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Isis, TargeGen Set Sights on Eye Treatments

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Federal approval of a competitor's drug to treat a leading cause of blindness has not blurred the path toward a multi-billion-dollar market for local innovators.

At least two local biotechnology companies, Isis Pharmaceuticals Inc. and TargeGen Inc., are charging forward with testing for their potential treatments for age-related macular degeneration, despite approval by the Food and Drug Administration on June 30 of Genentech Inc.'s Lucentis. Analysts expect Lucentis to be more successful than the other two currently approved drugs for AMD.

The painless disease affects more than 10 million Americans and is the leading cause of blindness in people older than 50, experts say. The number of people with AMD is increasing by about 200,000 annually, partly due to the aging baby boomer population.

But are the latecomers' efforts in vain, considering several years and millions more dollars are necessary to complete the required three phases of clinical trials? Consider the fact that the FDA could also deny their applications, striking down the entire effort in a flash.

And won't the market be more difficult to penetrate once "big pharma" advertising dollars make household names out of Lucentis and Pfizer's Macugen, approved a year ago?

No, says TargeGen Chief Executive Officer Peter Ulrich.

"Exactly the opposite," he said. "A few years of experience with injectable agents will only enhance people's ability to appreciate a drug that doesn't require seeing a doctor to be administered."

Targeting The Disease

Ulrich maintains that his company's therapy — administered as eyedrops instead of an injection through the eye — shoots down four targets of the disease, including inflammation and retinal detachment.

Lucentis works by inhibiting a protein believed to produce blood vessels that can leak blood into the eye.

"If you ask patients if they'd rather have a needle in their eye every few weeks for the rest of their life, or eyedrops, you can guess how that would turn out," Ulrich said.

AMD attacks in two forms, wet or dry, but wet is more serious because it is the type in which most vision loss occurs. Both Lucentis and TargeGen's drugs target the wet form, from which 1.7 million people in America suffer, according to South San Francisco-based Genentech, which has about 400 employees in Oceanside. However, there is a much larger number of patients with dry age-related macular degeneration. Dry often turns into wet AMD, according to companies specializing in this area. Another local firm, Sytera, Inc., plans to begin trials for an oral pill for dry AMD in October, said Jay Lichter, Sytera's chief operating officer.

While the dry form is associated with cell death of the central retina or macula, the wet form is caused by the growth of abnormal blood vessels under the macula. The disease essentially, over time, can ruin fine vision used in reading, driving or recognizing faces. Straight lines may appear curved or bent.

The exact cause of the disease is not known. Many scientists agree that the disease is hereditary, and smoking and an unhealthy diet can also play a role, research shows.

Major Market

Companies developing potential AMD therapies say approved treatments are either invasive — such as Genentech's Lucentis, or have limited long-term success. Like Lucentis, Macugen and Visudyne, the first approved product for AMD, are injections, but Visudyne is used in conjunction with light therapy. Existing treatments for AMD generate about \$500 million in annual sales, according to pre-Lucentis research conducted by Isis Pharmaceuticals.

Isis is in preclinical testing with a compound known as iCo 007. According to Isis, the potential treatment for AMD appears to reduce the formation of new blood vessels in the eye, which can obstruct vision. Isis did not return a call seeking comment for the story, and it was unclear from the firm's Web site if its AMD drug candidate is an injection.

TargeGen estimates that its compound, which has a pending trademark for the name Optikine, could bring in \$3 billion to \$5 billion annually. The amount is only for the wet AMD market.

Ulrich said several large pharmaceutical companies are knocking on TargeGen's door, but because the company is so well financed — the 57-employee firm has \$20 million in cash — it has gone it alone. Local, well-known venture capital firms such as Forward Ventures and Enterprise Partners Venture Capital are backing TargeGen.

"This has not escaped anybody that this is going to be big," Ulrich said of the technology, which was discovered by TargeGen's own scientists. "They're not going away. A drug of this magnitude doesn't come along very often."

Tough Competition

But Berkeley-based biotechnology analyst John McCamant said that Lucentis' strong clinical data impressed the investment community, and that companies in early testing such as Isis and TargeGen have a lot to prove. According to Genentech, 95 percent of the patients in two phase-three clinical trials maintained their vision, while 40 percent improved it.

"The key is that the hurdle goes up," said McCamant, who publishes the Medical Technology Stock Letter. "It's going to be harder to get into that market now."

But Ulrich said TargeGen will submit an investigational new drug application to the FDA within the next 60 days, whereby it will be able to begin human clinical trials. He expects the drug to be approved in the United States by 2011. In the meantime, the company has another compound for heart attack patients in human clinical trials and is testing two cancer drugs.

TargeGen's eyedrops would likely be far less expensive than Lucentis because no doctor would need to administer the once- or twice-daily treatments. Insurance companies, Ulrich said, would "be thrilled."

A Genentech spokeswoman, Dawn Kalmar, said while the company does not plan to research a treatment that would not require injection in the eye, the firm will likely test Lucentis for other eye diseases. She said the size of the protein in the drug requires the injection. Patients say injection in the eye is only slightly physically discomforting, she and Ulrich said.

Genentech began shipping Lucentis the day it was approved.

But Ulrich isn't worried. In fact, he expects more companies to join the market.

Perhaps there may be room for them. Genentech expects the number of people in America with wet age-related macular degeneration will grow to 2.95 million by 2020.

"The area is getting quite crowded," Ulrich said. "Yet, the drugs approved now treat the effects rather than

their causes.”

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