OPINION | COMMENTARY

Medical Miracles From FDA Inefficiency

The economist behind the 'priority review voucher,' which advances treatments for neglected diseases.

By Allysia Finley
Jan. 26, 2018 6:05 p.m. ET

Durham, N.C.

You've probably never heard of biallelic RPE65 mutation—and count yourself lucky. It's a genetic defect that causes a form of retinal dystrophy. People born with it gradually lose their vision, often while still children, until they go totally blind. But they are now fortunate: In December the Food and Drug Administration approved a new gene therapy called Luxturna that corrects the mutation and reverses the course of the disease. Patients don't get normal vision back but can read facial expressions and see stars for the first time. It's a partial cure for blindness.

The disease is very rare, afflicting only a few thousand Americans—and therein lies our tale. Spark Therapeutics , which developed Luxturna, charges $850,000 for a course. Even at that high price, a drug with such a small market might not have been economical to develop as recently as a decade ago. This medical miracle was helped along by a federal law enacted in 2007 with bipartisan support—a rare governmental success, for which economist David Ridley deserves much of the credit.

Mr. Ridley, 48, has spent two decades studying and teaching health-care economics at Duke. In 2006 he and two colleagues published a paper in the journal Health Affairs proposing a way to give pharmaceutical companies an incentive to develop treatments for so-called orphan diseases. Congress authorized the "priority review voucher" in 2007. The FDA has since issued 18 vouchers, including six last year: five for drugs to treat rare pediatric diseases and one for the tropical Chagas parasite, which afflicts more than six million people world-wide.

Here's how the system works: When the FDA approves a new treatment for a rare pediatric disease or an infectious tropical one, the drugmaker receives a voucher that can be used to fast-track FDA review on another drug. That allows it to bring the latter drug to market sooner, which can help increase sales, beat competitors and extend the patent's effective lifespan. The vouchers can be sold and never expire. Drugmakers are also required to pay a fee—$2.7 million in 2017—to cover the FDA's cost of expedited review.

In an interview at an on-campus hotel, Mr. Ridley explains that the voucher idea was a refinement of an earlier proposal by other economists: "If you developed a drug for a neglected disease, you'd be rewarded with a voucher for an extra six months on your patent." For companies making more than $1 billion a month on drug sales, "that was real value."

The problem? "That proposal was both inefficient and unfair," he says. A patent confers a monopoly, which encourages innovation by allowing inventors to recover their investment and make a profit. But patents are time-limited for a reason: If they're too

ILLUSTRATION: KEN FALLIN

companies from competition, deterring innovation and raising costs.

So Mr. Ridley and his colleagues focused on the front end. "We thought that was both fair and efficient, because people are getting access to a drug even earlier," he says. The patent clock is already ticking while the FDA reviews a drug, so earlier approval means more time in which the company has the market to itself. That's a win-win for consumers, who get new drugs faster without any additional wait for less-expensive generics.

The FDA's review process normally took 18 months, but Mr. Ridley and his colleagues projected that a priority voucher could speed it to six months, which would mean an extra year of sales. For a blockbuster drug, the 2006 paper estimated, a voucher could be worth as much as $322 million. Priority review, he emphasizes, does not make drugs less safe. Drugmakers still have to comply with all the FDA's clinical-testing and paperwork requirements.

The voucher idea became law after then- Sen. Sam Brownback, a Kansas Republican, heard of it, grew intrigued, and contacted Mr. Ridley. It was 2007, a time of divided government and wide public dissatisfaction with politics. Yet Mr. Brownback was able to assemble a bipartisan coalition with Sen. Sherrod Brown, a populist Democrat newly elected from Ohio.

It's easy to see how market-driven incentives in lieu of direct government funding would appeal to conservatives. The key to getting Democrats on board, Mr. Ridley says, was to make the argument that "the purpose is not to help drug companies get richer. The purpose is to help people suffering from diseases that would otherwise not get help."

The law initially provided vouchers only for infectious tropical diseases. Although scientists have performed plenty of molecular research on such ailments, large clinical trials are needed to bring a treatment to market—and they're expensive. Drugmakers are unlikely to recover the costs because the diseases mostly affect poor countries.

Consider Chagas, which the Centers for Disease Control and Prevention classifies as a "neglected parasitic infection." Most people with Chagas live in rural Latin America; few realize they've been infected. The symptoms are vague: fatigue, body aches, headache, rash. But if left untreated, the infection can kill. The promise of a priority review voucher gave Chemo Research an incentive to develop a treatment, approved last year, even though the company is unlikely to turn a profit off its sale.

