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DISPELLING THE MYTHS ABOUT PHARMA R&D

JOHN L. LAMATTINA, Ph.D.

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For Mary

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ACKNOWLEDGMENTS

THIS BOOK is based on the efforts and dedication of thousands of scientists from around the globe who use their talents every day to invent new medicines to treat the scourges of the world. We owe all of these people our respect and admiration. They are the ones on whom we depend to help cure us.

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INTRODUCTION

FOR MANY scientists a job in the Research and Development labs of a pharmaceutical company is a dream come true. After having gone to school for many years (more than 20 for some with Ph.D.s), scientists are finally able to utilize their talent and training in an organization where they can immediately act on their ambition to make a difference in the discovery and development of new medicines.

I knew from an early age that I wanted to be a chemist. I found the science involved in building complex molecules fascinating. Like the "baby boomers" of the late 1960s, I wanted to "make a difference." Working on the creation of molecules that potentially had important biological activity was very appealing. I pictured myself working in state-of-the-art laboratory facilities and having access to the finest equipment and technology available. I envisioned working with outstanding scientists from around the globe, all of whom would bring their special talents to bear on projects designed to produce new drugs to treat the scourges of mankind: cancer, Alzheimer's disease, heart disease, life-threatening bacterial and fungal infections, and so on.

I majored in chemistry at Boston College, where I received a B.S. degree in 1971. From there I entered the Ph.D. program at the University of New Hampshire, where I studied organic chemistry with Professor Robert E. Lyle. At UNH I specialized in the chemistry of heterocyclic molecules—the type of molecules that make up the vast majority of medicines. After graduating from UNH in 1975, I went on to Princeton University as a National Institutes of Health post-doctoral fellow, where I studied with Professor Edward C. Taylor, one of the leading heterocyclic organic chemists in the world. By 1977 I was ready for a job in the "real world" and I was fortunate enough to join Pfizer's Research and Development laboratory in Groton, Connecticut. Despite the many years of schooling that I had, I quickly found that I knew little when it came to the discovery of new drugs. I was fortunate, however, to be surrounded by experts in not just chemistry but also biology, toxicology, drug metabolism, and other key disciplines. While these early days were challenging, they were intellectually invigorating. I was working with great scientists committed to curing the world's diseases.

Interestingly, scientists aren't the only ones who relish the experience of working in such an environment. Being a part of this enterprise is sought by many others who play key roles, such as computer experts who design the systems needed to track and analyze data and facilities professionals who help in designing and maintaining laboratories that maximize efficiencies. Hundreds and hundreds of people are involved in this discovery and development process and, when a new medicine is approved by the regulatory agencies around the globe, all take tremendous pride in their respective contributions.

Not too long ago a cancer patient visited the Pfizer Groton labs to thank the people there for literally saving his life. He was diagnosed with malignant melanoma in 2002. The two most promising treatment options that existed then had both failed. His cancer was spreading and doctors gave him two months to live. In 2004 he entered an experimental study with a new Pfizer drug. His results are best described in his own words:

> "I could have been dead in April of 2004 without this drug," he told an audience more than two years later. "Each day I have had since has been an extraordinary gift. I wanted to come here to say thank you to each and every person. I don't care if you're working on anti-CTLA4 or not. With these tools you can't tell which of them is going to turn into something so important for someone in your family or a neighbor. So now I feel it's my job to remind you folks of how important what you're doing really is. And it is a tough time to be working in the pharmaceutical development industry. I know what's going on, I know the heat that you get. Let it go, and just focus on the benefit that you are providing. You should be able to go home and sleep at night, thinking, you know, this was a pretty good day."

This patient's words were both inspirational and motivating. To help people like him is what brings these scientists to work every day.

One would hope that this patient's view of the work done in pharmaceutical R&D would be shared by many others and valued highly. Unfortunately, that is not the case. Headlines about this industry during the last 10 years have questioned what contributions are really made by these scientists. It is not unusual to read stories claiming that drugs are not discovered by "Big Pharma" but rather that the true discoveries are made in academic or government labs or that the industry wastes resources by focusing on "me too" drugs. The innovation of these same scientists is often challenged with claims that real innovation occurs only in the biotech sector of the industry. Pharmaceutical R&D is even accused of inventing diseases in order to turn a profit. *None of these claims are true*.

