Steps to Getting a Drug to Market


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In the last century, we witnessed the emergence of industries dedicated to scientific and medical breakthroughs for new vaccines, medicines, and other therapies designed to prevent, treat, and even cure many of the diseases that afflict us. At the same time, starting in 1906, the U.S. Congress established basic federal laws regulating the sale of these products in interstate commerce.

These laws allowed the federal government to crack down on the sale of many elixirs, tonics, and so-called "snake oils" that claimed to cure a variety of ailments, but in many cases were ineffective—or worse—unsafe. Coupled with state regulations that govern the dispensing of pharmaceuticals, these laws provide drug safety protections that many describe as the worldwide "gold standard." But the United States' high standards also need to be balanced with the benefits and risks of new therapies, and a consideration of the need to provide access to medicines for serious illnesses where often none currently exist. Government policies on drug safety and access can literally mean life or death in some cases.

As the practice of medicine evolves, so do the expertise and techniques associated with researching and developing new products. Even now, scientific discoveries in human biology, such as the sequencing of the human genome, are creating dramatic opportunities for developing new medicines and techniques to combat many previously untreatable illnesses.

Through proteomics and genomics, we are gaining a more sophisticated understanding of how proteins and genes interact to cause disease in particular populations of patients, and how drugs affect patients in different ways. At the same time, advances in nanotechnology provide new opportunities to get a targeted treatment to specific cells in the body. With the help of advanced information technologies that can process and manage huge amounts of information, we are poised to further transform health care in a way that is revolutionizing personalized medicine.

In addition to combating illness and rare conditions, biotechnology is helping us design renewable resources from plants and enhance the production and durability of our food supply. The promise of biotechnology is real. We are already on our way to transforming many forms of cancer from a life-threatening disease to one that is

chronic, yet treatable. Today, there are more than 400 new cancer therapies under development. For breast cancer alone, fifteen-year survival rates have doubled during the past decade.

Even with the great promise of these medical advances, there is enormous uncertainty and unpredictability in the biotechnology field. The challenges of innovation are by no means the end of the story. After innovation comes rigorous product testing that can costs upwards of hundreds of millions of dollars. After testing comes government approval—another rigorous process—and then the new treatment must be sold at prices that not only enable access, but also recoup the costs of research and development.

While spending on biomedical research has more than doubled during the past decade, the number of new medicines reaching the marketplace has remained flat (at approximately thirty a year). Today, products actually face a lower chance of success than in the past. New compounds entering early clinical development today have only an 8% chance of reaching the market versus fifteen years ago, when it was 14%. Even more telling is that products that make it to late-stage clinical trials have a 50% failure rate today, up from 20% only ten years ago, and that is after many years of testing and millions of dollars spent in research.

Many new drugs take longer than ten years to develop, and with cost estimates ranging from $800 million to $1.3 billion to research and develop one product, there is considerable concern that some of the greatest innovations may never reach physicians and, ultimately, patients. Not only is there uncertainty at the clinical level, but companies often face skeptical and impatient investors, a complex and often opaque regulatory process at the U.S. Food and Drug Administration (FDA), and a marketplace where payment after approval can sometimes be hard to predict.

In order to deliver on the promise of medical innovation, we must look ahead and take on the following challenges:

- Planning for the health-care costs of patients who live longer as a result of new therapies and technology.
- Resolving the issue of how to pay for new drugs and treatments, and doing so in a way that assures affordability and access to medicines without endangering the financial incentives and intellectual property protections that enable the very research that drives the biotechnology revolution.
- Being careful to establish policies that avoid shifting the costs of these breakthroughs to future generations.

Consider these challenges carefully as you learn more about the drug discovery process in the United States in the pages ahead. If we can meet the challenges, we can ensure that America remains the "gold standard" in medical innovation without stripping the gold mine of medical innovation.

Steps in the Cradle of Invention

Ivor Royston, M.D.

Managing Member and Co-founder, Forward Ventures

Ivor Royston, M.D. in the lab

Scripps' recruitment of Frank Dixon, an immunologist, helped the institution earn a reputation as a major center of biomedical research.

