

# Indian Academy of Sciences

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### PUBLIC LECTURE

By

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At the outset, I would like to thank Dr. Kasturirangan and other members of Indian Academy of Sciences for inviting me to deliver this public lecture today.

A few months ago I was conferred 'businessman of the year' award by Business India. I am now invited to deliver a lecture at the Indian Academy of Sciences, which looks like a paradox; but it must be understood in the context of my business career spanning 25 years, during which I used science and technology to build a flourishing pharmaceutical industry.

Jawaharlal Nehru, the first Prime Minister of independent India believed that science and technology should be harnessed to build a strong and modern India. In fact, in one of his addresses he said, to do this, "scientists must come out of their shell". This was misunderstood by many. As I was building my entrepreneurial career, after completing PhD in Kinetics at NCL, Pune and a six-year stint in IDPL, I used to recollect his words very often and

felt that I was actually doing what he had in mind when he said, "scientists must come out of their shell".

The synthetic drug plant IDPL in Hyderabad had provided me opportunities to gain advanced skills in process development and implementation of process know-how on plant scale. Seeing an opportunity in the emerging scenario due to enactment of Indian Patent Act, 1970, I quit IDPL in the year 1973 and became an entrepreneur. In the next decade or so, I have developed many processes and produced many bulk drugs for the first time in the country.

However, by late 80s, I became quite conscious of the fact that it is the bounden duty of the pharmaceutical industry to make the medicines affordable to the common man of India. In 1988 while giving Prof. M.L. Khurana memorial lecture at 40<sup>th</sup> Indian Pharmaceutical Congress at Calcutta, I said, "The Patent Act, 1970 has given us an advantage which the industry must exploit to not only make profits, but also to bring the advanced medicines at a reasonable price to our poor people". I have practiced what I said. All the frontline drugs we brought for the first time in India were primarily priced based on affordability and not with profit as the motive.

For us in the pharmaceutical industry, it was a great opportunity to use science and technology as tools for the benefit of the society. What followed was a slew of pharmaceutical preparations ranging from anti-infectives to anti-hypertensives, all of them priced at a fraction of the prices prevailing in developed countries.

The entire pharmaceutical industry rose to the occasion and the result was that there was practically no medicine that was not accessible or affordable by the poor man in the country.

In the year 1991 India has accepted the challenge of globalization and many individuals and institutions were overwhelmed by this challenge. Pharmaceutical industry has been under the impression that the feast will continue and that the Indian patent Act 1970 will remain to generate profits. I was a loner at that time to take a completely different view. While delivering the presidential address of the 44<sup>th</sup> Indian Pharmaceutical Congress in this very city in January 1993, I said "the issue before us is not whether to accept the patent regime or not, but it is a question of time - 10 years as suggested in Dunkel amendments or more as demanded by our industry". I said the industry should take up this challenge and start drug discovery efforts. Everyone in the industry and the so-called international pundits said that drug discovery research is prohibitively expensive and is not within the reach of the Indian industry. One pundit even went to the extent of saying, "do not delude yourselves". I have given my own arguments and said that drug discovery is possible in India even with an annual expenditure of Rs.10 crores! This kind of expenditure was within the reach of at least a dozen pharmaceutical companies in India, but no one even believed that it is possible to carryout drug discovery research with this kind of investment.

In 1993, I have put together a team of brilliant scientists from various disciplines of life sciences and started Dr.

Reddy's Research Foundation. I must confess that even though I made bold statements, I was not very sure of the outcome. In order to ensure continuity and the future of my scientists, I kept aside a sum of Rs.100 crores and was prepared to allocate more funds to take care of the Foundation as long as it is necessary. In fact many of my colleagues remember my initial remarks, when I said ' God-willing, if we are successful, we will build a research-based pharmaceutical organization of the likes of Merck and Pfizer. God-forbidding if we are not successful, we will push the frontiers of science and publish path-breaking work!

I am narrating this story because I want to impress upon you that unlike any other business venture, pharmaceutical business requires a commitment of different sort. George W. Merck, founder of the reputed pharmaceutical firm Merck & Co, best brought this out, when he said, "Medicine is for people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear." When I look back, I must say that God is not only willing but was so munificent. We hit the first milestone quite early into the research, when we have licensed in March 1997 one of the most potent thiazolidinedione compounds (insulin sensitizer) for the treatment of diabetes to Novo Nordisk of Denmark, the world leader in diabetes, for an upfront payment of US\$ 3 million.

