Inside the Pipeline: Pharma Goes to Work

A n old joke about nuclear fusion research is that the technology for generating a cheap and plentiful supply of energy has been “just over the horizon” for the past 50 years. The drug industry is the focus of similar optimism but with a shorter time frame: Its research pipeline is invariably described as being on the verge of delivering novel and powerful treatments for dread diseases.

Unfortunately, that pipeline has a chronic leak that no pharma executive has been able to plug.

“What hasn’t changed in the past 25 years is that only one of five compounds that enter clinical trials comes out as a product. That’s amazing to me,” says Robert Gorman, former head of worldwide drug discovery at Upjohn-Pharmacia, who retired before the company was acquired by Pfizer in 2003. “I spent hundreds of millions of dollars on databases and other tools to try and improve that performance.”

What could the industry do to reduce the size of the leak? The answer is complicated. As the eight stories in this package and related articles in two of Science’s online publications, the Signal Transduction Knowledge Environment (www.stke.org) and Next Wave (www.nextwave.org), make abundantly clear, the process of discovering new drugs is fiendishly complex, vastly expensive, and wildly unpredictable. Some of the factors are beyond anyone’s control: Researchers are working at the frontiers of science, combining knowledge with educated guesses, and their companies are betting millions on untested compounds only to watch most of them crash and burn. Measuring inputs and predicting outcomes is a game that every research honcho plays but with limited success.

At the same time, some of the industry’s problems appear to be at least partially self-inflicted. The wave of mergers and acquisitions in the past decade has had a debilitating effect on morale and productivity, according to some analyses. Within companies, marketing departments are said to exert an undue influence at times on scientific decisions about which projects move through the lab and into clinical trials.

Training also seems suboptimal. Industry scientists typically learn on the job, not in school. “No university teaches drug discovery,” says Graeme Bilbe, head of global neuroscience for Novartis. “And many don’t give much credence to what we do.” At the management level, many pharma executives who joined industry after successful academic careers freely admit that they were shockingly naïve about what it takes to make a drug. “Even if you were thought of as a superstar in academia, the chances are that you don’t really know how things work in industry,” says Ben Shapiro, a retired research executive at Merck, who left the University of Washington in midcareer. “And if you’re deluded enough to think that you do understand, you’ll run into trouble.”

For all its problems, however, the drug industry appeals to thousands of scientists hoping for a chance, against long odds, to improve the lot of humanity.

“I was considered a sellout in 1980 when I went to work for Merck,” recalls Amgen’s Paul Reider. But he never regretted his decision, and over the next decade he helped the company develop Crixivan, the first protease inhibitor to treat AIDS patients. “It’s hard to give up on a drug,” he says, “if you know that thousands of people will die without it.”

—Jeffrey Mervis