Instead, the agency keeps safe treatment out of the hands of patients with no other options.

The FDA Could Help Save My Son From a Rare Disease

By Judy Stecker

My eldest son, Wheeler, has a rare genetic disease that will steal his vision, mobility, memory and, ultimately, his life. Every morning when he leaves for preschool, I worry it may be the last time he'll be able to see my face.

One in 10 Americans have rare diseases— defined as affecting fewer than 200,000 people in the U.S.—and 95% of these afflictions lack a Food and Drug Administration-approved treatment or therapy. Three in 10 children affected by rare diseases won't live to see their fifth birthday. Wheeler turns 5 in May.

When my son was diagnosed with CLN3 juvenile Batten disease at 4 weeks old, research into possible therapies offered hope. That hope is all but gone. The Beyond Batten Disease Foundation's planned 2023 Phase III clinical trial of a potential treatment is in limbo, seeking funding. (My family supports the foundation.) Earlier this month, Amicus Therapeutics abandoned its pursuit of the only proposed gene therapy.

These developments are devastating but unsurprising. Given this, the anti-innovation sentiment in Washington and unnecessary bureaucracy at the FDA have made it difficult for companies to justify investments in rare-disease therapies.

Rare-disease research is inherently hard—the science is challenging and the small population makes return on investment unlikely. Policies with a narrow-minded focus on lowering drug prices make it still harder. The Inflation Reduction Act's price setting will delay pharmaceutical launches and inhibit research into alternative uses of existing drugs. The march-in rights guidance the administration proposed in December to allow the government to seize patents from public- private partnerships will discourage their formation.

Though I know firsthand that the FDA's civil servants are committed to their mission, the agency's onerous bureaucracy impedes access to possible treatments with no meaningful gain for patients.

In December, the FDA had an opportunity to give patients with rare diseases more options when it issued a final guidance on research standards. While it's understandable to hold work on rare and common diseases to the same safety criteria, it's harmful to stick both with the same efficacy burdens. People with untreated rare diseases already have little prospect of seeing new treatments. Yet the FDA chose to keep the same outdated interpretation of efficacy criteria.

This standard simply doesn't work for children with rare diseases. Accurate diagnoses of rare diseases take four to nine years on average. By the time a clinical trial is available, children are too sick for a drug's efficacy to be assessed fairly. The answer is to get as many

diagnosed children treated as soon as possible so researchers can learn from them. Identifying patients earlier will become easier as childhood screening and genetic testing improve.

The agency's inflexibility with efficacy and trial design keeps safe drugs out of the hands of patients with no other options. Take the Beyond Batten Disease Foundation's paused clinical trial. Miglustat showed promise in slowing CLN3's progression in Phase I/II trials. The drug has a strong safety profile and has been approved for use against Gaucher disease in the U.S. for decades. Yet the FDA has insisted that the foundation conduct substantially more scientific and clinical development and applied additional complex requirements that significantly expanded the geographic footprint and cost of the Phase III clinical trial.

The FDA has the ability to adjust course and help kids with rare diseases right now. The FDA could modify the Expanded Access program for rare diseases. Currently, it allows experimental treatment only for single patients, but a broader version could reach more patients much quicker than a clinical trial.

The agency should also revise and finalize the March 2019 draft guidance on natural-history studies for rare-disease drug development and give natural-history data—research that tracks the course of a disease—weighted consideration. As former FDA Commissioner Scott Gottlieb has acknowledged, robust natural-history data could be used in lieu of a placebo group in clinical trials. This would allow for more open trials, in which everyone gets therapy, creating incentives for more patient participation and getting more children treated.

In approving treatment for diseases affecting small populations— fewer than 5,000 people—the FDA should apply a threshold similar to that used in emergency-use authorization. During an emergency like the pandemic, an emergency-use authorization allows the FDA to allow a treatment when the known and potential benefits of the drug outweigh the known and potential risks of the drug and the disease, and there is no other alternative treatment. The agency could also broaden the use of accelerated approval, a program that shifts more of the evidence requirement for efficacy to after the drug has been made available. The FDA has exercised these flexibilities before but on an ad hoc basis. Something more systematic and defined would encourage investment.

The pace of science is accelerating, but people struggling with rare diseases won't see that progress if the regulatory state can't keep up. Impeding access and stifling innovation isn't the answer. Time can't be wasted for anyone with a rare disease, and for children like Wheeler, time is swiftly running out.

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