce Pharmaceuticals Ltd. that could solve the problem of antibiotic resistance.

"We have a completely new class of antibiotics, and there has not been a new class of antibiotics worldwide for around 30 years," Recce Executive Director Michele Dilizia told *BioWorld*.

"Typically antibiotics are either derived from natural sources such as penicillin or they've been modified to give them additional spectrum of activity. Our antibiotic is completely different because it is entirely synthetic," said Dilizia, who is also a co-inventor of the technology.

"Not only is it a new class that will tackle all bacteria, including superbugs, but it will keep on killing and not be vulnerable to any attempt by bacteria to mutate and overcome our mechanism of action."

She explained that traditional antibiotics operate on a lock-and-key mechanism such that the antibiotic will look for a specific part of the bacterial membrane, lock into it, and destroy the bacteria. But as soon as the bacteria mutate, the antibiotic stops working.

Comparatively, Recce's mechanism of action is "universal," akin to a "master key" to the bacterial membrane so that the antibiotic adheres to the outside membrane of the bacteria, reacts with the protein, and destroys the bacteria.

"It will not only kill the bacteria, but because it is a universal means of killing, any mutation is rendered of no consequence," Dilizia said.

Executive Director James Graham said that traditional antibiotics have one, two or three active sites, but as a polymer, Recce's compound has millions of active sites.

"We have an extremely powerful antibiotic that has been able to kill every bacteria it has tested against," Graham said. "We are breaking the paradigm of antibiotic use through a completely different mechanism of action."

Lead candidate Recce 327 was developed for treating blood infections and sepsis derived from *Escherichia coli* and *Staphylococcus aureus* bacteria, including their superbug forms.

Sepsis affects around 30 million people worldwide, and one-third of them die within the first 24 hours, according to Recce.

Founder and inventor Graham Melrose, who now serves as the company's executive chairman, has a strong background in polymer chemistry and was formerly head of research with Johnson & Johnson. He wanted to continue the work he was doing at J&J and set up his own lab in Perth where he developed Recce 327. Dilizia joined him and helped set up a more intensive microbiology lab, growing bacteria, developing tests and confirming the activity of the compound.

The compound was tested against a wide range of bacteria, including a deadly strain of *E. coli* that was resistant to all antibiotics. Dilizia said the agar plates were spotless, and there was no organism they tested that could not be killed.

Preclinical results in mice for methicillin-resistant *Staphylococcus aureus* (MRSA) were also positive.

FDA QIDP status granted

The FDA awarded Recce 327 qualified infectious disease product (QIDP) designation as a broad-spectrum antibiotic, used intravenously against *E. coli* and *Staphylococcus aureus* bacteria in the blood, including their superbug forms. The QIDP designation provides for an expedited review and 10 years of market exclusivity.

QIDP designation is part of the U.S. Generating Antibiotic Incentives Now (GAIN) Act and was formed to encourage drug companies to develop new treatments for antibiotic-resistant organisms known to cause serious or life-threatening infections.

"The fact that Recce 327 meets the FDA's criteria for qualified infectious disease product designation is a tremendous validation of our strategy to invest in synthetic polymers as potentially a whole new-class of antibiotics, said Melrose.

In February, Recce submitted additional data to the FDA that included expanded preclinical data and a proposed phase I trial program.

The company has a meeting scheduled with the FDA in May to discuss the regulatory pathway for Recce 327. Graham said U.S. phase I trials could begin later this year. Recce plans on targeting the American market first since roughly 47 percent of the antibiotic market is in the U.S.

As a broad-spectrum antibiotic, the technology is applicable to a range of infections and formulations, and Recce plans on creating a portfolio of products, including an oral formulation for *Helicobacter pylori* and other applications. For now, it is focusing on the I.V. formulation first to treat the most urgent health needs.

"We are looking to break the antibiotic business model," Graham said. "Physicians are trying not to prescribe antibiotics for fear of them becoming resistant, but less prescriptions means less sales, and less sales means less return on investment, so less motivation to develop new antibiotics.

"If you have a drug that does not become resistant, no matter how many exposures, you break the current block on the industry, because the physician can prescribe the antibiotic without fear of it becoming resistant.

"This could be the biggest thing since penicillin," Graham said, noting that penicillin was discovered in Australia, but it couldn't find funding here; it finally found support in the U.S.

Meanwhile, governments around the world are taking both a carrot and stick approach to entice pharma companies to develop new antibiotics by trying to fine them for not developing new antibiotics and at the same time offering huge rewards.

Recce has its eyes on the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) global initiative, which is offering a $1 billion reward for each new antibiotic approved, as well as increased R&D funding.

The QIDP designation is making big waves among Australian investors, Graham said.

The Australian government awarded its R&D tax credit for Recce's clinical trials in the U.S., which is an unusual move, because it means that Australian taxpayers will pay 43.5 percent of the company's R&D expenses to support its international development. The tax credit is normally awarded for companies developing drugs in Australia and is intended to support clinical trials in Australia.

Manufacturing capability in Australia will allow Recce to control the process while also keeping the knowledge in Australia, Dilizia added.

With a market cap of A$21 million (US$16 million), Recce listed on the Australian Securities Exchange (ASX:RCE) in January 2016. It raised A$5 million in its IPO, and the funds raised helped the complete preclinical trials and establish a manufacturing facility to prepare for phase I trials. Graham said the company has completed those goals and will raise money to conduct phase I trials. ♦