The Salk Institute for Biological Studies brought in Nobel Prize winner Francis Crick, who quickly attracted other major talent and solidified Salk's reputation as a top research institute. Led by Roger Revelle, UCSD recruited top people from the top universities—and also hired faculty with experience in attracting research dollars.

The development of these institutions was not an intentional effort to create a biotech cluster. The collaborative environment in the institutions attracted top-quality scientists and it helped that San Diego also offered a quality of life and climate not found anywhere else, ethnic diversity, and strong arts and culture. Once here, these scientists provided both basic research and proofs-of-principal for treatment strategies.

In addition to UCSD, The Scripps Research Institute, and the Salk Institute, we now have the Burnham Institute, Sidney Kimmel Cancer Center, The Neurosciences Institute, and the La Jolla Institute for Allergy and Immunology. These attract nearly $700 million a year from the National Institutes of Health (NIH), putting San Diego in the top ten cities for NIH funding in the country.

While the research base is absolutely necessary for the success of the biotech industry, it can't support the industry by itself. The other legs that keep the industry standing are scientific entrepreneurship, venture capital, and skilled management talent to form companies that usher potential products through preclinical and clinical trials, approval by the U.S. Food and Drug Administration, and other aspects of the process of bringing a product to market.

Luckily, San Diego's close relationship between academia and business encourages an entrepreneurial attitude among scientists. An entrepreneurial attitude, when supported by universities, research institutions, and academic and professional colleagues, is a powerful force for creating a strong industry. The story of how Hybritech was founded is an excellent example of entrepreneurship supported by research.

But first, let's go back thirty years for a snapshot of San Diego. San Diego was a Navy town with beautiful beaches. The tuna industry was an important part of the local economy, but was showing signs of decline. The defense industry, with companies like Rohr, Convair, and Teledyne-Ryan, was a cornerstone of the economy. UCSD was only twelve years old. Like most adolescents, it was still defining itself and finding its place in the academic world.

In 1976, the world's first biotech company, South San Francisco's Genentech, was founded to capitalize on a new gene-splicing technique that could be used to create medicines. A year earlier, Georges Kohler and Cesar Milstein had invented monoclonal antibodies in England. I had been at Stanford doing postdoc work with Howard Birndorf, and I badly wanted to start my own Genentech. I thought monoclonal antibodies looked promising for cancer research and treatment, and they looked as promising as anything Genentech was doing.

In 1978, I was a professor at UCSD. I was treating patients as a practicing physician and doing oncology research. I convinced Howard to leave Stanford and work with me as a research assistant on the monoclonal anti-body project. It wasn't long before we figured out that we could base a business on producing monoclonal antibodies as research tools for other scientists. That way, we could fund the research it would take to develop monoclonal antibodies as cancer therapies.

Unfortunately, Howard and I had no idea how to start a company. We were scientists, after all, and there was nobody to mentor us in business. Not only that, we didn't have any money, and there wasn't any venture capital to be found in San Diego.

That is why I preach about the importance of the third and fourth legs of the biotech stool. Howard and I had the entrepreneurial spirit—but we didn't have venture capital and skilled management talent to attract talented employees and run the business.

Fortunately, my wife, Colette, knew Brook Byers, who had only recently landed a position at the venture capital firm Kleiner Perkins in San Francisco. I caught a flight to San Francisco for an initial lunch meeting. Brook was intrigued, and he persuaded his senior partners to come to San Diego to visit our laboratory. We sealed the deal with a handshake in a bar at Lindbergh Field.

But science and money alone don't make for a successful company. You must have superb management—starting with a chief executive officer (CEO) with outstanding strategic and leadership skills. We found such a person in Ted Greene, who became the first CEO of Hybritech. He moved the company from research reagents to higher margin, more profitable diagnostic kits.

These essential ingredients—outstanding biomedical research, an entrepreneurial attitude, local venture capital, and an assortment of talent—has grown a generation of serial entrepreneurs—individuals with the vision and energy to create one biotech company after another.

Today, the tuna boats are almost all gone, and the canneries are closed. The defense industry, a victim of the Cold War, lost 28,000 jobs. UCSD has an international reputation for excellence. And a six-square-mile area on the Torrey Pines Mesa now provides a critical mass of science and entrepreneurship.

