

## Fighting back at ALS

**In the middle of his business studies at Harvard, Avichai Kremer discovered he had ALS, otherwise known as Lou Gehrig's disease. Now he's applying what he learned to promoting the search for a cure.**

Gali Weinreb 14 Sep 05 18:03

Until he turned 30, Avichai Kremer lived a normal life. A year ago, he began studying for an MBA at the Harvard Business School. He thought that he would be able to found a successful company within ten years. He found his studies riveting. Everywhere he looked, he saw evidence supporting the theories that he heard in lectures about the reciprocal relationship between money and the way the world was run. He felt that he was on the right track. Then something went wrong.

"It started with pains and involuntary movements in my right arm. Suddenly, I noticed that in my workouts, I was unable to lift weights with my right hand that I'd been able to lift long ago with my left. After a long battery of tests, I was diagnosed with amyotrophic lateral sclerosis (ALS), a paralyzing neuro-degenerative disorder also known as Lou Gehrig's disease, or motor neuron disease. That was when they told me, 'You can go home; we can't do any more for you'."

The causes and mechanism of ALS are unknown. It affects one out of every 10,000 people. 500 people in Israel have the disease. The disease has a genetic source in 10% of patients, but, as far as is known, it strikes the other 90% randomly. "It's not because of anything I did," Kremer stresses. "I ate correctly, I exercised, I was careful about my health. It just happened." The disease affects the nerves, which gradually stop transmitting electrical signals.

When a muscle does not receive sufficient electrical stimulation, it degenerates. Patients initially have trouble moving their limbs, and later have difficulty swallowing (although digestion, which is an involuntary system, continues to work normally). Patients usually die eventually, because they are unable to breathe. The average life expectancy of ALS patients is three years from the outbreak of the disease, although some patients die much sooner, while others live far longer. One of the most famous and long-lived patients, in whom the disease progressed very slowly, and may even have been arrested, is astrophysicist Stephen Hawking. There is no treatment for the disease, and the only drug available extends the patient's life by an average of three months, although it is not clear how it does this.

In Kremer, the disease is not yet noticeable, although he says that he has lost 10% of his weight. Only his enormous will power enables him to continue performing the smallest ordinary actions. When we met, he ordered mineral water, and explained, "These are the daily struggles: to open the bottle, put a key in the door, put my hand in my pocket." He refused help in opening the bottle, but unhesitatingly solicits help from people he meets in fighting the disease in general. The help he receives from his environment is a redefinition of the expression, "That's what friends are for."

After Kremer was diagnosed with ALS, and after he spent a few days getting used to the bad news, he began to take an interest in the disease, and read on the Internet about its causes and treatments. "I began to wonder why research into ALS, a disease that has been known to science for 150 years, has made no progress, while research into AIDS, a disease with more or less the same number of patients, which was discovered only 20 years ago, has made such progress that AIDS is already considered a non-fatal disease. Multiple sclerosis, a disease that occurs with approximately the same frequency as ALS, is being researched by dozens of researchers around the world, and enormous progress has been made in recent years."

Kremer says that this is not a medical question. The reason is not that the disease is too complex, or because decades of focused research have achieved nothing. The problem starts much earlier. There are far fewer grants for ALS, far fewer researchers, and far fewer investors.

### "Globes": Why?

**Kremer:** "It's a vicious circle that begins with the size of the market. This is a parameter that is composed of several variables: the number of patients, their life expectancy, and their willingness to pay. As far as the number of patients and their willingness to pay is concerned, the situation is all right no worse than MS or AIDS patients. The problem is the three-year average life expectancy. Why should international drug companies invest in finding a drug to improve the life of a patient who will live only three years, when they can sell drugs for combating baldness, impotence, or acne

to millions of people for their whole lifetime?

"This vicious circle means that researchers interested in ALS have neither resources for carrying out research, nor any guarantee that someone will buy its results, if any, and turn them into a drug. Such researchers will therefore prefer to concentrate on related fields, such as Parkinson's disease or MS. Another problem is that donors are also not very interested in contributing to ISRALS, the non-profit organization for ALS. Since the disease is fatal, and the money is wasted, Israeli donors prefer to invest in cancer research, where progress is constantly reported. Because of the short lifespan, there's also a problem of public relations. Few people are familiar with the disease, or know people who have experienced it and suffer from it."

**Could it be that a concealed interest of foreign insurance companies is also involved? When a drug is discovered that makes chronic patients healthy, insurance companies have less to pay. When a drug is found that makes terminal patients chronic, insurance companies have more to pay.**

"I don't believe that foreign insurance companies were a factor in this. ALS is classified as an orphan disease an infrequent disease with no known remedy. When a drug is found such a disease, it automatically enters the National List of Reimbursed Drugs. Drug companies know that if they find a drug for the disease, they will be able to sell it, regardless of what insurance companies say."