In 2012 Congress extended the vouchers to rare pediatric diseases. Asklepion Pharmaceuticals received one in 2015 for developing the drug Cholbam to treat bile acid synthesis disorders. Children with those conditions can't properly absorb fats or the fat-soluble vitamins, A, D, E and K. That can lead to a variety of symptoms,

and liver disease.

Asklepion didn't use the voucher; it sold it, along with the rights to the drug, in 2015, to bio-pharmaceutical company Retrophin , which in turn sold the voucher to the French pharmaceutical giant Sanofi for $245 million. Sanofi redeemed the voucher later that year to fast-track review of a Type 2 diabetes medication, hoping to beat a competitor, Novo Nordisk , to market. (Both drugs were approved on the same day.)

Vouchers have sold for anywhere between $67.5 million and $350 million, though the price last year settled in the range of $125 million to $150 million. Mr. Ridley suspects one reason voucher values are lower than he originally projected is the FDA has become more efficient. Standard reviews now take only 10 months on average. "The FDA has been so great," he laughs, "this is a problem."

Another reason is the law's 2012 expansion to potentially thousands of rare pediatric diseases. Increasing the supply of vouchers would be expected to reduce their value—and thereby diminish the incentive to develop treatments for neglected diseases.

Thus the program's success may be self-limiting: If the vouchers succeed in encouraging novel drug treatments, a surfeit could reduce their value and discourage investment. Might this cause Congress to restrict the diseases that qualify for vouchers? And if so, how would politicians choose between, say, helping a few thousand American kids with neuroblastoma and millions in Africa with malaria?

"I could certainly understand a member of Congress saying, 'I want to help sick kids in this country,' " Mr. Ridley replies. "My preference would actually be the opposite, and part of the reason is I'm lucky and my kids are healthy." With rare pediatric diseases, drugmakers will likely recover some of their costs from insurers. But there's not much payoff for treating infectious diseases endemic to poor countries. "As sort of a coldblooded economist, I say, 'How can we help the most people?' "

Consider: The CEO of NanoViricides, Eugene Seymour, wrote to Mr. Ridley in 2015, saying that after learning of the voucher program, "I pushed my company to initiate development of a drug for dengue/dengue hemorrhagic fever." This investment would not have happened, Dr. Seymour continued, "had there not been a PRV program in place."

In 2012 the FDA approved the first drug in four decades to treat a resistant strain of tuberculosis, for which Janssen Pharmaceuticals received a priority review voucher. Nearly half of TB patients in Russia, Peru and Thailand have strains with demonstrated drug resistance. Killing resistant TB is exponentially more expensive and time-consuming than the normal first line of treatment. Drug resistance is becoming a bigger challenge for bacterial infections like TB because of the proliferation of antibiotics, so developing treatments could help millions of people.

While vouchers can't be revoked, there's a risk that Congress could fail to renew the program for rare pediatric diseases when it expires in 2020. Mr. Ridley acknowledges this could create uncertainty for drugmakers and investors. The last time the program was up for renewal, in December 2016, one researcher at Duke's School of Medicine was told she wouldn't receive funding from investors until the program was reauthorized.

Another potential problem is that governments and insurers could use their negotiating power to drive down drug prices, leading pharmaceutical companies to produce fewer new drugs for common ailments. "If there aren't the blockbuster drugs

Ridley says: "Even though I worry about the end of the blockbuster, we just had Sovaldi a couple of years ago." That's the hepatitis C treatment that earned Gilead Sciences Inc. $10.3 billion in sales in 2014, its first full year on the market.

The potential problems notwithstanding, the voucher program must be reckoned a success. And Mr. Ridley thinks the principle could be applied in other regulatory areas. In 2010 he proposed a priority review voucher for Europe that would include faster regulatory review and decisions about how much national health services will pay for new drugs. "Part of the delay in getting to market in Europe is not just the regulators wanting evidence of your safety and efficacy, but the payers making you jump through some hoops," he says. Perhaps that's why European officials have expressed little interest.

He suggests a priority review voucher for the Environmental Protection Agency, also aimed at preventing infectious tropical diseases: "Our proposal is that if you develop a new pesticide to kill the pests carrying malaria or dengue or Chikungunya or Zika, then you get faster review at EPA for another product, say, for a herbicide to treat crops."

Regulatory agencies tend to move at a snail's pace, but Mr. Ridley says he's seen significant improvements at the FDA over the past decade, and especially within the last year under new Commissioner Scott Gottlieb. Which points to the paradox at the heart of Mr. Ridley's idea. The voucher, he says ironically, is "fundamentally built on inefficiency in regulation." If the FDA were more efficient, priority review wouldn't be valuable.

So why not simply allow all drug companies to pay for priority review? Don't economists prefer efficient markets? "Well, we could," he says, but "if companies could just pay for it, the voucher program would go poof."

Ms. Finley is a member of the Journal's editorial board.