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Drugs to Help Smokers and Block Heart Attacks Show Promise

By ANDREW POLLACK

Two experimental drugs developed by biotechnology companies - one to prevent heart attacks and the other people quit smoking - have shown promising preliminary results, executives said.

One company, [AtheroGenics](#), said yesterday that its drug for atherosclerosis had significantly reduced the volume of plaque that can clog arteries. The results, in a midstage clinical trial, sent the company's stock soaring in after-hours trading.

The other company, [Nabi](#) Biopharmaceuticals, is expected to announce today that its vaccine against nicotine helps people quit smoking in a small clinical trial.

The results of the AtheroGenics trial had been eagerly awaited because removing fatty plaque from the arteries is considered a new goal for cardiovascular drug therapy. Even the statins, the widely used anticholesterol drugs, can do little if anything to reduce plaque.

AtheroGenics said its drug, AGI-1067, reduced plaque volume about 3 percent to 4 percent after a year, as measured with ultrasound. The reduction was statistically significant compared with the patients' starting levels, but not as much as with the lesser reductions in patients who got a placebo.

Doctors in the trial cautioned that the preliminary results covered only 133 of about 260 patients, but nevertheless promising.

"We want to see the final data but at the same time, I'm encouraged," Dr. Steven E. Nissen, a cardiologist at the Cleveland Clinic, said on a company-sponsored conference call with analysts. "It's a substantial change."

Dr. Nissen said that while it could be misleading to compare the results of different trials, the reduction in plaque achieved by AGI-1067 was roughly equivalent to that recorded in a 47-patient trial last year using a drug developed by [Esperion Therapeutics](#). In December, shortly after the results of Esperion's trial were announced, [Pfizer](#) agreed to pay \$1.3 billion to acquire the company.

Speculation that AtheroGenics might also be acquired - or at least will sell the rights to AGI-1067 for a large sum - helped fuel the rise in the company's stock. The stock closed down 43 cents at \$23.16 in regular trading but soared as much as 80 percent in after-hours trading.

AGI-1067, which fights the inflammation involved in heart disease, is in some sense more attractive than Esperion's drug because it is taken as a pill rather than given by intravenous infusion. AtheroGenics, based in Alpharetta, Ga., is already in a final-stage trial to determine if the drug actually does prevent heart attacks. If so, it hopes to apply for approval at the end of next year for approval from the Food and Drug Administration.

As for Nabi's nicotine vaccine, 33 percent of those who got the highest dose quit smoking for at least 30 consecutive days compared to 9 percent who got a placebo, Dr. Henrik S. Rasmussen, Nabi's senior vice president for clinical, medical and regulatory affairs, said in an interview. Still, the trial was small, with only 68 patients, and it could

ruled out that the difference between the vaccine and the placebo resulted from chance.

Two investigators in the trial, Dr. Stephen I. Rennard of the University of Nebraska and Dr. Dorothy Hatsukami of the University of Minnesota, called the results encouraging.

Smokers find it hard to quit because the nicotine binds to receptors in the brain and gives them a positive feeling, Dr. Rasmussen said.

The vaccine, which was given by four injections over six months in the trial, consists of nicotine connected to a detoxified bacterial protein, which, when injected, causes the body to form antibodies against nicotine. (Just injecting nicotine by itself would not elicit the antibodies.) After that, if a person smokes, the antibodies would bind to the nicotine and prevent it from reaching the brain.

"We're basically taking away the positive enforcement, which is the main reason people can't stop smoking," Dr. Rasmussen said.

Nabi, based in Boca Raton, Fla., will do more studies to determine the best dose and hopes to begin final-stage trials by the end of next year, Dr. Rasmussen said.

[Xenova](#), a company based in Britain, and Cytos, based in Switzerland, are also working on nicotine vaccines, while Pfizer and Sanofi-Aventis are testing drugs that work by other means. The therapies already approved to help people quit smoking are [GlaxoSmithKline's](#) drug Zyban, and a variety of patches, gums and other products that contain nicotine, Dr. Rennard said.