A Passion for Tough Medical Problems

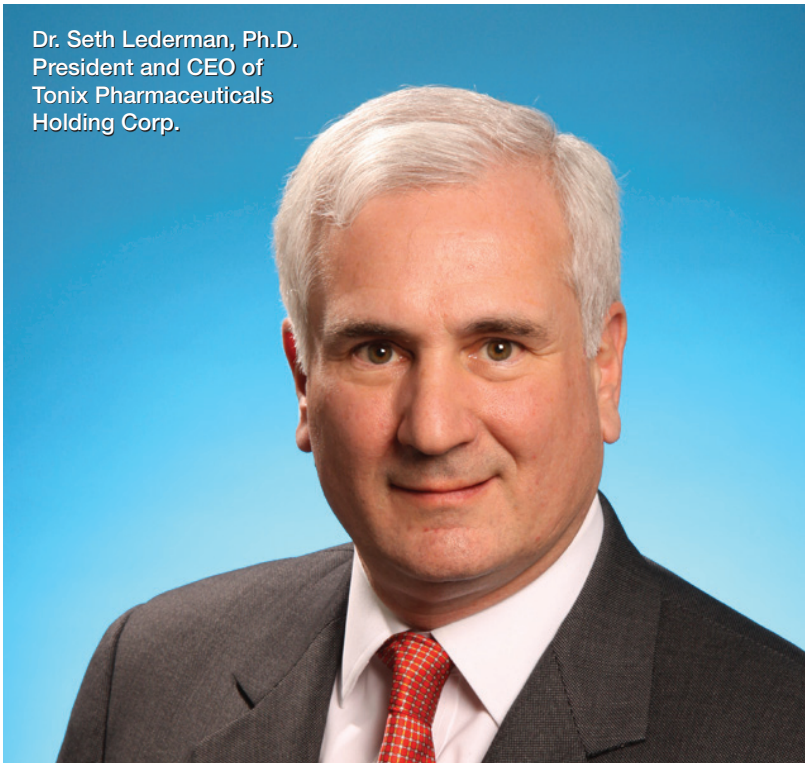
Dr. Seth Lederman and his company Tonix Pharmaceuticals Holding Corp. aim to ease the pain and suffering of millions of patients with fibromyalgia

Dr. Seth Lederman has always been drawn to tough medical fights. In the 1980s, he did work in AIDS, working to keep patients alive before effective drugs were available and helping to figure out how HIV infects cells. Now, he's taking on the challenge of fibromyalgia, a condition that brings often-severe pain and fatigue to more than five million Americans. Many doctors don't even like to give patients a diagnosis of fibromyalgia because there are few available treatments. That hasn't stopped Lederman. "I got into science to be a foot soldier in the war against the greatest medical problems of our era," he says.

But Lederman believes he and the company he founded, Tonix Pharmaceuticals, Inc., now are on the verge of a major advancement in the field. They are developing a drug that, in a Phase 2 trial, dramatically reduced the pain suffered by fibromyalgia patients. Moreover, the drug appears to work by improving a key type of sleep—a mechanism that suggests that the drug may be effective against other types of pain as well. "I am very passionate about this product," says Lederman, chairman, president and CEO of Tonix Pharmaceuticals Holding Corp. ("Tonix"). "We're talking about a non-addictive treatment for chronic pain, which may be the biggest medical problem we face today."

The next step for the drug is conducting the two large-scale trials needed to get approval from the U.S. Food & Drug Administration. Lederman and Tonix plan to begin the first pivotal trial in early 2013. Moreover, if the two trials prove that the drug, which Tonix now calls TNX-102, is effective, Tonix believes approval by the FDA should be relatively straightforward. That's because the product is actually a reformulation of a drug, cyclobenzaprine, that's already been on the market for 35 years. The drug was first approved by the FDA in 1977 under the brand name Flexeril® for the treatment of acute muscle spasms. Lederman and Tonix are proposing to use the drug in a new way, for the management of fibromyalgia.

