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Portola Valley,
Woodside and
Menlo Park.

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Beyond pills

Cell by cell,
Tom Okarma and
Geron are on track
to regenerate
failing organs.

And maybe
beat cancer.

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News This Week

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Apple CEO Steve Jobs
withdraws appeal over
demolition of 1926
Jackling house, but he
still wants to tear it down.

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The town may get a
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Matching funds are
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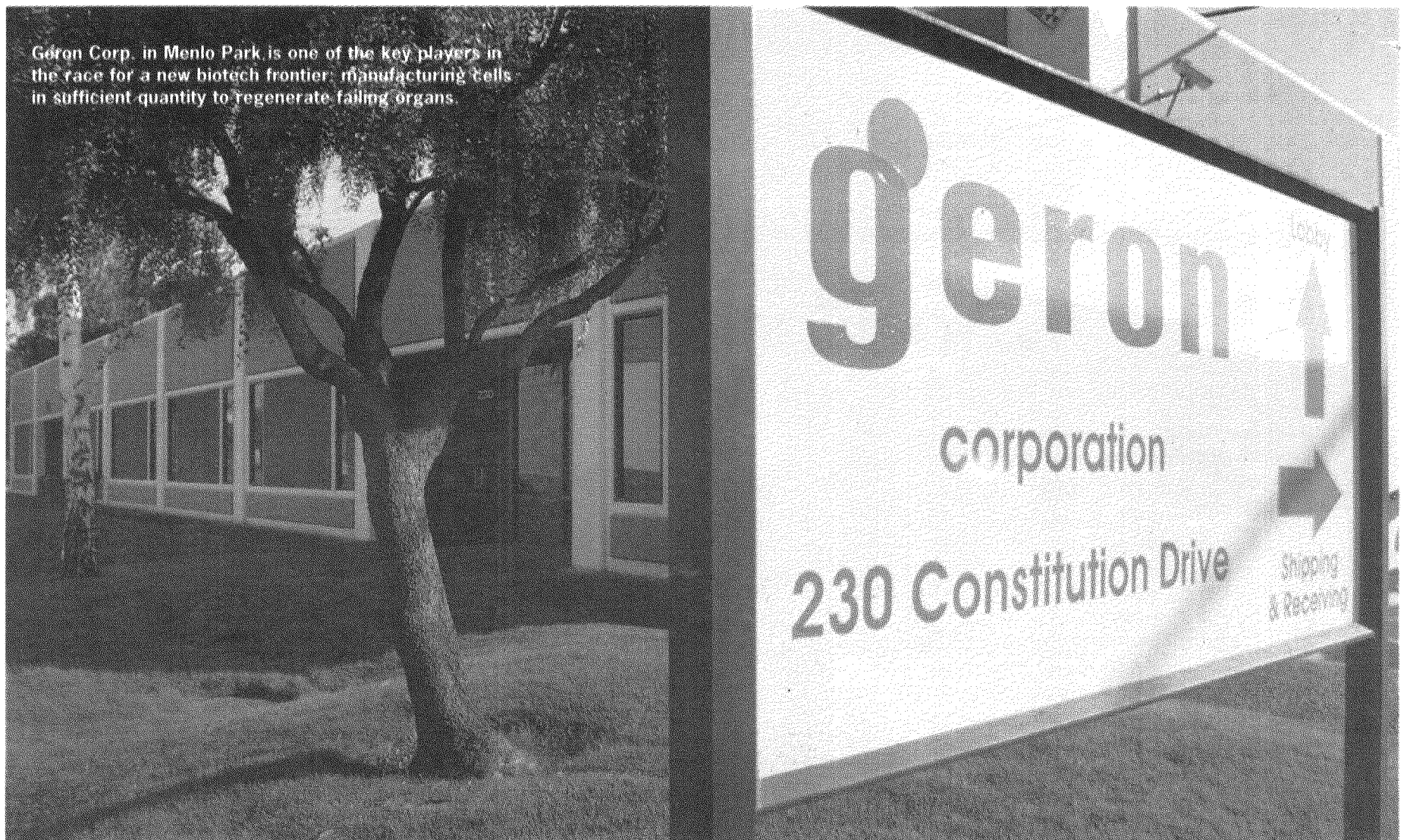
SECTION 2



■ Health & Fitness

Portola Valley's Matt
James heads up Kaiser
foundation's online health
policy information
service.

Geron Corp. in Menlo Park is one of the key players in the race for a new biotech frontier: manufacturing cells in sufficient quantity to regenerate failing organs.



