If I examine my early youth, I can detect hardly any signs of entrepreneurship. Sure, critical decisions had to be made: first, to leave Hungary to study in Switzerland over the strong objections of my parents; later, to abandon my academic career, my wonderful mentor, Leopold Ruzicka, and the old continent for an essentially unknown future. In retrospect, I consider the causes of these events, speaking in chemical terms, more the push-pull effect of the grave political circumstances of that time than entrepreneurship.

When Pearl Harbor was attacked, I was in Havana waiting for a boat to Ecuador, where I had been offered a chair in organic chemistry at the University of Quito. Since the University of Havana showed no interest in me, I tried to get a job at the largest local pharmaceutical firm—Laboratorios Vieta-Plascencia.

The reaction of the owner, Angel Vieta, dean of the University of Havana medical school, was negative. To quote: “In the 18 successful years at my firm, I never had a chemist. Why should I hire you now?” My answer was short and bold: “Give me a chance and I’ll show you.”

Apparently impressed, he offered me the glorious salary of $20 a week. I did not fail him. A dozen products later, I was making $1,000 a month and 15% on those products’ sales. The university offered me a professorship. I declined but eventually agreed to direct a research program for Ph.D. candidates in my laboratories. The most famous of my two dozen students of those days was Ernest Eliel, who became a president of the American Chemical Society.

My Zurich-born interest in steroids led me to look for domestic sources of steroidal sapogenins suitable for hormone synthesis. Finding none, I imported sarsaparilla and learned how to extract diosgenin, the substance needed to produce steroid hormones, and Mexican yams. Rumors of these activities led to an invitation to visit a start-up firm in Mexico named Syntex.

My life started in Montevideo, Uruguay, many years ago. Uruguay is a small country; today it has three million people. Back then life in Uruguay was wonderful. It was a great place to live—safe and peaceful—and the standard of living was high. For many years, Uruguay was known as the Switzerland of South America. The social and political organizations were very progressive: women were allowed to vote; it had the highest rates of literacy; it was the first social democracy on the continent; primary, secondary, and university education was free.

The population was and still is mainly of European descent, mostly Italians and Spaniards. My grandfather emigrated from Italy and arrived in Uruguay when he was 16 years of age. My father was in the banking business, and our family enjoyed a good standard of living. Early in my life, I lost both my parents. My mother passed away when I was 12 years of age, and my father when I was 18. Now, when I look back, I think that loss forced me to learn to be on my own. I was also lucky enough to have an uncle and an older sister who supported and encouraged me to continue my education.

After earning a B.Sc. at the University of Montevideo in 1941, I began studying at the school of medicine. I soon realized, however, that anatomy was not one of my favorite courses. I had taken some chemistry and biochemistry courses while in premed, and I decided to study biochemistry instead. Since there was no biochemistry degree in Uruguay or South America, I started to inquire about studying abroad.
The Early Days of Syntex

After World War II ended, I boarded a Liberty ship in Montevideo, Uruguay, and arrived in the United States at the port of New York on 16 August 1945, two days after the Japanese had surrendered. For me, arriving in New York at that time was an unforgettable experience. It was like a big party: people were celebrating on the streets, there was music, and it was incredible. After a couple of weeks I went on to Harvard. There I met a young professor who explained my options. I would be part of a group of six students following a research program under the guidance of the professor. I then went to visit the University of Rochester. During those times, the entire medical school was working on the Manhattan Project. As a foreign student I could not participate in that project, so the chairman of the chemistry department at Walter R. Bloos, told me they would give me a lab, and that the professor would visit me every now and then to the field of lipids. Having my own lab and the freedom to choose what I wanted to work on, it convinced me to decide on the University of Rochester.

At Rochester I became interested in my area of expertise, I started from square one, developing my own processes. Soon we were in production. I was offered $1,000—a huge sum by today’s standards—and we began manufacturing hormones with the exception of estrone. While tackling this last problem, my attention was drawn to a young chemist, Carl Djerassi. Following a hunch, I invited him to Mexico. He was charmed and accepted. This cooperation was one of the most significant events in our lives, the empathy and friendship we built has carried through all these years.

Since profits selling hormones and steroid intermediates were significant, nobody questioned my budget. I invested in research, bringing the most talented scientists available to Mexico. Interestingly, organic chemists, in contrast to biologists, were more ready to assume risks. One of them was Alejandro Zaffaroni. We met at the 1951 Laurentian Hormone Conference in New Hampton, New Hampshire, after a long correspondence involving steroid samples for Alex’s paper chromatography. This encounter turned out to be one of the most significant events in our lives, the empathy and friendship we built has carried through all these years.

I will not describe in detail the two monumental events in Syntex’s history: the cortisone race and the pill. They are well known. For a short time, they focused the attention of the world on our company, our achievements, and Mexico.

At this stage we had an outstanding team of scientists and consultants, an astounding number of patent applications and publications, and an impressive number of new compounds that resulted from what I used to call “molecular acrobatics.” Our scientific reputation allowed us to attract the best talent. But all this was not in line with the operation of a small-sized chemical producer of steroid intermediates. Prices fell and other steroid manufacturers became competitive.