What followed was much more than anyone imagined. When we continued our work on insulin sensitizers, we started seeing some interesting results. Some of the compounds that we designed and synthesized (non-thiazolidinediones)

have shown remarkable activity in reducing not only plasma glucose but also many lipid parameters. When we researched further, we found that these compounds represent a new class, which we termed as "dual acting PPAR alpha-gamma activators".

Peroxisome Proliferator-Activated Receptors (PPARs) are members of the nuclear hormone receptor super family. PPAR has three subtypes: PPAR *alpha*, PPAR *delta* (also called *beta*) and PPAR *gamma*. While the exact role of PPAR *delta* is not known to-date, the PPAR *alpha* and PPAR *gamma* play a critical role in lipid metabolism and carbohydrate metabolism. Agonist-induced activation of PPAR *alpha* is known to influence the reduction of triglycerides levels whereas, agonist-induced activation of PPAR *gamma* is known to stimulate reduction of insulin resistance and hyperglycemia in type-2 diabetes.

One of the PPAR alpha-gamma compounds was licensed again to Novo Nordisk in June 1998. Discovery of this new class of compounds has proved that it is not 'we' but 'they' who deluded themselves.

It is now almost four years since we have licensed this compound, which is now in phase-3 clinical-development. Incidentally, this compound is now regarded as the first-in-class of a series called 'Glitazars' and is aptly named as "Ragaglitazar" (Reddy *alpha gamma*).

Not only have we pioneered the discovery of this new class of antidiabetic compounds, but also succeeded in designing and synthesizing second-generation compounds of this new

series. One such compound was licensed to Novartis, the 8<sup>th</sup> largest pharmaceutical company in the world, in May 2001.

As a result of these brilliant discoveries in a short period of time, we are now increasingly being recognized as world leaders in PPAR Research. In addition to the work in diabetes, we at Dr. Reddy's are also working in the field of cancer, Infectious diseases and inflammation. As per current indications, we expect to have a research pipeline by next year, which can be compared to that of a mid-size pharmaceutical company.

This is what can happen to a Scientist who can see an opportunity and take bold decisions to create a future for his own organization as well as for the country. It is somewhat astonishing and astounding that just about 25 years back, I was drawing a salary of Rs.1500/- a month, working for the Government-owned IDPL and today I am the proud owner, holding a significant 26% of equity, of a Rs.8000-crore worth company that is listed on the New York Stock Exchange.

I have narrated this to show how one can earn enormous profits by harnessing science and technology and plough back those profits, as I have done, to the benefit of science and also for the benefit of the society.

While this is my own story, there are many and more successful examples to prove that 'Science for profit is profit for Science!' I would now like to draw your attention to a few such stories.

## **Herbert Boyer – Creation of a new industry, Biotechnology:**

Herbert Boyer and Stanley Cohen discovered “scientific cloning” and reported their historic experiment in November 1973 in the proceedings of the National Academy of Sciences. Soon after this publication Robert Swanson, a venture capitalist, approached Herbert Boyer. Was it possible, Swanson asked, not just to use cloning technology to create countless identical strips of an entire gene, but to exploit the technique to make the gene’s product? Boyer’s answer to Swanson’s question about the possible manufacture of human proteins using genetically altered micro-organisms was a “yes” because a plasmid could code for a protein and use the bacterium’s internal protein-making machinery to produce it. And in giving this answer, Boyer set in motion forces that were to establish an entire new industry, now known as Biotechnology industry. Boyer borrowed \$500 and joined Swanson in forming a company that would exploit this new science. They called it Genentech, for genetic engineering technology.

Today the US Biotechnology industry is worth more than 200 billion dollars (market cap of the biotech industry).

## **Paul Janssen: Janssen Pharmaceutica**

Look at the success story of Paul Janssen, the Belgian organic chemist who started his research laboratory with an investment of 1000 USD, one hot plate and a few mice. His company Janssen Pharmaceutica, which became an MNC and

later a part of Johnson and Johnson, has discovered 80 new drugs in 30 years and Paul Janssen is credited to be the most prolific discoverer in the pharmaceutical industry. Not only has he benefited the world by inventing life saving drugs that include the first antidiarrhoeal LOMOTIL (diphenoxylate), but also created wealth for the organization and for himself. It is estimated that the value of his holdings in this company today is a cool one billion dollars!