Biotech: the next

In Menlo Park
Tom Okarma
and Geron are
growing cells
to rebuild
organs in
people with
failing hearts,
livers, brains
and other
organs

The boxy building near Bayshore Freeway in Menlo Park's industrial area hardly looks like a house of dreams. Yet here, under tight security, scientists at Geron are nursing vats of cells that give promise of providing new, healthy organs to people suffering from heart failure, stroke, Parkinson's, and other degenerative diseases.

The power of that promise has propelled scientists, politicians, money managers and moralists into the high-profile debate over human cloning, stem cells, and genetic engineering that occasionally shares front-page space with Afghanistan.

Geron is a leading player in this new wave of biotechnology known as regenerative medicine.

"Regenerative medicine moves from pills, which stop symptoms, to cells, which actually rebuild organs and restore their functions to normal," says Geron president and CEO Dr. Thomas Okarma of Portola Valley. "They are the self-renewing source for manufacturing replacement cells for chronic diseases."

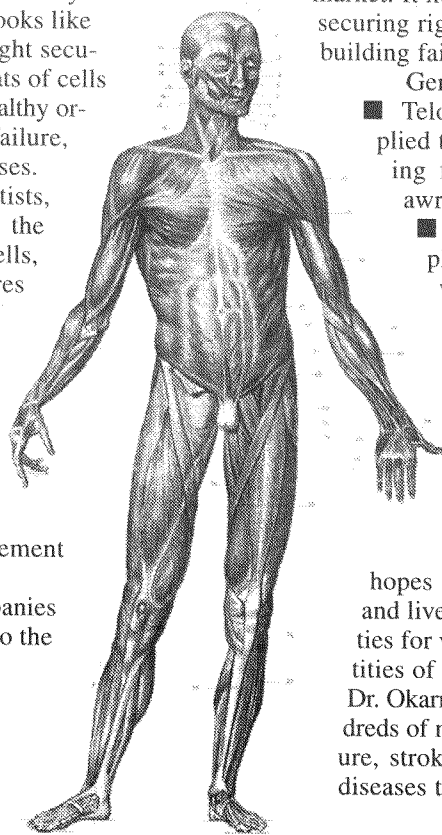
Geron is well-placed among the dozens of companies scrambling to bring these futuristic technologies to the

market. It holds more than 100 patents, here and abroad, securing rights to three key technologies essential to rebuilding failing or diseased organs.

Geron's three basic technologies cover:

- Telomerase, an immortality enzyme, can be applied to the ends of body cells to keep them dividing forever, instead of aging and dying. Gone awry, telomerase is also involved in cancer.
- Human embryonic stem cells, taken from surplus embryos from in-vitro fertilization clinics with parents' consent, can be coaxed to grow into any cell in the body. They are called "pluripotent."
- Nuclear transfer, the cloning technology that created Dolly the sheep, could allow cells to be adapted to individual patients to avoid immune rejection. In 1999, Geron bought the Roslin Institute in Scotland, where Dolly still thrives.

Building on these platforms, Geron hopes to manufacture heart muscle cells, neurons, and liver cells — among others — in sufficient quantities for widespread use. "We can make infinite quantities of them. That is what is so revolutionary," says Dr. Okarma. "It makes it possible for us to service hundreds of millions of people with liver failure, heart failure, stroke, spinal chord disease — just to name the diseases that are affected by those cell types."



By Marion Softky
Photographs by Cindy Chew

In the long run, Dr. Okarma dreams of stocking hospital shelves not with pills, but with bottles of frozen heart, liver or Parkinson's cells that are young, healthy and ready to treat patients. "We want to demonstrate how we can make these cell types with as much precision and control as Big Pharma makes pills," he says.

Meanwhile, Dr. Okarma takes a dim view of the recent announcement of cloning a human embryo by his former colleague, Mike West, of Advanced Cell Technology in Worcester, Massachusetts. Dr. West founded Geron in 1991 to study the aging process at the cellular level, and left in 1998.

The achievement is scientifically trivial, and politically disastrous, Dr. Okarma says. It may lead the U.S. Senate to vote to criminalize cloning – as the House of Representatives has already done – and block an important field of research.

"It's a very damaging contribution to the field politically, and adds nothing scientifically," he says. "It's a tragedy."

Geron itself should not be seriously affected by political fallout. It already has several stem cell lines approved by President Bush for research using federal funding. It also plans to create new lines. "We will use our own money to make more," Dr. Okarma says. "To disallow the National Institutes of Health from studying the lines that we develop is crazy."

