THE PHARMACEUTICAL INDUSTRY IS AILING, AND CONCERNED LEGISLATORS IN THE U.S. government have offered a panoply of remedies with names such as NCATS, PCORI, and CAN. Some claim that these therapies are ill-conceived and will make matters worse. Others hail them as bold new solutions that will eliminate impediments to innovation. Still, most agree that something must be done to restore the industry’s preeminence and its contributions to public health. Here, I examine how the National Center for Advancing Translational Sciences (NCATS), the Patient-Centered Outcomes Research Institute (PCORI), and the Cures Acceleration Network (CAN) might bring about the changes that will reinvigorate pharmaceutical innovation.

The diagnostic is grim: The pharmaceutical industry has spent $1.1 trillion in research and development (R&D) over the past 10 years, but the value of its pipeline is barely $293 billion (1). Some chief executive officers warn that drug R&D has become an unwieldy enterprise that destroys shareholder value—as much as 30% of each dollar spent on R&D (2). Globally, drug companies spend $135 billion on R&D annually to produce 25 to 30 new drugs, many of them with mediocre health outcomes and often sold at staggering prices. Governments and payers worldwide are pushing back and curtailing reimbursements and rescinding patents. How could this happen to an industry that, 20 years ago, was much respected? The short answer is that it walked away from the translational research model that made it great: risk-taking and breakthrough science (3).

A RISKY PROPOSITION

Translational research consists in taking cutting-edge scientific discoveries and turning them into medicines. Antibiotics, vaccines, and protein therapeutics are some of the iconic advances that were brought to market through successful translation. For most of the past century, this model created enormous value for society. Unfortunately, true translation is no longer practiced by industry (4), largely for two reasons. First, it carries huge risks. Companies that overcome translation’s daunting challenges are rewarded by 10 to 20 years of prosperity; those that fail disappear. Second, it is disruptive because the next translatable innovation seldom coincides with a firm’s market franchises, forcing the company to start anew. For many chief executives, this combination of challenges was too much. They tried to remake R&D to lower risk and render innovation predictable. The result was a rise in incremental advances and retrenchment from some of the more difficult therapeutic areas (for example, infectious, cardiovascular, and psychiatric diseases) (5).

A LITTLE BOOST FROM GOVERNMENT

Given the industry’s plight and difficulties in regaining its footing, there is a need for an honest broker to foster initiatives that keep innovation moving. This is what NCATS is all about (www.ncats.nih.gov). It is not Big Pharma in government clothing. It is a catalyst for much-needed changes. For instance:

More collaborative research. Some firms are exhausting themselves on challenges that are too big for one organization to tackle alone, such as Alzheimer’s disease or the development of RNA interference–based therapeutics. Other companies repeat mistakes already made by competitors. The resulting waste weakens the industry and heightens its risk aversion. Collaboration reduces the risk of R&D by enhancing the collaborators’ understanding of the science they want to translate and by enriching this understanding with insights from regulatory scientists and patients. Collaboration increases the likelihood of designing better drug candidates that fail less often in clinical trials.

Faster innovation. Since 2002, the U.S. Food and Drug Administration (FDA) has approved 27 drugs for 20 rare diseases, an all-time high. But at that rate, it will take 350 years to address the 7000 rare diseases that affect 10% of Americans. The scientific community must do better. Drug repurposing—a key focus of NCATS—is a cheap and powerful innovation engine that can speed the delivery of affordable therapies to patients who badly need them.

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**Bolder innovation.** Across the U.S. National Institutes of Health (NIH) and industry, innovation is often dulled by conservative decision-making designed to avoid failure rather than achieve breakthroughs. NCATS has the authority to nurture a different culture, and its $575 million budget can do much to restore support for bolder science and the young investigators who often spearhead it.

**Speedier R&D.** Research is hampered by lack of tools and standardization. Each clinical trial is treated as one-of-a-kind, and costly resources are spent replicating processes that have seen little innovation in decades. NCATS helps by developing tools that promote common standards and best practices (for instance, in patient-recruiting and consenting, data capture, and study management). It has also partnered with FDA and the Defense Advanced Research Projects Agency (DARPA; www.darpa.mil) to develop tissue chips that speed drug toxicity assessment, a notorious stumbling block in drug research (6). To aid NCATS in its mission, Congress gave it CAN, a unique program that not only funds some of the initiatives described above but also seeks to uncover impediments to innovation in government (www.ncats.nih.gov/funding-and-notices/can/can.html). CAN is assisted by an advisory board that consists of 24 members—11 with extensive industry experience—who know where to look for such roadblocks.

While NCATS and CAN concentrate on innovation, PCORI focuses on the quality of care achieved with this innovation by funding research that enables evidence-based medicine (www.pcori.org). At present, PCORI spends much of its $160 million budget on developing methods to assess how therapies work in various patient subpopulations. However, the hope is that one day it will be possible to link patient-reported outcomes with genotypes and data in electronic medical records to better decipher the mysteries of pharmacology. Such quick feedback will offer scientists rich insights upon which to keep innovating.

The angst caused by the innovation crisis has given collaborative research a major impetus. By prodding competitors, NIH, regulators, and patients to cooperate, collaboration has reset innovation on a stronger foundation and gives us hope that tough public health challenges ahead will be conquered.

— Bernard H. Munos

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