

BioMarin forges business from 'orphan' malady

By Ron Leuty

December 5, 2008

Dr. Emil Kakkis' research project on a treatment for a rare, potentially deadly disease has proved a franchise for BioMarin Pharmaceutical Inc.

Now the Novato company is diving deeper into MPS, a family of rare lysosomal storage diseases, hoping to detect the inherited disorders and deliver enzyme replacement treatments earlier.

"We have solutions," said Kakkis, BioMarin's chief medical officer.

On the table are a treatment trial to put a BioMarin enzyme directly into spinal fluid of younger patients with the connective tissue disorder MPS VI and creation of a database to get a clear picture of the depth, breadth and complexities of MPS IV, also known as Morquio Syndrome.

"Most young patients are identified because they have a sibling with it," said Dr. Paul Harmatz of Children's Hospital Oakland Research Institute, which has worked with BioMarin on basic MPS research. "We're close to having the technology for infant screening."

That could have implications for BioMarin's treatments, and it comes as Kakkis, who joined the company 10 years ago, plans his February retirement.

BioMarin's two FDA-approved MPS drugs, Aldurazyme and Naglazyme, are expected to account for more than two-thirds of the company's expected 2008 revenue of \$288 million to \$326 million.

Aldurazyme was the center of Kakkis' research as an assistant professor in the genetics unit of the pediatrics department at Harbor-UCLA Medical Center. That led him in September 1998 to BioMarin, which at the time was less than two years old.

The drug targets MPS I, an inherited shortage of an enzyme that breaks down certain complex carbohydrates, leads to respiratory or cardiovascular complications, joint stiffness, slow mental development and other problems. It was BioMarin's first approved drug, in April 2003.

“BioMarin was offering me work on genetic disorders, and I realized that I’d never get that much money and opportunity to make that happen (at a university),” Kakkis said.

Now BioMarin, which less than four years ago was teetering on the edge of financial ruin, is at the top of many analysts’ lists of Big Pharma takeover targets.

The company, led by CEO Jean-Jacques Bienaimé, has more than 600 employees and in October opened a 20,000-square-foot drug-development center in Brisbane.

Through the first nine months of this year, it recorded a \$6.3 million profit, with projections of a \$30 million to \$42 million profit for the full year.

Next year, Kakkis said, the company is expected to have four products in the clinic and about six in preclinical development.

Orphan diseases — maladies that affect 200,000 or fewer patients, but carry tax and intellectual property benefits for companies that develop treatments — are the cornerstone of BioMarin’s portfolio.

In addition to Aldurazyme and Naglazyme, approved in May 2005 to treat MPS VI, BioMarin has developed Kuvan. That is aimed at the genetic disorder phenylketonuria, or PKU, in which abnormally high levels of an amino acid found in most protein-containing food accumulates in the blood and other tissues.

Kuvan was approved in December 2007 by the Food and Drug Administration and could win European approval this month.

BioMarin’s strong financials are supporting programs like the Phase I/II treatment trial of Morquio Syndrome, set to begin early next year on about 20 patients.

The trial size is small because Morquio, like other MPS diseases, is hard to detect — and even then it often isn’t pinpointed until children are 8 to 10 years old.

Morquio is estimated to occur in as few as one in 300,000 live births worldwide.

“We started with teenagers and now we’re treating younger and younger patients,” Kakkis said. “We’re getting closer to the time they’re diagnosed.”

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