Margaret Taylor, director of health services for San Mateo County, also feels strongly that such research should be encouraged, not forbidden. "Any research that helps us deal with debilitating disease is worth looking at more closely," she says. "I have no interest in banning research that may help people lead more productive lives."

wave?

Meanwhile, Geron is already entering clinical trials at Duke University with a prostate cancer vaccine based on telomerase. Since out-of-control telomerase is common to most cancer types, a vaccine that instructs the immune system to recognize and destroy cancer cells, holds promise to help most kinds of cancer, Dr. Okarma says. "That's the power of telomerase. It should be effective against all cancers."

When could a cancer vaccine hit the market? "I don't predict. It's too early," Dr. Okarma replies.

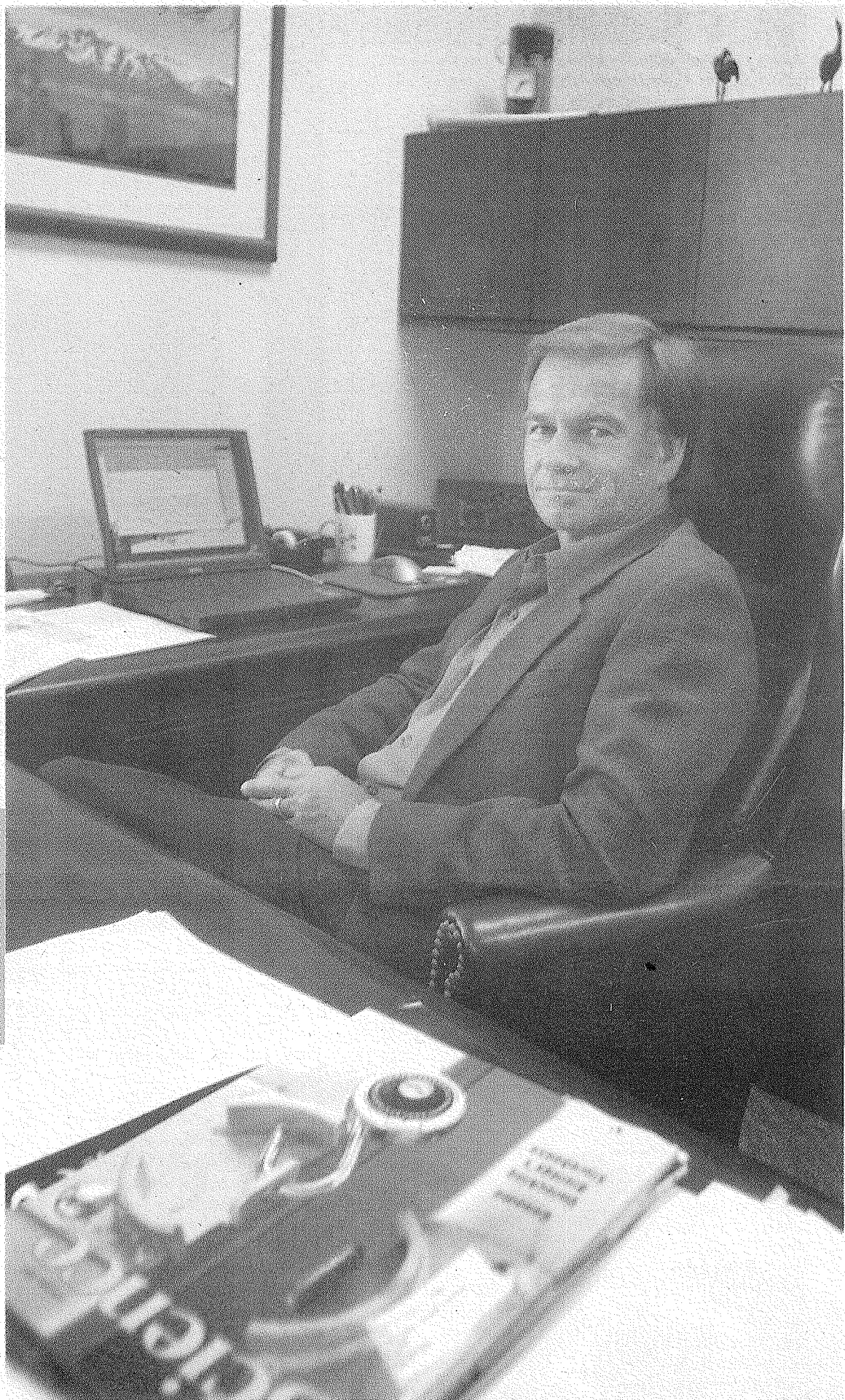
Salesman of hope

Dr. Okarma seems to fit naturally into his role as physician, scientist, executive, and missionary. He's also efficient, organized, and a popular speaker.