#### **William Rutter: Chiron**

Bill Rutter, a PhD in molecular biology, along with two other scientists shared a common vision to use the emerging tools of biotechnology to create products for use in human medicine. Thus, as early as 1981, he founded Chiron Inc., a biotech company that has focused its energies on the development of vaccines mainly for hepatitis. Today, Chiron is one of the world's largest biotech companies with a market cap of over 6 billion dollars.

#### **Alejandro Zaffaroni : Alza Inc, Affymetrix Inc.**

Al Zaffaroni has an impressive career as an inventor and entrepreneur on controlled-release drug delivery, a now common method of treatment that he was one of the first to support. After a successful career with Syntex Laboratories, in 1968 he founded his own drug delivery

company ALZA Inc. In a thirty-year career at Alza, Zaffaroni performed double duties of research and management. Zaffaroni faced an uphill climb, because the medical and pharmaceutical industries were still hesitant, through the 1970s and into 80s, to accept controlled drug delivery.

Today, controlled drug delivery is widely recognized as the most safe, efficient and cost-effective means of many types of treatment. Alza, merged with Johnson & Johnson in 2001, is one of the leading drug delivery companies with over \$950 million in revenues in 2000.

Apart from Alza, Zaffaroni has founded over half-a-dozen biotech companies including Affymetrix (1991, market cap of 1.3 billion dollars) whose recent innovation is the GeneChip system for computer-aided analysis of genetic information.

As I speak at this Faculty Hall in this great Institute, the path-breaking discoveries and contributions of Sir C. V. Raman and G. N. Ramachandran come to my mind, the former a Nobel Laureate in Physics and the latter a stalwart in structural biology. The contributions of these two great scientists have left an indelible mark on Science throughout the world. There is a need to re-enact such path-breaking scientific contributions from India. It is unfortunate that independent India has not produced a Noble Laureate in Science. We all are aware that India suffered a lot due to shortage of resources, import restrictions and lack of infrastructure for pursuit of scientific research. But today, the scenario in the country is entirely

different and we have no such excuses, thanks to the liberalization and globalization of our economy and industry.

Let us, for a moment turn to Stanford University and Herbert Boyer. It is true that America had great scientific institutions as well as a culture of venture capital even as early as the 70s, which is most important to build big industry. I have reason to believe that India also possesses equally great scientific institutions, the foremost being your own Indian Institute of Science. The spirit of venture capital is gaining ground in the city of Bangalore. Is it then possible that a Herbert Boyer may rise from this great Institute to help create wealth and pave the way for the advancement of science?

Coming to the future of pharmaceutical research, all of us know that sequencing of the human genome has generated a vast body of knowledge at a very basic level. It will require much greater effort and resources to actually translate this knowledge into practical solutions for human health.

Normal genes and their variations known as polymorphisms need to be studied in relation to their corresponding proteins in order to understand how biochemical pathways are altered in a diseased state. This will lead to the identification of proteins that could serve as:

- Markers for use in diagnostics.
- New drug targets for designing novel drugs

- Therapeutic proteins such as streptokinase, tissue plasminogen activator etc.
- Gene therapy, the ultimate goal of genomics wherein defectives genes are corrected

India has advantages enabling the pursuit of such opportunities. These are -

- Intellectual capability
- Strong basic education
- Cost advantages
- Multiple sources of funding

In my opinion, what we need are the following:

- Revamping/strengthening higher education
- Specialist skills for multi-disciplinary research
- Infrastructure for cutting edge drug discovery
- Employment opportunities to prevent brain drain (*The Organization of Pharmaceutical Producers in India estimates that more than 15% of the scientists engaged in Pharmaceutical R&D in the U.S. are of Indian origin*)

In conclusion, I would like to observe that in addition to all these resources, we need to bring entrepreneurial perspective to scientific research. I compliment the faculty members of this Institute for taking a lead in this direction and founding Strand Genomics a Biotech company. This was unthinkable in academic settings until recently. In a small measure, we have recently taken a new initiative to establish a center of excellence in life sciences that will cater to the requirements of the research-based pharmaceutical organizations in the country. This

initiative is being pursued with the support of the Government of Andhra Pradesh and in collaboration with the University of Hyderabad. The institute will be located on the campus of University of Hyderabad.

Let us hope that there will be more such initiatives in future to help advancement of science in this country.

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