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Going to the United States

I managed to get a scholarship to come to the United States thanks to the Institute of International Education. My two options were Harvard University or the University of Rochester. I boarded a Liberty ship in Montevideo while World War II was still going on and arrived in the United States at the port of New York on 16 August 1945, two days after the Japanese had surrendered. For me, arriving in New York at that time was an unforgettable experience. It was like a big party: people were celebrating on the streets, there was music, and it was incredible. After a couple of weeks I went on to Harvard. There I met a young professor who explained my options. I would be part of a group of six students following a research program under the guidance of the professor. I then went to visit the University of Rochester. During those times, the entire medical school was working on the Manhattan Project. As a foreign student I could not participate in that project, so the chairman of the chemistry department at Walter R. Bloos, told me they would give me a lab, and that the professor would visit me every now and then to the field of lipids. Having my own lab and the freedom to choose what I wanted to work on, it convinced me to decide on the University of Rochester.

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The Early Days of Syntex

Continued from page 10

for survivors, only to find us roaring with laughter.

The results of the brilliant amateurs with a "can do anything" attitude. We were like stem cells (though then none of us really knew what they were). We could differentiate into anything we desired. Production, finance, sales, marketing—all held no fear for us.

The source of all these activities had to be our chemists. We rapidly turned the risk-taking volunteers into executives. This movement resulted in a healthy effect on our research. Talented youngers moved up rapidly, allowing new ideas to blossom and preventing our research from becoming stale.

EXPANSION

Profits from sales of our bulk steroid products, now on a much larger scale, still provided our basic income. Yet in 1958 we started a pharmaceutical company in Mexico based on novel topical and systemic steroids. Our first hit was Synalar. This topical corticoid for treatment of psoriasis later became the first product of our U.S. venture. Innovative research collaborations with large pharmaceutical firms provided another source of income. Apart from becoming eventual providers of the so-called active ingredients, we wanted full and great foresight in retaining the right to market under our own label. Nobody thought of us as a competitor to the pharmaceutical market.

Alex and I were traveling the world, writing new collaboration and license agreements. Our biggest coup was to create a worldwide distribution of our novel compounds practically overnight and without a cent of investment. This novel approach consisted in becoming a partner of the so-called "big five" drug firms in a European country. We proposed to provide them with the "raw drug", the active ingredients, and have right of first refusal for our future products. But again, we retained our right of the research and development on our own label. This arrangement was unwieldy in those days, but our research produc-

tivity proved to be convincing. Eventually among others, Syntex-JCJ, Syntex-ICI, Syntex-Astra products were launched.

The year 1961 marked the start of the inevitable changes Syntex was undergoing.

It began with the decision to begin moving the company to the United States to become an important factor in the domestic and world market. We all accepted...I remained in Mexico, but was in daily phone contact with Palo Alto, and every month went for a week to the West Coast.

Slowly the era of gifted amateurs yielded to outstanding professionals. A host of new talent entered the picture.

The growth of our business was meteoric, ever expanding domestically and internationally.

RETIREMENT—AND

Thoughts on Management

In 1982, strictly adhering to the rules I established, I relinquished my executive positions, but continued on the board of directors with the title of founding chairman.

I also became chairman of the newly created board of science. This move sent a forceful message to employees and the outside world about the importance of science for our company. The board enabled brilliant scientists, such as F. J. Corey and other Nobel laureates, not only to provide their invaluable scientific input into Syntex's search for new medicines but also to pursue their passion for science within a pharmaceutical industry.

The value of our company rose astronomically. After a large number of stock splits, at its maximum an original investment of $2 per share was worth $16,750. In 1994, Syntex was acquired by Roche Holdings for $3.5 billion.

Talented young researchers and colleagues, who found their way into new business ventures, embraced many of these ideas—and my management philosophy lives on.

The success of the controlled drug-delivery technology can be seen by the size of the market and the number of companies and products that use the wide range of drug-delivery technologies. Looking back to the early days of this technology, I am amazed at how large the current size of the market is and how much it promises to grow, and also of how many drug delivery technologies and patents now exist. Even today, controlled-release technologies are being used in new fields such as consumer products and agriculture.

Since ALZA, I have been blessed with the opportunity to start many other companies. Some of these technologies stemmed from my own ideas, but in large part they resulted from the collaboration of a large number of very capable scientists with whom I had the fortune to be associated.

The companies are too numerous to list them all, but we have developed many novel technologies, for example, computational chemistry and combinatorial chemistry; gene shuffling; biomarkers, including nano bar codes, and much more. I am also proud that many ALZA alumni have branched out as I did and created their own companies.

My most recent endeavor, Alexza Pharmaceuticals, I founded Alexza in 2000 to explore the idea of delivering existing drugs via a rapid-onset-of-action device. We began with a shortlist of existing medications, focusing on the potential of Glucotrol XL, and Ditropan XL. The company currently has more than 900 active patents and about 1,200 patents pending.

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