"Regenerative medicine is a whole new value paradigm," he recently told a standing-room audience at Woodside Village Church. "Think heart attack. Drugs can reduce pain; they cannot restore function. This could have the power to reverse chronic loss of function. We can play the tape backward."

Tom Okarma was born and raised on a dairy farm in New Jersey, and attended high school there. A degree in biology from Dartmouth College led

See **GERON**, next page



Dr. Thomas Okarma of Portola Valley has a dream for regenerative medicine. Some day hospital pharmacies may be stocked with bottles of frozen cells to replace failing cells that can rebuild whole organs for patients with chronic disease.

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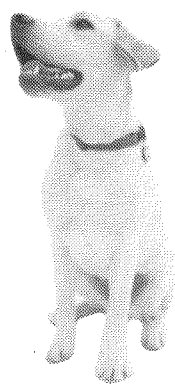
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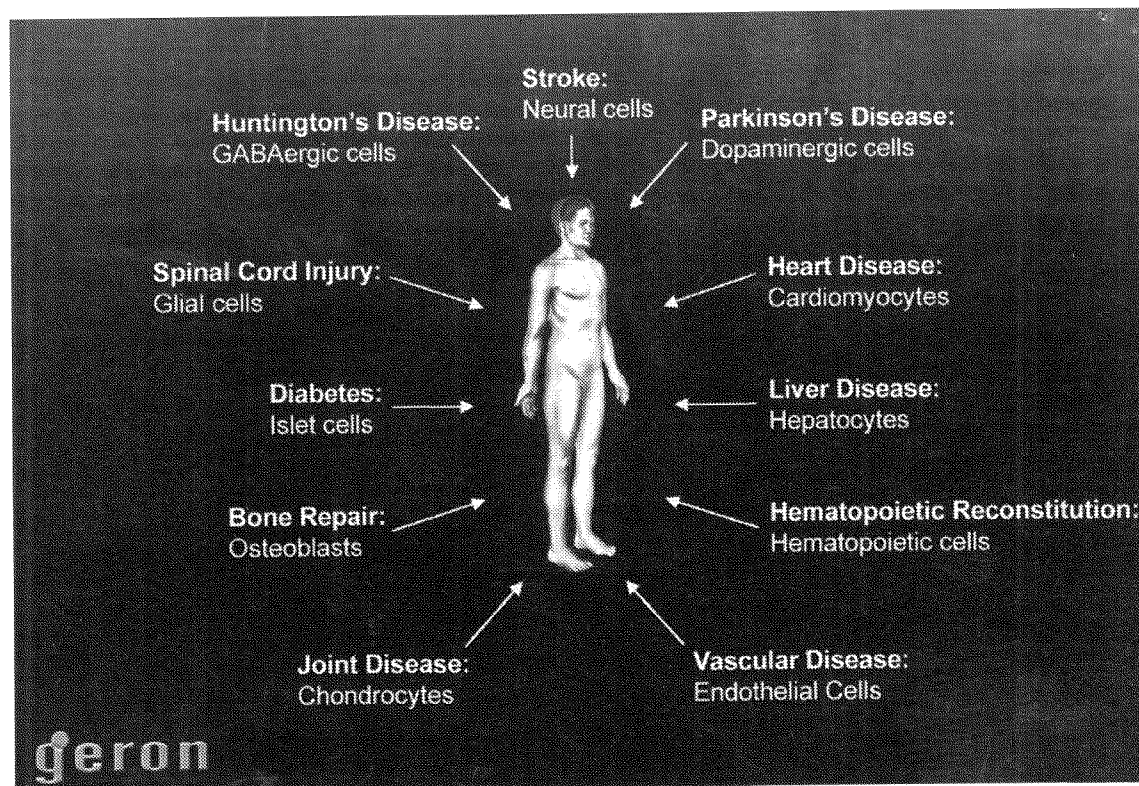
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Courtesy of Geron Corp.

Possible applications of human embryonic stem cells being grown by Geron Corp. in Menlo Park are shown above. These cells may be coaxed to grow into any cell in the body, and substituted for cells in failing organs.

GERON

continued from previous page

him to Stanford, where he earned a Ph.D. in pharmacology in 1972 and an M.D. in 1974.

