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## '83 law called big boost for rare-disease drugs

By Diedra Henderson

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WASHINGTON\_\_ More drug companies are embracing the challenge of creating therapies for rare diseases, despite the pint-size potential markets for those drugs.

So-called "orphan diseases" can affect just a few thousand people. In the past, people suffering from conditions such as orthostatic hypotension (it causes blood pressure so low that sudden moves can rob the heart and brain of blood) or thrombocytopenia (a rare blood disease, it causes bleeding even when there is no injury) went begging for treatment.

But federal regulations that give incentives to pharmaceutical companies that invest in treatments for orphan diseases have brought hope to patients and their families. Even people who suffer from orthostatic hypotension and some forms of thrombocytopenia today have treatments.

Just last week, Cambridge-based Genzyme Corp. got the nod from the Food and Drug Administration to sell an intravenous drug to treat a rare neuromuscular disease that afflicts no more than 10,000 worldwide.

That places Genzyme's Myozyme among the nearly 200 drugs that earned FDA approval to treat "orphan" diseases in the past decade, according to a report issued last week by Pharmaceutical Research and Manufacturers of America. (Orphan illnesses are defined as ailments that afflict fewer than 200,000 Americans.) That's a jump from the 108 orphan-disease treatments the FDA approved from the mid-1980s to the mid-1990s. In the 1970s, the FDA approved fewer than 10 drugs to treat orphan ailments

"That's only part of the story," said Lori Reilly, PhRMA's vice president for policy and research. Hundreds of experimental drugs are in development for rare conditions, Reilly said. Those include treatments for a deadly brain cancer and for Crohn's disease, an inflammatory bowel disease.

The Orphan Drug Act, which Congress passed in 1983, lowered financial hurdles, provided tax relief, and gave the first drug maker to treat a given rare disease up to seven years of marketing exclusivity meaning no generic competitors would nibble at its profits.

Reilly and Abbey S. Meyers of the National Organization for Rare Disorders agree that the 1983 law is the main reason so many drug companies target orphan diseases. Small biotechnology companies can leverage their venture capital funding and finance postmarketing clinical trials with drug sales revenue.

"They can get on the market quicker and at a lower cost," said Meyers.

Meyers, president of the Connecticut-based group that champions the cause of rare diseases, also said she expects more orphan-drug approvals in the future.

"We've seen so many of these biotech companies that start this way and, later on, they may move to more common diseases," she said. "But they start off with rare diseases."

An FDA staffer who reviews orphan products said more biotech companies are targeting rare diseases due the success of other biotechs that followed that strategy.

"There are several biotech firms who focus only on rare diseases or that were established on the marketing approval of an orphan product," said Janet Whitley, a product reviewer in FDA's Office of Orphan Products Development. "Industry has learned from this history. In short, the Orphan Drug Act works."

Emil D. Kakkis, chief medical officer of BioMarin Pharmaceutical Inc., a California biotech firm, told NORD's annual banquet last week that the company's pivotal trial to earn the FDA's approval for Naglazyme in June 2005 involved a mere 38 patients. The small trial size was crucial, since only 1,000 people have the disease, mucopolysaccharidosis VI, that the drug treats. People with the condition lack a key enzyme that breaks down complex carbohydrates.

Typically, thousands of patients participate in a late-stage clinical trial. In some cases, the firms seeking approval for treatment of orphan diseases can combine early stage safety trials, saving time and expense.

Still, Kakkis proposed an "Ultra" Orphan Drug Act during his speech that could help companies, like BioMarin, that seek remedies for diseases that affect as few as 1,000 Americans. Additional incentives could include allowing the FDA to approve a drug based on results of just one clinical trial.

"I think the Orphan Drug Act has been incredibly successful. I don't deny that," Kakkis said. "I do think, though, there are diseases for which even the Orphan Drug Act is not sufficiently incentivized to generate new drugs."

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