SYMPOSIUM

Transition from Academia to Industry: A Personal Account

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A career in industry has become a widely accepted alternative for those of us trained in medicine and/or science who have traditionally focused on careers in academia. Like any career decision, consideration of a position in industry should include asking yourself a series of fundamental questions. A few of the key questions should include: 1) What kind of work environment do you find most enjoyable (e.g., patient care setting, basic research lab, team-oriented setting)?; 2) What are you focused on accomplishing in your career (basic research discoveries, contributions to clinical medicine, compensation)?; 3) Are you team oriented in your interactions or are you more of an individual contributor? A successful career in any endeavor, including industry, starts with a careful and honest examination of what you are best suited for and inspired to do. Exp Biol Med 231:1682–1684, 2006

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Background

Like many physicians, my aspirations for a career in medicine began with an interest in science. Growing up in the 1960s on a 25-acre farm in Huntsville, Alabama, I was number six of eight kids. We often said that life was boring, but in retrospect, I had everything I needed to start a wonderful life. I developed a keen interest in learning and understanding things around me and a healthy sense of confidence that would come in handy during the many years of professional training.

Through a series of improbable circumstances, in 1977 I found myself at Haverford College on the swanky Main Line just outside of Philadelphia. While the competitive environment was more intense than that to which I was accustomed, the quality of the teaching was first rate, and I enjoyed my first introduction to cutting-edge science. I graduated in 1981 with a B.A. in molecular biology and headed off to Yale University for medical school.

The next 4 years were spent doing the traditional training in medicine, with the addition of a required research thesis. I focused my research on folate metabolism and a novel anticancer agent under the mentorship of Joseph Bertino, M.D. Graduating in 1985, I set off for a residency in internal medicine at Massachusetts General Hospital (MGH).

I spent 7 terrific years at MGH, 6 completing an integrated internal medicine/basic research/clinical cardiology fellowship and 1 as a faculty member. My research focused initially on understanding the molecular mechanism and clinical properties of plasminogen activators like tissue plasminogen activator (tPA) and urokinase (in collaboration with Edgar Haber, M.D.) and later on understanding the genetic and molecular bases of various hypertrophic cardiomyopathies (in collaboration with Christine Seidman, M.D.). At the time I believed I would be at MGH forever, unraveling the basic science of important topics in clinical cardiology.

Early Years in Industry

In the spring of 1988 my mentor, Edgar Haber, M.D., then Chairman of Cardiology at MGH, called me to a meeting in his office. He informed me that he would be leaving his position at MGH to become President of Research and Development at E.R. Squibb and Sons (later became Bristol-Myers Squibb). I was surprised by Ed's career change but did not think it would have much impact on me. Over the next several years I continued my basic and clinical science activities at MGH and also kept in close contact with Ed. When I visited Ed in New York we strolled

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through Central Park and he said to me, "A guy like you would be very valuable in industry." Typical of my interactions with Ed, his comment about industry left me thinking. I believe one of the greatest roles for a mentor is to help you continue to ask the right questions.

Someone once said to me, "MGH is a great place to be on the bottom (training) or the top (distinguished faculty), but in the middle you can get squeezed." In my first year on faculty, I may have felt some squeeze, but more importantly I began to ask myself fundamental questions relevant to making thoughtful career choices. What did Ed Haber see in me (or not see) when he said "a guy like you"? What experiences did I want to have in my daily work environment? (I was spending more than half of my time in the lab and the remainder in patient care.) How does my mind work, and how might this apply to my career choices? Am I focused on publication of important basic research or is there an equally or more satisfying alternative which could leverage my training in medicine and science? As I pondered these questions, I began to consider alternatives to the traditional career in academic medicine, much to the dismay of some of my academic advisors and colleagues.

After dismissing a broad range of considerations (e.g., business school, venture capital, investment banking), I decided to join the clinical research group at Genentech, Inc. in1992. This decision was based upon a number of factors:

1. Dave Stump, M.D., a great mentor and person, would be my boss;
2. Genentech was highly regarded for its science and rigor so I felt it would be a great environment for training in industry;
3. I would be the only cardiologist in the company when Genentech's most important product was a cardiac drug, Activase (r-tPA), for the treatment of patients suffering acute myocardial infarction (MI);
4. Activase was in the midst of a head-to-head trial (GUSTO) against its key competitive product, streptokinase, and I would lead the U.S. Food and Drug Administration (FDA) submission if the trial results were positive as I bet they would be.

Like most things, my transition from academia was not without challenges. For example, Genentech was much more teamwork and team decision oriented than I was accustomed to at MGH. While I brought a great deal of clinical experience, I had to learn to embrace the multidisciplinary approach required in drug discovery and development. It takes much more talent and experience than any one individual can master to file a successful investigational new drug application, design a robust clinical development program, and file a new drug application. Fortunately I started my career at Genentech at a very junior level so I had time to learn to become an effective team player with strong influencing skills. After a rocky start during which I sometimes asked myself if I should go back to Boston, I began to realize that I prefer and am more effective in a team-oriented environment.

In April 2003 the GUSTO trial was completed and the results were indeed positive: r-tPA was superior to streptokinase in improving 30-day survival in patients who present with acute MI or heart attack. Over the next weeks and months I was in for the time of my life analyzing, debating, and presenting the results to a range of audiences including the FDA and academic centers. GUSTO was one of the first and most important of the megatrials in medicine. It consisted of 41,021 patients with acute MI and was designed to test whether r-tPA's proven advantage in recanalizing occluded coronary arteries would translate into superior mortality reduction. The trial demonstrated a 15% relative (1% absolute) reduction in mortality by r-tPA compared with streptokinase, and it was my job to lead the effort to obtain a superiority claim over streptokinase from the FDA. We received our superiority claim for the treatment of patients with acute MI, and more importantly almost all patients in the United States began to receive the benefit of getting this life-saving therapy. Superiority claims are rarely granted by the FDA.