Another 11 years treating patients and teaching at the Stanford Medical School and Veterans Affairs Medical Center left Dr. Okarma frustrated at the limits of conventional medicine and drugs in treating immune disorders and diseases of aging.

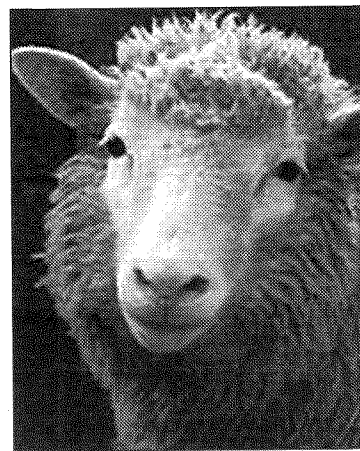
"The power of cells came home to me," he says in an interview in his Geron office. "I view cells as therapeutic entities."

Dr. Okarma slowly realized he could not pursue such revolutionary theories in an academic environment. "NIH does not fund research that far ahead of its time," he says.

In 1985, Dr. Okarma left the practice of medicine to found a start-up biotech company, Advanced Immune Sciences (AIS), the first company focused on commercializing cell-based therapies.

During the next 11 years, Dr. Okarma and AIS invented some therapies for cancer, bone marrow transplants and breast cancer, and began testing them in the clinic. After AIS was bought by pharmaceutical giant Rhone-Poulenc-Rohr (RPR), he got a taste of working for what he calls Big Pharma.

The problem with the cell therapies developed at AIS was scale, Dr. Okarma reflects. They had to be applied individually, patient by patient. "We couldn't commercialize them because they were too expensive to compete with pills, which were less



Geron is doing cloning research for agricultural applications at the Roslin Institute in Scotland where Dolly, the sheep, still thrives.

effective, but much more cost-effective," he says.

Enter Geron

By 1997, Dr. Okarma found that Geron, a company that was studying telomerase, and its role in both aging and cancer, might hold the key to manufacturing cells in sufficient quantity. He left RPR, took an MBA from Stanford, and joined Geron.

About that time Dr. Okarma and his family also moved to Portola Valley, where they live in one of the old houses on the Lauriston estate, in the middle of the Windy Hill Open Space Preserve.

At Geron, the concepts and techniques of regenerative medicine have come together.

Key to manufacturing cells in commercial quantities was the isolation of stem cell lines from human embryos by the University of Wisconsin, with funding from Geron. These cells could be persuaded to double indefinitely, and could be turned into

any cell in the body.

Several lines of these cells have been growing continuously in Geron labs for more than two years. "That's more than 450 population doublings," Dr. Okarma says, gesturing expansively. "We could fill this room with cells."

The purchase of the Roslin Institute, with its scientific team and rights to the cloning technology that produced Dolly, was aimed at the third big problem in developing practical cell therapies: immune rejection; cells need to be matched to the system of the patients receiving them.

In pursuing his dream of manufacturing large quantities of cells to treat many diseases in many people, Dr. Okarma hopes to leapfrog the Dolly technology. Cloning cells so they won't be rejected has to be done individually, patient by patient, and is difficult to scale up.

Instead, Geron is pursuing research toward genetically engineering the stem cells they already have to make them neutral to the host immune system. "Nerve cells, liver cells made from such a null embryonic stem cell could be transplanted to anyone without immune suppression," Dr. Okarma says. "So it becomes a universal donor cell."

He warms up to his dream. "Now you've got an engineered immortal, pluripotential stem cell that's silent immunologically."

"So we can make any cell in quantity, freeze it and put it in a bottle, and put it on a pharmacy shelf in a hospital for off-the-shelf use for anyone who needs it."

Dr. Okarma's dream

Dr. Tom Okarma gives his views on the promise of stem cells

"All the diseases we plan to treat – diabetes, stroke, heart failure, liver failure, spinal chord injury – are chronic illnesses. So we have to demonstrate over the long haul that these cells work consistently and permanently.

"It's not like taking a pill for high blood pressure, which in three days will lower your blood pressure. We have to follow the improvement in patient function for a long time before we have data the FDA will believe that supports our claim.

"We want to put these cells into a Parkinson's [patient's] brain to have a permanent cure. We want to put these cells in the heart of a patient with heart failure once, and permanently fix the failing

heart.

"That's the power and promise of this technology. The promise, the value, is so much greater than any pill you can think of – any 10

pills added together. You're fixing a broken heart.

