

## **Stem-cell drug gets shot in arm**

### **FDA puts city lab's drug on 'fast track,' boosting chance of being pioneer**

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The Food and Drug Administration has granted "fast track" clearance to Osiris Therapeutics Inc. to expedite development of a stem-cell drug to thwart a sometimes fatal reaction to bone-marrow transplants.

Osiris said the FDA's action improves its chances of becoming the first to bring a stem-cell product to market.

The fast-track designation, granted only to therapies showing promise in treating life-threatening conditions, is thought to be the first for a stem-cell-based medication.

Osiris, which employs 40 people at its waterfront lab and offices in Canton, announced the approval yesterday.

The company predicted the action could allow it to commercialize Prochymal by 2007 - a year earlier than it previously thought.

"Our patients, they are dying, and this is probably their last chance," said Alla Danilkovitch, a senior Osiris scientist working with Prochymal. "This is what physicians and the pharmaceutical industry want."

Prochymal is designed to treat graft versus host disease, or GVHD, which affects about half of the 8,000 to 10,000 Americans who receive bone-marrow transplants yearly as a treatment for some form of blood cancer, such as leukemia.

The transplants - considered the original stem cell therapy - essentially give patients a new immune system, which sometimes rejects the recipient, causing GVHD. Symptoms of the condition, which kills more than half of those who acquire the most severe form of it, include liver disease, intestinal bleeding and peeling skin.

"It's a horrible way to die. ... If you see it once, you don't want to see somebody else go through it again," said C. Randal Mills, Osiris' president and chief executive officer. As a student at the University of Florida in the early 1990s, Mills held an internship in a bone marrow transplant ward, where he saw GVHD firsthand. "It's very personal to me," he said.

Prochymal, which was tested on 46 individuals in the first clinical trials beginning in 2000, fights GVHD by suppressing the symptoms and then regenerating the damaged tissue. Unlike other rejection-fighting drugs given to organ transplant patients, it does not suppress healthy immune responses.

Dr. Richard W. Childs, senior investigator at the hematology branch of the National Heart, Lung and Blood Institute of the National Institutes of Health, gave Prochymal to a patient who had the worst case of GVHD he'd seen. No other therapies had helped her, but this one did.

"There was evidence of tissue regeneration we had not seen before. We raised our eyebrows and said, 'Hey, this looks different,' " Childs said. "This could represent a big advance in the way that we treat any kind of autoimmune condition. ... We'll have to see how the study goes."

Mills said the drug could make it possible for more people to undergo bone marrow transplants, many of whom forgo the treatment to avoid GVHD. It may one day also be used to treat Crohn's disease, which causes painful inflammation of the small intestine, and rheumatoid arthritis.

Prochymal, made from stem cells extracted from the donated bone marrow of adult volunteers, is entering the second of three clinical trial phases the FDA requires to commercialize a product. Most companies testing adult stem-cell therapies are in the very early stages of Phase I.

"Certainly with the FDA, they are farthest along," said Dr. Joshua M. Hare, director of the cardio-biology section at the Institute for Cell Engineering at the [Johns Hopkins University](#) School of Medicine. "Osiris is clearly the leader."

A Massachusetts company, ViaCell Inc., is working on a similar therapy, but its drug is still in Phase I trials, as is a therapy being developed by Michigan-based Aastrom Biosciences Inc. to use bone marrow stem cells to treat fractures.

The fast-track designation, one of about 80 granted by the FDA since March 1998, will enable Osiris to speed the approval process by allowing the company to submit advancements to the agency's review as they happen, rather than at the end of a trial. It also means the agency will work closely with Osiris to design the trials. The company has already devoted a dozen years and about \$50 million to bring Prochymal to this point.

"This is such a big milestone for this company, this industry and this product," Mills said.

Osiris, which was founded in Ohio in 1992 and moved to Baltimore in 1994, is testing two other therapies - Chondragen and Provacal - using the same kind of adult stem cells.

Chondragen is aimed at preventing osteoarthritis and regenerating the meniscus, the crescent-shaped cushion in the knee that is injured by about 800,000 people annually because of trauma or aging.

Provacal, entering Phase I clinical trials, is designed to treat heart damage in the millions of patients who've suffered heart attacks.

"It's an absolute revolution in medicine because we now conceive of treating chronic diseases in a way that we never thought would be possible," Hare said of stem cell therapy. "We're at the brink of a new era here."

Stem cells, known as "primitive" or "precursor" cells, are found naturally in the body and prized for their regenerative abilities. They can renew themselves over and over and have the ability to develop into different types of cells. Scientists believe they could be used to regenerate and rejuvenate damaged tissue, and one day to grow spare body parts as needed.

Much has been reported recently about the ethical implications of using embryonic stem cells, derived from fetuses or embryos, in therapeutic research.

The federal government pays for research with human stem cells, but only for work with 22 lines; each line is the progeny of a single embryo. That restriction dates from Aug. 9, 2001, when President Bush issued a directive saying the government would pay for research, but only with cell lines created before that date.

No embryonic stem cell treatment has made it into clinical trials. The issue emerged during the last presidential campaign.

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