CHAPTER ONE

The Puzzle

I WAS THE HEAD OF RESEARCH AND DEVELOPMENT AT Merck & Co., Inc., when two of the company's scientists dropped a puzzle in my lap. The puzzle had an important ethical component, but that was not what concerned the scientists who had come to see me. Bill Campbell was a parasitologist who was involved in the discovery and development of ivermectin, a remarkable substance that was active against the worms that plague livestock as well as household pets. He and Mohammed Aziz, an infectious disease specialist, weren't concerned about cattle or horses, however. They had a more intriguing problem in mind. They wanted to spend some of the company's money to see if ivermectin could be used against the parasite that causes river blindness in people.

Mohammed had a good, firsthand knowledge of the disease. He had worked with the World Health Organization (WHO) in Sub-Saharan Africa, where the black fly breeds in the continent's fast-flowing rivers – hence *river* blindness. The flies pick up a tiny parasite (microfilariae) from infected humans and spread it to

others. In the victim's skin, the parasites develop into adult worms that can reach two feet in length. They produce millions of microfilariae that crawl through the skin and produce intolerable itching. Even worse, when they enter the eyes, they cause inflammation and then scarring that leaves the victim blind. As Mohammed and Bill explained, there was a good chance that ivermectin might be the first effective treatment for this terrible disease. The drug, they said, was working against a related parasite that attacks horses.

But there was a catch. At that time, it was estimated that 18 million people were infected in Sub-Saharan Africa alone, and in some West African villages 60 percent of the population over fifty-five years old was already blind. According to WHO's estimates, there were over 100 million people living in areas of Africa and Latin America where they were threatened by the disease.[1] If ivermectin worked, there was bound to be a tremendous demand for it. But there was no way either the people at risk or their governments could pay for the treatment.

That was the first part of the puzzle, and I found it relatively easy to solve by saying "Yes." There was a potential downside for me personally. I hadn't been on the job very long and I was still learning how to promote new drug development in a corporate setting. While we had some big innovations in our pipeline, I was still an unproven rookie in the business world. I would be spending a considerable amount of company money in a field, tropical medicine, that few of us other than Mohammed Aziz knew very well.

Still, I had good reason to be confident of what we could accomplish with ivermectin. Merck & Co., Inc., had an impressive

[1] The scientific name of the parasite is *Onchocerca volvulus*, and thus the disease is onchocerciasis (pronounced onco-sir-KI-isis).

long-term track record in new drug development. The year I joined the company (1975), it was spending over $120 million on research and development out of total revenue of almost $1.5 billion. Revenue had increased by 12 percent over the previous year, and Merck was doing particularly well in overseas markets, which accounted for 45 percent of the firm's sales. But CEO Henry Gadsden had become worried – with good cause – about Merck's pipeline of new products, and he had hired me to solve that problem. It was as obvious to me as it was to Mohammed and Bill that even if ivermectin was successful against river blindness, the drug wasn't going to pump up the firm's revenue and make the stockholders happy. So I was being asked to take on some risk for myself and for the laboratories.

Nevertheless, I decided to crawl out on that limb. This decision reflected the fact that I was so new to the business world that I still thought of myself as a physician first, scientist second, and president of an industrial laboratory third. So I didn't hesitate and sent Mohammed and a small group of Merck people to Dakar, Senegal, to find out if ivermectin could indeed control river blindness.

The second part of the puzzle would be more expensive, more risky, and more difficult to solve. But before I faced that problem, Mohammed would have to find out if ivermectin worked against river blindness and I would have to learn how to do an entirely different job at Merck. I would have to become a business leader and would have to rearrange my priorities: I would have to become a corporate leader first, a medical scientist promoting innovation second, and a physician concerned about healing third. Before explaining how that happened, what kind of leader I became, and what Merck decided to do with this new drug, I want to tell you a bit more about myself and my background before I got into the pharmaceutical business.

CHAPTER TWO

The Professional Path

MY LIFE HAS IN MANY WAYS BEEN THE CLASSIC American dream: Poor immigrants come to the United States and work very hard; their children receive an excellent education and lead a better life. Like most such myths, the story has some truth to it, as it certainly does in my case.

I was born just before the start of the Great Depression, in October 1929, in Westfield, New Jersey, where my Greek father and one of his brothers owned a shop that sold candy, ice cream, and snacks. Times were hard for all of us, but I grew up in a family that was extremely supportive, even in the harshest days of the 1930s.