Today, San Diego also possesses an essential biotech infrastructure that allows start-up companies to move directly into appropriate facilities rather than building lab space from scratch. The engine of growth and talent is in motion, propelling San Diego's biotech industry forward.

The results have been tremendous. Now, nearly 500 biotech/medical companies provide 30,000 jobs for San Diegans. Of the $1.4 billion invested in San Diego by venture capitalists, 50% has been in biotech. In 2004, a study by the Milken Institute and Deloitte & Touche LLP named San Diego as the number one biotech cluster in the United States. In fact, San Diego has the largest number of biotech companies of any city in the world.

For San Diego and for me, it has been a terrific journey—one that is not over yet.

A Career in the Life Sciences—A World of Potential

Chancellor Fox

Dr. Marye Anne Fox

Chancellor, UCSD

If you are considering a career in the life sciences, you are considering a vibrant area in which huge discoveries are about to be made. Many people say that the 21st century will be the century for biology, as the 20th century was the century for physics.

My interest in the sciences was in part sparked by world events. I grew up around the time that Sputnik, the first manmade satellite, was launched by the Soviet Union. As a result of this new frontier of discovery, many young people were considering careers in science and engineering. I loved research, so that is what I did. Science, in my case organic chemistry, was a great choice for me.

Students who have the potential to succeed in the sciences will be creative, innovative, and open to new ideas. They will be hard working, diligent, and able to pay attention to details. Does this describe you? If the answer is "yes," a career in biology or related fields may be a great match with your strengths.

Opportunities in the life sciences abound, especially in the San Diego area. Even if I weren't chancellor, I would have to point out the outstanding resources available at the University of California, San Diego (UCSD). UCSD offers top-quality education at the graduate and undergraduate levels—it is one of the top-ten public institutions in the United States. UCSD's researchers bring in one of the highest amounts of federal support per capita of any institution in the country. UCSD boasts a medical school dedicated to research, superb bioengineering and neurosciences groups, and biological investigations ranging from research on the cellular and molecular levels to translational medicine that brings discoveries to bear on treatments.

Harvard researcher Michael Porter has proposed the idea of "clusters of innovation," a critical mass of research and entrepreneurship that propels a region's biotechnology sector forward. San Diego is a case in point. The area has become one of the country's leading biotechnology centers because of the excellent research institutions in the region—including, of course, UCSD, whose contributions to the industry have been substantial and deep. UCSD faculty and alumni have spun off approximately 200 local companies, including over one-third of the region's biotech firms.

In this spirit of academic-industry partnership, many resources are available to those interested in transforming

technical ideas into businesses. CONNECT is renowned as a biotech and technology company incubator. UCSD's Rady School of Management also recently introduced its FlexMBA program, a two-year executive MBA program tailored for budding entrepreneurs and working professionals, particularly those in science or technology-driven organizations.

Even if you are just starting out, these resources are good to know about, although you may have more immediate concerns—like which classes to take to prepare for college. In this regard, if you are interested in the sciences, I recommend signing up for advanced mathematics courses. Learn algebra well, and study calculus. But also learn literature and languages—Spanish, for example. The individuals who will succeed in the future will understand global cultures in addition to specialized technical knowledge. Aim for a broad education.

One of the first steps in exploring a career in the life sciences is to take a laboratory course. Your laboratory work will give you some insight into the life of a scientist. Then you can ask yourself: Do I enjoy these tasks? Do I enjoy focusing on these kinds of details? Do I work well in this environment? Do these scientific questions fascinate me or do my passions lie elsewhere?

If you already know the life sciences are for you and you are in the process of earning a degree, I encourage you to work hard in your studies, and to look ahead to the world of work. Join research teams. Take advantage of internship opportunities. Enroll in summer work programs. These can be rewarding and offer you valuable insights into the opportunities available.

Wherever you are on your path, I wish you the best of luck. If you are reading this book, you are already showing the initiative and curiosity that will contribute to your success.

Future Life Science Career Enthusiasts