Furthermore, such uninformed views are not just aggravating but are also insulting to the thousands of people in the pharmaceutical industry who dedicate their professional lives to discovering new medicines. The R&D carried out in pharmaceutical companies is critical in the overall advancement of medical science. In fact, one might argue that it provides the crucial link because it is the work of pharmaceutical R&D that actually proves or disproves medical hypotheses that result in new treatments or cures.

If this is true, why isn't the important role of this research universally recognized? There are many reasons for the current state of affairs, but the primary reason is a lack of understanding of what pharmaceutical R&D actually does, how technically difficult it is, what the process entails, and how long and costly the drug discovery and development process really is. Not too long ago, I was able to see this problem first hand.

In March 2006, I was asked to be the Harold A. Iddles lecturer of the Chemistry Department at the University of New Hampshire. This was a great thrill for me and I accepted this opportunity excitedly. For one thing, I myself had listened to Iddles lec-

turers some 30 years earlier as a graduate student at UNH, hearing some of the outstanding chemists in the world such as Nobel Laureate Robert Merrifield. To be asked to now actually be an Iddles lecturer myself was an honor I had never envisioned.

But there was another intriguing aspect to this opportunity. One of the requirements for an Iddles lecturer was for one of the lectures to be a presentation of a general nature, one that would be of interest not just to the UNH community but also to people in the southeast New Hampshire region as well. The title of this talk was "Pharmaceutical R&D: The Worlds' Hope for Tomorrow's Cures." Some of the questions addressed in this talk included:

- What value do new medicines bring to society?
- Where do medicines come from?
- What innovation does Big Pharma bring?
- How are risks and benefits of medicines evaluated?

This 45-minute talk began at 4 PM to an audience of a few hundred people. The question and answer period that followed lasted another hour and a quarter when the meeting organizers had to end it. Nothing like this had ever been seen before at an Iddles lecture. The questions covered the entire spectrum of what is done in Pharmaceutical R&D. People were more than curious—they had dozens of questions and wanted answers. They were stunned to hear how long and costly it is to discover new drugs. People had little appreciation of the cutting edge science involved in pharmaceutical R&D. They asked how scientists stay motivated when, after spending years on a program, it suddenly dies. By 6 PM, it became pretty clear that the audience suddenly had another view of what pharmaceutical companies did, the challenges they face, and, most importantly, the critical nature of their work in bringing forward new medicines. The audience began to see a major piece of the health care debate in a totally new light.

This curiosity is not unique to this group of people in New Hampshire. Everyone expects something from the drug industry. If the industry doesn't deliver, people take it personally. Is there any other industry in which this is true?

Physicians and patients, investors, regulators, and administrators all have an active interest in the drug industry. Everyone wants to know what makes drugs work medically and economically. Why are drugs so expensive? Why do drugs take so long to develop? Is it the drug companies or investors who demand high profits? Does patient safety really take a back seat to profits?

This book attempts to answer these questions by focusing on the discovery and development of important new medicines. In effect, it paints an insider's account of the pharmaceutical industry drug discovery process, the very real costs of misperceptions about the industry, the high stakes—both economic and scientific—of developing drugs, the triumphs that come when new compounds reach the market and save lives, and the despair that follows when new compounds fail. It is hoped that this book will broaden the views of many readers as happened with the UNH audience.

Why is this important? To the extent that the misperceptions of pharmaceutical R&D continue, overall healthcare is undermined. As the reader will see in the

ensuing chapters, major new treatments for AIDS, heart disease, nicotine addition, rheumatoid arthritis, and others have emerged solely from this industry. Eroding of support for pharmaceutical R&D will result in delays for the discovery and development of even better new medicines. Ironically, this is coming at a time when medical science has unprecedented opportunities thanks to the unraveling of the human genome.

Finally, the Presidential election in 2008 will again thrust the pharmaceutical industry into the spotlight. The value of medicines and the importance of pharmaceutical R&D will be debated and will undoubtedly be scrutinized as a new President takes over in 2009. It is now a critical time to level the playing field.