I needed support because in elementary school I was a cutup who entertained the other students – but not, of course, the teachers. They were interested in teaching Pindaros Roy Vagelos (they wouldn't use my nickname, Pindo) to read and write in English, goals that seemed formidable to a first grader who spoke only Greek at home. I was a slow learner. I just wasn't interested in learning. Since my last name begins with a "V," I sat in the back

of the class, where it was hard to hear. I got used to not paying attention to the lessons, although I pretended to work when the teacher was watching.

The year 1936, when I was in first grade, was an especially difficult one for my family. My father and his oldest brother owned the Westfield Sweet Shoppe in the center of an affluent bedroom community about an hour's drive from New York City. Like many other Greek immigrants, they had gravitated to the candy and small restaurant business because startup costs were small and they were largely uneducated. They could thrive with minimal English, making up with hard work and warm personalities what they lacked in education and capital.

But the hard times of the 1930s didn't spare Westfield or our family business. When the market collapsed, we lost our house. We moved into an apartment above a drugstore about two miles from Westfield, and I thought my life was coming unhinged. My sister and I changed schools. I lost my room and had to sleep on a sofa in the living room.

I remember it like it was yesterday. My parents, Herodotus and Marianthi, never discussed their financial problems in front of me. But I absorbed every sign of urgency in our family. My father and his older brother tried to keep the Sweet Shoppe going by cutting expenses and working longer hours. My mother, who had stayed home before I entered school, took a job ironing clothes in a laundry. After a full day there, she came home and made elaborate evening dresses for the few women in that part of New Jersey who could still afford them. As soon as we could work, we all helped with the family business. I washed windows and swept out the store. I think I learned more about life from these early experiences in my family than I did in school, where I continued to lag.

I learned a great deal from just being around my father. He taught me something about community and interdependence. Watching him help other members of the family come over from Greece provided important lessons about our responsibilities to others. I also learned something about endurance and optimism. Even during the worst years of the Depression, my father considered himself fortunate to be in a place where people could build new lives and had access to greater opportunities for themselves and their children. If you work hard, my father said, you can achieve anything here.

At first, it looked like this lesson was not going to take. I was an able young musician, playing my violin in the school orchestra and singing in the chorus. It encouraged me to think of myself as an entertainer. My father remained gentle but firm. He kept telling me about relatives whose sons had received scholarships to college. He spoke of the advantages of working with a pen behind a desk instead of working long hours on one's feet in a store or a factory.

Gradually, I began to get the picture and started to concentrate more of my energy on schoolwork. Especially when I discovered that mathematics came easily to me. Reading was still a problem. Nevertheless, my academic performance improved steadily, and to my surprise I found myself among the top group of students at Roosevelt Junior High School.

When the economy was recovering in the early 1940s, my father and mother were able to buy the Estelle Luncheonette from another Greek family. So we moved from Westfield to Rahway, a working-class town just five miles away. For me, this move was providential. It threw me into the hands of Miss Brokaw, my high school algebra teacher. Miss Brokaw was young, enthusiastic, and interested in her students. She began to make me feel that I could

do something important in life. She constantly challenged me with extra homework assignments, and I responded to that positive pressure by doing exactly what she had in mind.

I also was able to upgrade my position in the family business: Now I was a soda jerk. When I was working the fountain and helping with the tables, I got to know our customers, especially the people who worked for Merck & Co., Inc., which was Rahway's leading business. Merck was only a few blocks from the luncheonette, and many of its scientists and engineers regularly came over for meals. They impressed me with their intelligence and ability to talk about different ideas. The common language seemed to be chemistry, and for the first time I saw people truly excited about the intellectual aspects of their work. I started to see an interesting path opening ahead of me, and it led directly to college, as Miss Brokaw and my father had understood long before I did.

Academic accomplishment brought out a fiercely competitive streak in my personality, something I can't remember having during my early years. I became an honor student on a fast track in science and mathematics, both of which played to my newfound ability in analysis. I was not a geek – the luncheonette prevented that from happening – but I now had all of the energy and determination of a religious convert. My newfound zeal didn't keep me from being turned down when I applied to go to Johns Hopkins, but I had better fortune with the University of Pennsylvania, which became the next leg on my path to a profession.

