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How Failure Leads To Innovation In Drug Discovery

By Robert Popovian — March 7, 2016

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"Success is the result of perfection, hard work, learning from failure, loyalty and persistence." – Colin Powell

In my 20 years with Pfizer, I have been directly involved in several late stage clinical development programs both as a medical director and a health outcomes scientist. Most of my engagement began during the submission of a medicine for regulatory review by the Food and Drug Administration (FDA). The medications ranged from treatment for pain to cures for infectious diseases and drugs for the management of diabetes and diabetes complications. All of them were novel medicines with great potential to change the way we treated patients. Some of them were first in class while others were significant improvements compared to treatments already available for patients.

Unfortunately, despite their great promise, only three out of the six compounds I worked on are still in the U.S. market today. A 50% attrition rate was not a great achievement since most of these drugs were in the latter stages of development or had received FDA approval. In addition, the failure rate was high compared to other industries that rely on research and development such as technology companies developing the latest phone application.

Now consider this: my 50% attrition rate is an incredible accomplishment compared to the overall research and development model currently in place for biopharmaceuticals where investigative failure is the norm. Indeed, most scientists employed by biopharmaceutical companies carrying out the basic science or early human research will go through their entire career without discovering or working on a single molecule which will ultimately appear on the shelves of a pharmacy and on a patient's night stand. Successful research programs in the biopharmaceutical industry often follow a complicated path of multiple failures, where only 0.2% of molecules show enough promise for testing in humans and only 20% of medicines starting phase I human clinical trials receive FDA approval. A successful research program is where researchers learn from the failures and apply their learnings in discovering new or improved therapies.

This "failure leads to innovation" reality is especially true when one is conducting scientific research in areas of significant unmet need such as treatments for dementia and cancer. For

example, since 1998, there have been 127 projects started by the biopharmaceutical industry which have produced only four approved medicines for the treatment of symptoms associated with Alzheimer's disease. A mere 3% success rate with no cure in sight! Yet patients suffering from serious ailments should take heart in the recent breakthroughs in lung cancer research. A slew of approvals in the past several years demonstrate that persistent research is paying off. Due to the sequencing of the human genome and the advancement of precision medicine, lung cancer patients now have several medicines that target specific forms of the disease based on genetic mutations.

Another great example of many years of failed research leading to improved care is in Chronic Myelogenous Leukemia (CML). After the approval of the first breakthrough therapy for CML and multiple agents afterwards, the five-year survival of patients afflicted with this deadly disease has increased from 31% to 89%. This achievement is due to the resiliency of researchers who did not give up because of initial failure and believed in incremental improvement of medicines that followed.

Another way to look at the challenges of biopharmaceutical research and development besides its failure rate is to quantify the research steps required to successfully bring a new medicine to market. For a single approved product by the FDA, researchers had to have tested a minimum of 10,000 promising compounds while conducting almost two dozen non-clinical safety studies. On average, over 200 scientists had to have a hand in the development program working for close to 15 years; conducting over a dozen human clinical trials involving over 3000 patient volunteers.

Finally, rates of failure not only vary by disease area but also by the size of the company. In addition, failure rates are a misleading barometer for a successful research and development program. Large established biopharmaceutical companies have significantly higher failure rates because they stay in business after several iterations of unsuccessful tries. On the other hand, smaller companies that do not succeed immediately tend to quickly faze out of the arena of medical research.

Biopharmaceutical companies understand that failed experimentation is an inherent part of discovering and developing new medicines. It is a risk that biopharmaceutical companies have accepted, and one that motivates researchers to continue to work to discover treatments that change people's lives and give families hope, despite the deeply disappointing setbacks. So next time you hear about a failed clinical trial do not despair. The cure may be right around the corner.

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