

Untapped potential

After 20 years of false starts, Emisphere is shaping up

BY GEORGE E. JORDAN
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For two decades, Emisphere Technologies has struggled to get its footing.

The Cedar Knolls biotechnology company has no products on the market, despite spending tens of millions of dollars in a failed effort to turn injectable drugs such as insulin and the blood-thinner heparin into easy-to-take pills and tablets. On Wall Street, the company had a reputation as a severe underachiever.

Enter Michael Novinski, the former president of Organon BioSciences who decided to move on last year when Schering-Plough bought the Dutch pharmaceutical company. After 28 years working at drug giants such as Organon and Wyeth, Novinski was ready for the challenge of running a smaller company.

"There were a lot of promises delivered by (Emisphere's) past management team, and a lot of promises not kept," said Novinski, who arrived last April and quickly revamped the company's upper management. "Basically, we've been around 20 years and couldn't get a Phase II clinical trial right. It was a classic case of knowing what you know, and knowing what you don't."

By most accounts, Novinski is an executive who knows what he knows. The company now has a co-development deal with Novartis, which is in Phase III testing of osteoarthritis and osteoporosis therapies turned into tablet form using Emisphere's technology, called eligen. It could be ready for Food and Drug Administration approval within a year or two.

"You have to say to yourself, would Novartis spend that much on something they have no confidence in?" said Steve Brozak, an analyst at WBB Securities. "If it works for one product, how many others does it work for?"

Separately, Emisphere is exploring development of a diabetes tablet made from a compound called glucagon-like peptide 1, which induces cells in the pancreas to churn out insulin. And it is developing tablet forms of popular nutrients such as

vitamin B12, which is administered worldwide via hundreds of millions of injections annually. FDA approval of vitamins and nutrients is less rigorous, and cheaper and less time-consuming, than winning marketing approval for pharmaceuticals.

FUTURE PLANS

Because Emisphere's technology potentially works with such a wide range of compounds, Brozak said the company may emerge as a takeover target for Big Pharma, which has been on a biotech buying spree.

"It will become a bidding war," Brozak said.

Novinski, who insisted Emisphere plans to remain an independent company, replaced former Chief Executive Michael Goldberg, a physician who continues to serve on the board. He presided over a publicly held company for 17 years using consultants as chief financial officers, no chief legal counsel, less-than-desirable financial controls and no broad-based pre-clinical de-

Emisphere
\$1.63 ▲ \$0.14

velopment program, according to Novinski and Wall Street analysts.

Goldberg and other members of Emisphere's board declined to comment through the company's spokesman, Bob Madison.

Wall Street analysts pan Goldberg for a missed opportunity. They argue the company never raised enough money to carry its development of oral insulin and the blood thinner heparin through to FDA approval.

"The past management probably promised too much and didn't deliver enough," said Rahul Jasuja, an analyst who follows Emisphere at MDB Capital, an investment bank in Santa Monica, Calif. "There have been strategic mistakes. They were penny wise, pound foolish."

Emisphere's research, focused almost exclusively on the potentially lucrative heparin and insulin products, showed its techniques could indeed turn the injectable proteins into oral tablets that delivered medicine to the bloodstream. The technology was so compelling it attracted the interest of Eli Lilly, which made a takeover bid for the company several years ago. Emisphere rejected the bid.

Ultimately, Emisphere's insulin and heparin tablets failed in Phase II trials because they were too bitter or the formulations the com-

pany tested did not consistently deliver a high enough dosage. Emisphere lacked the capital to go back to the drawing board, revise the formulation and start the tests anew, Jasuja said.

As a result, the company's share price went into a freefall after reaching a high of about \$80 eight years ago. It has been stuck below \$10 for the past two years. Jasuja estimated Emisphere's share price today would be between \$40 and \$60 if it pressed ahead with development of oral insulin and heparin.

"When you have a few failures, you've got to make sure you finance the company to bounce back to do those experiments again," he said. "These guys never did that. They handicapped themselves that way. They always had half-baked stuff."

A LUCKY BREAK

Emisphere got into its current position through classic scientific serendipity.

A scientist at the company, whose name has long been forgotten, was working on perfecting super-small capsules when he stumbled on what the company calls "chemical chaperons," according to Richard Connor, Emisphere's assistant vice president for quality control and one of the company's most senior employees.

Connor said the scientist was struck by a whim. Why not fill some of the microcapsules with his diabetes medicine and feed them to a laboratory mouse?

He figured the mouse would be unaffected, because insulin cannot be taken orally. Digestive juices in the stomach make the drug ineffective. That's why diabetics inject their medicine directly into the bloodstream.

But the mouse's blood sugar dropped, Connor said. Something in the microcapsules had allowed insulin to pass through the mouse's gastrointestinal tract unmolested. It was later discovered synthetic chemicals in the microcapsules "stun" cells in the intestines and stomach to allow the medicine to pass into the bloodstream unaltered.

Two decades later, Emisphere finds itself stuck in place, touting a technology that has never made it to market.

"The technology is not commercialized," Novinski said. "That explains the single-mindedness to get the B-12 product on the market."

"I think you do that, the fortunes of the company will change dramatically. It only takes one product."

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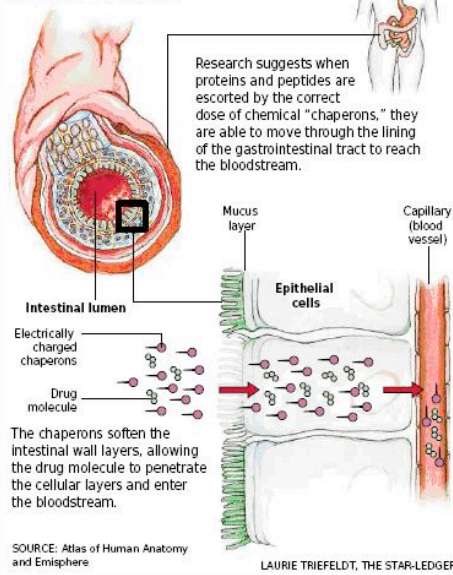
PATTI SAPONI/THE STAR-LEDGER

Michael Novinski, Emisphere's CEO, is trying to turn the company around.

Breaking the intestinal barrier

A new biotechnology called eligen has been developed by Emisphere, which is being used by Novartis in Phase III testing of an osteoarthritis drug. The technology would allow a variety of medicines that presently need to be injected to be administered in pill form.

Traditionally, proteins and peptides do not work when ingested orally because they cannot penetrate the gastrointestinal wall before being destroyed by juices in the digestive tract.



SOURCE: Atlas of Human Anatomy and Emisphere

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