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ORPHANS IN DANGER

For rare diseases and orphan products, the future looks promising, but as **Peter Saltonstall** finds, significant research, educational and policy challenges remain. A view from one of the patient community's staunchest advocates

This is an encouraging time for people who have a rare disease. One third of the new drugs approved in recent years by the FDA have been orphans. For some rare diseases, such as Gaucher disease and homozygous familial hypercholesterolemia, there are now multiple approved therapies.

The genomic revolution promises to identify innumerable opportunities for new therapies. Investors have recognized that there is a business model for a company that makes drugs intended for patients with rare diseases. Many of the major drug companies have created divisions devoted to orphan drugs.

At the same time, there is a long way to go. There are nearly 7,000 diseases that are categorized by the NIH as rare—that is, affecting 200,000 or fewer Americans. Only a few hundred of these diseases currently have approved treatments. While each rare disease affects a relatively small number of people, rare diseases collectively affect nearly 30 million Americans, or one in 10.

We all know someone who is alive today because of the remarkable medical advances of recent years. But the patient advocacy community still faces a remarkable number of challenges:

1 **More research dollars for rare diseases:** It is ironic that we are on the cusp of so many scientific advances at a time when federal and private industry research dollars are becoming scarcer. Most rare diseases are genetic in nature. The human genome project has opened up so many new avenues for research. We will never have unlimited dollars, but if only we could pursue additional potentially fruitful leads, we would see an acceleration in new therapies.

2 Diagnosing rare diseases: Unless a physician specializes in diagnosing and treating rare diseases—and comparatively few do—most practicing physicians have little experience in diagnosing one. In some cases, a blood test is all that is needed, yet I hear story after story from parents about how challenging it was for them to secure an accurate and reliable diagnosis for their child. For many diseases, it can take half a dozen years or longer before an accurate diagnosis is made.

Systems should provide broader education for physicians in enabling them to diagnose rare diseases more quickly and with greater accuracy. The companies that make drugs for rare diseases conduct extensive education programs for physicians; these educational efforts are central to their marketing efforts, because an accurate and early diagnosis almost always leads to prescribing a therapy.

3 Expediting clinical trials: Testing new treatments is always time consuming, especially when little is known about a disease, and when there are few patients to test. There are certain new tools that are designed to expedite the clinical trial process and generate data that will pass the appropriately careful scrutiny of the FDA. NORD (the National Organization for Rare Disorders) is committing significant resources to increasing our knowledge about how certain rare diseases naturally progress, with no intervention or with existing interventions, because we can then more easily assess the effectiveness of new treatments. And we also have established networks of patients with rare diseases so that recruitment for clinical trials can be expedited.

4 Expediting new drug approvals: We are fortunate that officials at the FDA who deal with orphan drugs understand that, sometimes, it is not feasible to test a new treatment for a rare disease in the same way that a treatment for a common disease would be tested. The FDA has demonstrated great flexibility in assessing new treatments for rare diseases.

A study recently published in the *Journal of the American Medical Association* evaluated the evidence supporting FDA approval of novel therapeutic agents and found it to be less rigorous than the data supporting the approval of drugs for more common diseases. This study generated debate about FDA exercise of flexibility and judgment in approving new drugs. FDA Commissioner Margaret Hamburg, MD, wrote a blog explaining why FDA supports a flexible approach to drug development.

The patient community avidly supports FDA's exercise of appropriate flexibility. While all drugs must be shown to be safe and effective before approval, there are different ways to demonstrate this. The same clinical trial that might be used for patients with a well-understood, highly-prevalent disease would not be appropriate or feasible for a disease that affects few patients, or in whom the natural progression is not well understood.

FDA clearly seeks to strike a balance between protecting patients from unsafe or ineffective drugs, and making new therapies available expeditiously. But that balance is a delicate one. Approving new drugs requires the kind of careful judgment that FDA has exercised. Currently, FDA is listening to the patient voice more than ever before.

Camp threatens orphan tax credit

A proposal made public recently by Rep. Dave Camp (R-MI), chair of the House Committee on Ways & Means, would repeal the Orphan Drug Tax Credit, one of the crucial incentives in the Orphan Drug Act to encourage the development of treatments for Americans with rare diseases.

The proposal highlights the need for providing advocacy on public policies.

The repeal of this tax credit would be an anti-patient, anti-public health policy, and would squelch medical research and innovation.

NORD (the National Organization for Rare Disorders) has mobilized support for its position on this, and many other patient organizations have signed onto a letter we will be sending to the House Ways & Means and Senate Finance committees on this issue. We will vigorously oppose any attempt to repeal this important incentive for orphan product development.

5 Assuring access to new treatments: Our healthcare delivery and reimbursement systems are changing. More patients are entering the system, and better and more expensive treatments are being developed. We are challenged to assure that new treatments reach patients quickly after approval and are reimbursed appropriately. At NORD, we are working with all insurers to assure that treatments become available in a timely way. We instituted a program to educate elected officials at the state level, recognizing that states play an increasingly important role in reimbursement decisions. We are soliciting support from companies and patient organizations in this initiative.

NORD also pioneered patient assistance programs, and we have recently enhanced and expanded our capacity to administer programs that are collaborative, innovative, credible and tailored to the specific needs of our industry partners. These programs provide medication assistance, premium and co-pay assistance, travel and lodging assistance for clinical trials, and other services.

6 The empowerment of the patient: We are seeing more personalized drugs—drugs created for an individual patient. As personalized medicine becomes a reality, patient involvement in the development process becomes ever more important. The word that I use is "patient-centricity." We have always been advocates for patients, and are committed to making the patient the center of the healthcare system.

There are many reasons why everyone should be attuned to what is happening in the rare-disease community, but one particular reason is especially compelling: rare-disease research and orphan-drug development very often have provided the knowledge that leads to the development of drugs for more common diseases. NIH Director Francis Collins, MD, a strong advocate for rare-disease research, has made this a cornerstone of his priority-setting.

I am optimistic that scientific advances will let us learn more about rare diseases and how to treat them, and our public policies will create a friendly environment. This is what keeps us going every day. ■

Peter Saltonstall is president and CEO of the National Organization for Rare Disorders (NORD).