The idea for the product came from Dr. Iredell Iglehart III, a Baltimore, Maryland rheumatologist, in the late 1990s. In his private practice, Iglehart saw many patients with unexplained pain, tenderness and fatigue—the classic symptoms of fibromyalgia. But he noticed another symptom that many other doctors missed: Fibromyalgia patients typically don't sleep well. "A lot of doctors don't take enough time with their patients to ask about sleep," says Lederman. "As a result, the sleep problems of fibromyalgia patients have gone largely unnoticed."



Dr. Seth Lederman, Ph.D.
President and CEO of
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Iglehart also knew that cyclobenzaprine seemed to have an effect on sleep. But he thought that when it came to the sleep problems, the originally approved dose of Flexeril®—a 10 milligram tablet given three times a day—was like hitting a nail with a sledgehammer. What if patients were given just one small dose right before bedtime, he wondered? He tried it with

his patients. It worked. They slept better and had less pain.

In fact, the approach worked well enough for Iglehart to patent the idea of low dose cyclobenzaprine given at bedtime. And the idea seemed promising enough for L&L Technologies, a company Lederman had founded with partner Dr. Donald Landry. L&L Technologies acquired the rights to the idea from Iglehart.

Lederman and Landry then assigned the rights to Vela Pharmaceuticals, another company Lederman had co-founded. Vela then did a study in 2000, giving low dose cyclobenzaprine to 36 patients for 8 weeks.

The results "were beyond our wildest expectations," says Lederman. The study showed that the patients' pain dropped by 26%. Just as important, the data revealed that the quality of the patients' sleep had been significantly improved. The full results were published in December 2011 in the Journal of Rheumatology [http://jrheum.org/content/early/2011/08/30/jrheum.110194.full.pdf+html]

What did the analysis show? Non-dreaming sleep has three basic rhythms, Lederman explains. Two of them are associated with disturbed, non-restorative sleep. The third is the stable sleep that leads people to wake up feeling refreshed and restored. The trial showed that the low dose cyclobenzaprine decreased the length of the disturbed sleep, and increased the amount of restorative sleep. "For the first time, we showed that a drug treatment could improve the quality of sleep—and the symptoms of fibromyalgia," says Lederman.

But while the trial was enormously encouraging, the drug's development quickly ran into a roadblock. In 2001, Vela Pharmaceuticals hired a prominent former ex-FDA official to evaluate the company's drug portfolio. The consultant told Vela that the agency would never approve a product for fibromyalgia. The reason: "A lot of people were skeptical that fibromyalgia was even a real condition," explains Lederman.

So Vela put the project on hold. Lederman and Landry still believed in the idea, however. They eventually managed to get back the rights to low dose cyclobenzaprine for fibromyalgia from Vela in 2005, returning the asset to L&L Technologies.

Then, in June of 2007, the agency approved a Pfizer drug called Lyrica (which had already been on the market for pain in diabetics and for epilepsy) specifically for fibromyalgia. "That was good timing for us," says Lederman. "The approval of Lyrica improved the value of our asset dramatically."

The fact that the FDA was open to approving drugs for fibromyalgia enabled Lederman to raise the money to start his current company, Tonix, to continue developing the low dose idea.

It also helped that the potential market for the drug is very large. Fibromyalgia patients and their insurers spend about $1.3 billion per year on prescription drugs. Yet neither Lyrica nor the other drugs now approved for fibromyalgia, the anti-depressants Cymbalta and Savella, target the sleep problems that may underlie the other symptoms. That's why Lederman expects many patients currently taking those medications to try his drug when it becomes available, and many more patients who don't take those drugs at present may consider trying the new alternative. What's more, the availability of an effective treatment might bring more people to doctors' offices with fibromyalgia symptoms. "When a good therapy is available, more people are happy to get the diagnosis," explains Lederman. Finally, the sleep quality improvement could reduce other types of pain as well.

Now Lederman is focused on the next step—preparing for the first of the two required large-scale studies. Once that study is done, Tonix could be acquired by a big pharmaceutical company, which would then conduct the second required study. Or, Tonix could go ahead itself to bring the drug to market on its own.

Either way, Lederman is excited about the prospects—and the impact that this drug could have on solving a once intractable medical problem. "It's an exciting opportunity," he says.