Kremer explains that if one drug is found that extends the life expectancy of ALS patients by three years, the market will begin to attract large international drug companies, or at least medium-sized ones. Finding the first drug is the key to setting market forces in motion to continually improve the lives of ALS patients. This process has already taken place with other diseases.

### **Being a good salesman**

How can that first drug be developed? "Drug companies look at return, but also at risk. If we bring them a product with a much lower risk, they can develop a drug, and be satisfied with the small return offered by the market of ALS patients, as it is at present," Kremer says. He is not asking the market for a contribution amounting to tens of millions of dollars. The organization he founded is now seeking only an initial sum of a few million dollars - \$500,000 for each research project that it plans to bring from the laboratory stage to just before clinical trials.

The assumption is that if he offers international drug companies for free, or for a nominal price, a molecule or treatment developed by well-known researchers that has gone through animal trials, the companies will be eager to conduct clinical trials. "Teva has already expressed interest," members of the organization say, "and even introduced us to the researchers that they regard as leaders in the field. Other companies are also interested."

Kremer and his friends have analyzed motives and trends in both the market for donors and the researchers market. They learned that donors prefer to put their money where it will have the greatest effect. When Kremer talks about ALS, he gives you the feeling that relatively little money will suffice to jump-start the process, and market forces will do the rest. Who will object to donating a few thousand dollars under these circumstances?

Another consideration of many donors is keeping as much of their donations as possible in Israel. For that reason, all the researchers in the project that Kremer and his group are planning are Israelis. Fortunately, Israel is a mini-power in neuro-degenerative disease research, as shown by Israeli-developed drugs Copaxone and Rasagiline.

How will Kremer find researchers? "The disease is a total mystery, and what is more interesting to a researcher than a mystery? They're curious, they want to know, and they want to save patients for whom no one is doing anything right now. Furthermore, it's also a matter of ego. Finding a drug within a few years for a disease that is incurable today means worldwide fame perhaps even a Nobel Prize."

### **Uzia Galil takes up the challenge**

Only two months ago, Kremer came back to Israel for a visit. He told several friends about his disease, and about his theory of the market factors affecting possible treatments for it. He explained that he wanted to do something about it. He didn't expect that he would have an active organization within a few days.

His friends, all young people in their 30s, recruited within a short time an amazing number of leading figures, both

from within the pharmaceutical industry, and outside it. Uzia Galil's grandson is a friend of Kremer's, and is taking part in the efforts. Uzia Galil heard about the project, and immediately offered to help. "He was the first leading figure who helped us, and he introduced us to donors and leading researchers," Kremer says. Among the prominent sources of concrete help, Kremer lists Pitango Venture Capital, Gemini Israel Funds, Jerusalem Venture Partners (JVP), Proneuron Biotechnologies scientific founder Prof. Michal Schwartz, and Teva chairman Eli Hurvitz through the Pontifax fund.

Help has also arrived from unexpected directions. JVP managing partner Erel Margalit, who took an interest in the venture, explained to Kremer's group that his fund did not specialize in life sciences. "He promised us that if we found an incubator or fund that would invest in our projects, he would provide supplementary financing," explains Idan Geva, one of the leaders of ISRALS, and a childhood friend of Kremer. "Following his offer, we appeared a month ago at a conference of life science incubators."

As part of their efforts to raise money, the ISRALS team began an exhaustive search for a Palestinian ALS patient, so that they would be able to request aid from European funds that donate to cooperative efforts between Palestinians and Israelis.

ISRALS has already managed to raise \$250,000 out of the \$500,000 originally planned, and looked for two suitable projects. They were quickly inundated with projects, and had to reject several, at least until they receive additional donations.

The main weak point in Kremer's plan is that, statistically, only 20% of projects reaching the pre-clinical phase become drugs, which means that ISRALS must promote at least five projects. This will cost \$1.25 million, assuming that each research project produces a molecule suitable for a trial. This fact makes the initial selection of research projects extremely important.

"We have a team of expert advisors that includes one of the leading researchers in ALS, who is also the doctor who treated me in the US," Kremer says. "One of the factors that led researchers to make proposals to us was the possibility of exposure to such a senior team. The team helps us select the projects. One criterion is that only projects capable of reaching the clinical trials phase within two years will receive financing from us. Theoretical research about the disease is important, but we can't afford to finance it."

"All in all, it's quite fun," Kremer sums up. "While I was studying for my degree, I thought I'd found a start-up within ten years. I never thought that in the middle of my degree, I'd already lead significant activity, and work every day with my best friends. We've created something amazing within two months that is also very important. If our venture really succeeds, and we discover that first drug, we can do the same thing for patients suffering from other rare diseases."

Kremer is talking about a process, but also never forgets the goal for a moment. "We have to discover a drug. If we don't discover a drug, we may have made a big splash, but we won't have really accomplished anything. In the end, it's clear everything will be measured by the results."

*Published by Globes [online] - [www.globes.co.il](http://www.globes.co.il) - on September 14, 2005*