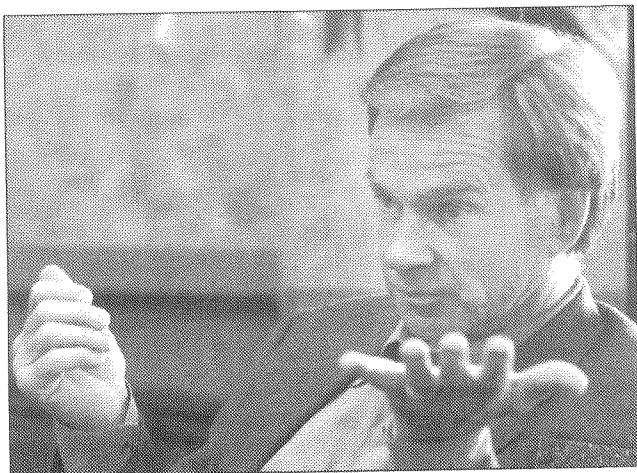
"Patients who were immobilized by stroke become mobile again. It will allow diabetic patients to throw away their insulin and lead normal lives.

"That's the promise, and a pill can never achieve that.

"Our view is it's worth the extra time, effort and

cost to commercialize products of regenerative medicine because the value is so extraordinary.

"That's what's touched everybody's imagination."



Dr. Okarma adds, "This is something I just dreamed about when I was a medical student at Stanford."

Floating hope

For all its dreams, Geron is still a long way from showing a profit. Its nine-month financial report for 2001 shows \$615,000 in operating revenues and \$11.1 million in expenses. Its stock is wobbling between \$9 and \$10. Its 52-week high was \$35.75 in September 2000.

Geron is also involved in a lawsuit with the Wisconsin Alumni Research Foundation, which holds the patents for embryonic stem cell work done with funding from Geron.

"We are so far away. We are talking about things way down the road," says Crispin Littlehales, director of communications for Burrill & Co., a life sciences merchant bank in San Francisco.

Ms. Littlehales sees Geron as promising in the long run. It is building value with its technologies and patents and some products. "When Geron has a product, it's going to be a blockbuster," she says. "Its big challenge is floating hope."

Geron already has products and license agreements that get its name out and bring in some revenue. It is selling a product that measures telomerase in cancer cells, and is selling liver cells to drug companies to use in testing new drugs, Dr. Okarma says. It also licenses the Dolly technology to agri-

culture companies to clone livestock for food-production, pharmaceuticals, or disease resistance. "It's a way of creating high-value agricultural products," he says.

Geron's near-term hope of turning red ink to black is with one of its cancer products – possibly the vaccine now starting clinical trials.

"We hope to release a blockbuster cancer drug in the near term to help fund the company for the longer, more expensive trials in regenerative medicine," Dr. Okarma says.

"You have the potential for this company to become Merck. It's real," he says. "This is a story that will have huge impacts worldwide in medicine and in agriculture."

Issues

Like many revolutionary technologies, regenerative medicine brings with it a host of political, economic, social, legal and moral issues. In particular, it touches "how we understand ourselves as human beings," Dr. Okarma told the rapt audience in Woodside.

To help guide regenerative medicine, Geron has appointed an Ethics Advisory Board made up of five prominent ethicists from different traditions. The board has prepared guidelines that would, for example, prohibit the company from cloning to create new human beings.

Will the new technologies lead to people living longer and potentially sicker?

Not so, responds Dr. Okarma. New cells could help regenerate one, maybe two organs; there is no way they can replace all cells in the body that contribute to aging.

"We are not interested in expanding your life span," Dr. Okarma adds. "We want to expand your health span – the fraction of your life on earth that is spent independently in health."

Another troubling aspect of the new technologies relates to access. Who gets the new liver, or Alzheimer's treatment, or fix for osteoarthritis? Will only the rich and well-insured be able to afford these cures? Or will they go to those who need them?

"There's a big problem here," Dr. Okarma acknowledges. "The Ethics Advisory Board is very worried about this becoming therapy for the wealthy – which again is why scalability is so important. If we can make these cells as efficiently as drug companies make pills, we won't have an access problem."

Dr. Okarma also acknowledges the U.S. health care system is not set up to provide equal health care for all, including the poor and uninsured. "In this country we have not come to the position that health care is a right," he says. "Health care is a luxury in the U.S."

Reflecting on the challenges of the new medicine, Dr. Okarma observes, "When science makes a huge paradigm advance, it's threatening." ■