

## Stem Cells Inc.

Stem cell research is expensive, and researchers can't count on government grants. President Bush limited federal funding for stem cell research, and the National Institutes of Health budget is shrinking. Even though California voters authorized spending \$3 billion over 10 years, the California Institute of Regenerative Medicine still needed to raise money to help get projects going in the short run.

"There's an overall crisis for scientific research that is incredible right now," said Dr. Renee Reijo Pera, professor and director of the Center for Human Embryonic Stem Cell Research and Education at the Stanford University School of Medicine. "Eight percent of applications are funded. Ten years ago, it was 22 to 25 percent. We've reduced the level of funding to a level that is unsupportable. There is a tremendous need for funding for medical research."

But there is another source. Biotech companies see some promise in stem cells, with the hope that breakthroughs in the lab could lead to new drugs and therapies. Private enterprise is kicking in millions of dollars in the effort.

"We definitely need private companies in this area," Reijo Pera said. "Even at Stanford University, it's extraordinarily difficult to fund an FDA clinical trial."

Dr. Warren Hoeffler, PhD, the founder of Xgene Corporation, a company commercializing discoveries in tissue engineering, told the Dominican University of California conference on Feb. 9 that in Northern California alone, 800 life sciences companies employ 80,000 people, paying \$5.8 billion in wages.

This region accounts for 10 percent of the world's 8,000 life sciences companies, he said, and of those, 180 are dedicated stem cell companies.

"There's a lot of momentum in the business environment toward stem cell companies," Hoeffler said.

Because of the powerful nature of what stem cells accomplish in the body, the research is critical, Hoeffler said. "This is not going to go away," he said. Yet so much is unknown, and the research is so expensive and time-consuming, that businesses are really taking a chance when they place their bets on stem cells.

"In business, there's a strong relationship between risk and reward," he said. "If you take a lot of risks, you often expect a big reward," if the risks pay off. "If you reduce your risks at the beginning, you're more likely to bring products to market," he said.

The biotech industry has already shown it can hit home runs, such as Tenofovir, a drug from Gilead Sciences of Foster City that is used in AIDS cocktails and has "alleviated a lot of suffering and is a great generator of wealth," Hoeffler said, or Gleevec, from Novartis Pharmaceuticals of Switzerland, which saved the life of one of Hoeffler's friends who had gastrointestinal tumors.

"Stem cell research has the promise of curing diseases," he said. "Blockbuster drugs can bring in \$1 billion a year in revenue, and can reduce human suffering.

California's investment in Stem Cell Research is to be \$3 billion over 10 years, so the size of the investment is reasonable in terms of the earnings potential of leading therapies"

Yet the risk is great.

“Currently, the number of applications for any kind of cell therapy are very limited,” Hoeffler said. “How does one treat patients using cells? We’re used to drugs. The idea of cell therapies is quite new.”

Hoeffler cited some of the key companies working on stem cell therapies:

- Geron Corp. of Menlo Park is developing cell-based therapeutics for several diseases based on differentiated cells derived from human embryonic stem cells, including cells for spinal cord injury and Parkinson's disease, cardiomyocytes for heart disease, pancreatic cells for diabetes, osteoblasts for osteoporosis, and other cells for osteoarthritis, for blood diseases and to prevent immune rejection of the other cell types. Because investors are so taken with the promise of stem cells, Geron, which is publicly traded, has a market capitalization of more than \$370 million even though it lost \$27 million in the first three quarters of 2007. “Geron has the ability to issue new shares and fund the things they think are important,” Hoeffler said.
- OncoMed Pharmaceuticals of Redwood City is focused on cancer stem cells. OncoMed believes that cancer stem cells in tumors grow in the same way as regular stem cells, but that differences between the cells can be exploited to attack the cancerous cells. OncoMed last year announced a partnership with pharmaceutical giant GlaxoSmithKline that could pay OncoMed \$1.4 billion if it successfully discovers, develops and markets novel antibody therapeutics to target cancer stem cells.
- Advanced Cell Technology, in Alameda, is a publicly traded company investigating using adult stem cells to fight heart disease, and embryonic stem cells to fight retinal degenerative disorders. It lost \$16 million in the first three quarters of 2007.
- StemCells Inc. of Palo Alto, another publicly traded firm, is focused on the discovery and development of stem cell therapeutics to treat damage to or degeneration of major organ systems such as the central nervous system, the liver and the pancreas. It lost \$17 million in the first three quarters of 2007, and has a market capitalization of more than \$120 million.
- Xgene, which is Hoeffler’s firm, concentrates on tissue engineering. It is based in Sausalito and remains privately held. Hoeffler’s research interests focus on 3-D organ models that work on the inner and outer layers of tissue.

Hoeffler has worked on both the academic and the financial side of the equation. Hoeffler has served on the faculty at the Department of Dermatology at Stanford University School of Medicine. He conducted postdoctoral research at Genentech.

Xgene is working on skin cells, which have drawn increasing interest since James Thompson's announcement at the University of Wisconsin last year that some skin cells can mimic stem cells, without destroying embryos.

Skin cell work has already taken place in the form of skin grafts. "Now, in hospitals, if you're lacking skin in one area, they can take it from another area and graft it on," Hoeffler said. "They can take skin from your buttocks and put it on your torso."

Building on that work, Xgene has developed something it calls AccuSkin, in which it has "re-created skin from skin cells packaged in an incubator," he said.

AccuSkin is built on Xgene's patented platform AccuOrgan, which harnesses cell mechanisms to accurately re-create cell layers from a variety of sources representing organs from throughout the body. Other Xgene products include AccuGraft, an upside-down version of AccuSkin that's used for skin grafting studies, and AccuCornea, a three-dimensional human corneal equivalent.

Some of Xgene's experiments have led it into therapies that it did not anticipate. "Sometimes when you do science you come up with some pretty amazing things," he said. "We set out to make skin, and we ended up with a structure we didn't quite understand."

This new structure had an epithelium, a tissue composed of layers of cells that normally are on top of the skin, instead at the bottom. Xgene scientists saw that the epithelium a spongy material formed that "creates a scaffold that may be crucial required for establishing the blood supply during wound healing," Hoeffler said, and they were able to harness this into AccuGraftWound, a proprietary therapy. Harnessing this method may be crucial for grafting stem cells back onto patients too.

"It's quite spectacular that by doing experiments mixing cells, you can come up with an understanding of how wound healing works," Hoeffler said.

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