I spent 6 years at Genentech in increasing roles of breadth and responsibility. I was able to learn a great deal about the biopharmaceutical industry, from the drug discovery and development process to the various drug regulatory systems around the world. Ultimately, as head of the drug development process, I had great pride and pleasure in leading the development of a vast portfolio of drugs, some of which are now marketed (e.g., Herceptin, TNKase, Xolair, Rituxan) and helping to save and improve patients' lives.

I left Genentech in 1998 to help build a new and exciting company called Theravance (formerly Advanced Medicine, Inc.). The company was being organized by an extremely successful group of former Merck executives (including former Merck Chief Executive Officer [CEO], Roy Vagelos, M.D.), distinguished academic leaders, and venture capitalists. This was a golden opportunity for me to build a drug development organization from the ground up and to be a key member of an executive team who would build a world-class company. Indeed, Theravance has done extremely well, a result of its success in attracting top talent at every level and its focus on drugs which provide truly superior benefits to patients. Today Theravance has a broad drug development portfolio, several major corporate partnerships, and a market capitalization value of more than $1.5 billion.

Recent Years in Industry

In 2001, having spent 9 years in industry, I took on the challenge of trying to build and lead a company in the position of CEO. The key reason why I accepted the position was the fact that the Chairman was George B. Rathmann, Ph.D. George is arguably the most successful

biotech CEO of all time, having founded and built both Amgen and ICOS. I was not only confident that George and I could turn a struggling life-science tool company (Hyseq, Inc.) into a successful biopharmaceutical company but knew I was availing myself of the opportunity to learn from a great mentor.

However, the problems at Hyseq were significant. The company was near bankruptcy with only $2 million in cash, while it was spending about $60 million per year. It was also embroiled in litigation with DNA chip leader Affymetrix, which was a huge distraction and expense and made raising additional funding nearly impossible. Finally the company had long promised products, but none were in near sight. Saving the company was a complex task to say the least.

However, George and I began to tackle the problems in an orderly fashion, based upon immediacy of the problem and sequencing what needed to happen first to begin to build a new foundation. We were able to solve the litigation with Affymetrix by building trust during negotiations with them, and we turned a former enemy into a business partner. We were able to raise modest amounts of money based largely upon George's reputation. Unfortunately, to keep the company alive, I had to reduce the number of employees to less than 60 from a high of approximately 385. Finally we were able to acquire an exciting early-stage drug development candidate from Amgen which did not fit their strategic business focus and redirect our internal research team to be more oriented on product discovery.

Despite a great deal of effort and hard work, it was impossible to raise cash at the rate required to keep the company afloat because the financial markets at that time were difficult for biotechnology companies. In 2003 George Rathmann lent the company $40 million from his personal accounts. In early 2004 Hyseq merged with another company that had approximately $50 million in cash, and the merged company was renamed Nuvelo, Inc. Shortly after the cash infusion of the merger, we were able to acquire two more product candidates to strengthen our drug development portfolio, and we were able to raise cash in increasingly large amounts and on better terms.

We have come a long way. This year Nuvelo expects to complete two phase 3 trials for its lead product candidate, alfimeprase, and the company has an impressive portfolio of product candidates at earlier stages of development. Recently we announced a major deal with Bayer HealthCare for ex-U.S. alfimeprase commercial rights and completed financing that provided the company with more than $200 million in cash. The pride and confidence of people within and outside the company about its prospects have never been higher.

Although a turnaround of this magnitude and in this short period of time is unusual, it is not at all unusual for a biotech company to have a period of severe difficulty before its ultimate success (e.g., IDEC, Genentech, Gilead). Therefore, anyone who considers a career in biotechnology, particularly a smaller company without product revenues, should be comfortable with the associated risks of the company struggling to find its way forward.

Over the past 5 years, my expectations for my first job as a CEO have been realized or exceeded. George has not only been a great mentor but has become a friend and role model for me professionally and personally; the company's prospects appear stronger than anyone would have expected 5 years ago; Nuvelo is attracting the very best and brightest talent, and the market value of Nuvelo is approaching $1 billion. Although there have been many difficult challenges along the way to build Nuvelo, the result has more than justified the efforts.

Summary

A career in biotechnology can be an exciting and rewarding alternative to the traditional career paths for individuals with training in medicine or science. However, the talents, interests, and skills required for success in industry are different than those that predict success in academia. In addition, the rewards and daily challenges differ significantly in industry compared with academia.

Fundamentally, success in industry is driven by multifunctional teams that cooperatively navigate the complex, regulated, and high-risk drug development and approval process. In my experience, the most successful individuals in industry have a blend of strong interpersonal and scientific skills that allows them to become effective leaders in the team-driven industrial environment. Not only are such skills required to be successful within the company, they are even more important when it comes to influencing one's peers and colleagues within the FDA, investigational sites, and corporate partnerships.

Intellectually, the challenges in industry and academia differ significantly as well. Much of my time in academia was spent becoming more expert on a focused topic. In industry, much of my success has been driven by my interest and ability to think very broadly. In certain situations in industry. I have become an expert on a topic; however, on many more occasions it has proved more expedient to hire deep expertise through consultants and advisors. There are simply too many issues coming too fast in a successful industry environment for anyone to expect to be an expert on every important topic. Consequently, the skills required to attract and leverage outside or internal expertise are critical.

In closing, I want to acknowledge the tremendous help I have received from my mentors. I often advise to seek the mentorship of someone who is where you would like to be; these individuals are most likely to be able to show you the way. Finally, your career is a major part of your life, and if life is to be fully enjoyed, you should pursue a career that you enjoy.