Drug approved to treat cystic fibrosis' root cause

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The first drug that treats the root cause of cystic fibrosis won approval Tuesday, offering a life-changing treatment for a handful of patients with the deadly illness and broader hope for thousands more patients with the inherited disease.

About 30,000 Americans live with cystic fibrosis, a disease that causes sticky mucus buildup in the lungs and other organs, leading to infections, digestive problems and death in young adulthood. The typical life expectancy is about 37 years, according to the Cystic Fibrosis Foundation.

The Food and Drug approved Vertex Pharmaceuticals Inc.'s Kalydeco for patients with a rare form of the disease that affects just 1,200 people in the U.S., about 4 percent of affected population nationwide. These patients have a protein defect that prevents their cells from properly absorbing and excreting salt and water. Studies of the drug showed it significantly improved lung function and reduced other symptoms of cystic fibrosis.

"Even though this drug isn't for the majority of people, it proves that you can look at the mistake in the genes and design a drug in a rational way that will fix the problem," said Dr. Drucy Borowitz of the State University of New York at Buffalo, where she directs the cystic fibrosis program.

The twice-a-day pill is among the first drugs designed to a correct a

specific genetic defect. Its development characterizes both the promise and challenges of that approach. Scientists first identified the gene that causes cystic fibrosis in 1989, but it took more than two decades and more than $75 million in outside funding to develop a drug to treat the disease.

Borowitz enrolled several of her patients in the key study for Kalydeco, which showed that patients taking the drug increased their lung strength more than 10 percent when compared with patients taking a placebo. Patients also had fewer infections and gained nearly seven pounds on average, a significant amount for patients who typically have trouble retaining weight. All patients in the study continued taking older medications that help loosen mucus.

"Two weeks after using the drug my lung tests were above average for a healthy 15-year-old who didn't have cystic fibrosis," said Nick Mangano, 17, a Borowitz patient who has been taking the drug for two years. Before starting on Kalydeco, Mangano said he was hospitalized for lung infections five times in four years. Now he says he usually recovers from a cold within a week or two.

"I don't really need medicine for it anymore, it's totally different," said Mangano, who is considering leaving Buffalo for college next year - a step he hadn't previously considered because of his dependence on his family and physicians.

Only a few decades ago, children with cystic fibrosis seldom survived elementary school. Today, thanks to earlier diagnosis and new focus on diet and physical therapy, 47 percent live to be 18 or older.

The FDA approved the drug for patients 6 years old and up, though Vertex is also planning to study the drug in patients as young as 2 years old. Researchers hope that by using the drug earlier they will be able to

prevent permanent lung damage, which is the primary cause of death for cystic fibrosis patients.

Mangano and others with the so-called G551D mutation have a defective protein that fails to balance the flow of chloride and water across the cell wall, leading to the buildup of internal mucus. The vast majority of cystic fibrosis patients have a different genetic defect, in which the protein does not reach the cell wall. Vertex is developing another drug to try and address that problem. Study data for that drug is expected later this year.

Kalydeco is part of a growing number of new medicines that target rare genetic variations found in subgroups of patients. Last year Pfizer launched a new lung cancer drug called Xalkori, which targets cancer linked to a genetic mutation found in less than 7 percent of patients.

After scientists identified the genetic sequence that causes cystic fibrosis in 1989, many experts hoped the disease could be cured by replacing the gene with a normal one. However, attempts at so-called gene therapy proved unsuccessful, and researchers began looking for ways to correct the genetic defect.

"I think it took the field about a decade to realize we had to look for other options," said Paul Negulescu, vice president of research at Vertex Pharmaceuticals.

In 1998, the Cystic Fibrosis Foundation approached Aurora BioSciences, now part of Vertex, to help screen potential drug candidates for a cystic fibrosis drug. In 2000, the foundation awarded the company more than $45 million to study and commercialize an experimental drug for the disease, the largest grant of its kind by a nonprofit disease group. To date, Vertex has received over $75 million in research and development funding from the Cystic Fibrosis Foundation. Vertex said it also spent

hundreds of millions of dollars of its own money, though it did not specify the exact amount.

Cambridge, Mass.-based Vertex has only one other drug on the market, the hepatitis C drug Incivek, which launched last May. The company said it would announce the drug's price and potential financial assistance programs later Tuesday.

Company shares rose $3.06, or 8.8 percent, to $37.80 in midday trading.

The most common side effects with Kalydeco include headache, stomach ache, rash diarrhea and dizziness.