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I had never even seen the Penn campus before my parents drove me and my single suitcase down to Philadelphia in September 1947 and dropped me at the gate on 37th Street and Woodland Avenue. Beyond the gate were dormitories built around large quadrangles

of green lawn. The classrooms and laboratories that absorbed my time over the next three years sprawled on both sides of Woodland Avenue, which divided the campus.

At Penn I found exactly what I was looking for, including the opportunity to set my own pace and to explore what intrigued me. When I found difficult problems to solve in chemistry or physics, problems that sustained my interest, I became even more energized. I learned how to concentrate, to stay focused for longer and longer periods of time. Did the memory of my mother bent over her sewing, my father's long hours in the shop, have anything to do with my drive? I believe they did. Studying late at night, I would recall how hard both my parents worked and reflect on the difference between their lives and those of the professionals who ate at our luncheonette.

The only significant break in my schedule was rowing. I rowed my whole time at Penn with the lightweight crew. I discovered that the discipline of rowing – the physical exertion and team coordination – fit my personality. My teammates became my closest friends. From rowing I learned the benefits of being in peak condition, the importance of teamwork and team leadership, and the positive impact physical fitness could have on my intense studies in chemistry. After I rowed, my concentration was always better.

When I wasn't rowing, I focused with great energy on my studies and was able to graduate in three years. Playing to the hilt my role in the classic American immigrant story, I had become the classic American high achiever. Then, rather suddenly, I had to decide what I was going to achieve after I left Penn. The top two contenders were graduate training in chemistry or medicine. I loved chemistry. Organic chemistry in particular was incredibly exciting to me, and I could see opportunities to make important intellectual and practical contributions through a scientific career.

But inside my head I heard my parents and relatives saying, "You have to do things for others." This was the kind of deeply grooved voice that stays with you for an entire lifetime. Now it guided me away from chemistry and toward medicine. My family was especially proud (as was I) when I was admitted to Columbia University's College of Physicians and Surgeons. Their son was pointed toward an honorable profession, and that was important to the Vagelos clan. The tug-of-war between science and medicine was not over, but for the moment, medicine was the winner.

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Then in the fall of 1950, my triumphant march through academia came to an abrupt halt. Like many other high achievers, I hit a wall. At the College of Physicians and Surgeons (P&S to us), I quickly rediscovered academic anxiety. I found that I was launching my study of the ultimate biology – the anatomy of the human body – with the least possible preparation. What I had mastered at Penn was problem solving in science, my strength, but medical school required memorization, my weakness. I was deeply distressed and uncertain what to do. Returning home at Christmas break, I was on the edge of failing and I contemplated ending my medical career before it began.

Fearful of failure, I returned to New York and ground my way, inch by inch, through anatomy. I survived my first year in medical school, but I had regained some of the humility I seem to have lost at Penn.

I spent the summer after the first year of medical school at home in Rahway working as an intern for Merck & Co., Inc. I would like to claim that the work engaged my imagination, but it wasn't like that at all. Though I had great respect for the company's scientists and I knew that the Merck laboratories were widely respected as

a state-of-the-art operation, the rote tasks they assigned me were deadly dull. After that summer, I had no intention of ever returning to Merck or any other pharmaceutical company. The only positive result was to make medical school and a career in medicine look even more attractive.

In my third year at Columbia, I encountered the legendary Dr. Robert F. Loeb, chairman of the Department of Medicine. This towering figure was coauthor of the *Textbook of Medicine* used in many medical schools and revered at Columbia, where it was the bible for both faculty and students. We all studied Loeb's bible with care and also learned a good bit about the author. We knew, for instance, that he had a sadistic streak that emerged when he did medical rounds. Terrified by these encounters, we worked very hard to master the Loeb medical dogma. I survived his rounds relatively unscarred. In fact, I enjoyed clinical medicine so much that I began to set my sights on internal medicine, possibly leading to a specialty in cardiology.

One afternoon toward the end of my fourth year, I was finishing my work in obstetrics and, with no delivery scheduled, I joined the rounds with Dr. Loeb. Most students avoided him after their third year, but I had always done well in his classes, and unfortunately I wasn't afraid. As we stopped at the bed of a patient with inflammation of the kidney, Loeb asked one student after another for the incubation period of the disease. As each confessed ignorance, Loeb's anger mounted. Finally, wheeling to me, he said, "Vagelos, tell these third-year students what *every* P&S student should know!" I had to admit I didn't remember either, and Loeb berated me.

I was stunned at my foolishness in putting myself on Loeb's firing line so casually. Later that day, I walked past Dr. Loeb and