

# *Innovation in the Pharmaceutical Industry — Future Prospects*

**Talk by Dr Franz B. Humer, Chairman of the Board of Directors and CEO  
of F. Hoffmann-La Roche Ltd, to the *Zürcher Volkswirtschaftliche  
Gesellschaft*  
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Ladies and Gentlemen,

Anyone who has read the papers in recent months could easily get the impression that the pharmaceutical industry as a whole is not doing very well. Internationally, serious problems with world-famous drugs have hit the headlines. Prices and costs have come in for scrutiny in some countries including – and fairly vehemently of late – Switzerland. Confidence in the industry and its reputation have been damaged, mainly in the USA but also here in Switzerland.

Over the past five years, the market capitalisation of the global pharmaceutical industry has halved to CHF 1.5 trillion. Of course the market value of other sectors also plummeted when the stock market bubble burst. However, it shows that the financial markets have greatly reduced their assessment of the industry's prospects. Last year, the market capitalisation of pharmaceutical companies declined further. Pleasing exceptions to this trend were Roche and the other Basel-based pharmaceutical company.

For the industry as a whole, therefore, 2004 was not a good year. However, that is no reason to grumble. A sector which needs 10 to 15 years to bring a new product to market readiness thinks, acts and plans in longer-term dimensions. It is commercial, scientific and political trends that are decisive for us. The political framework is particularly important, as there is probably no other industry that is as strictly regulated as the research-based healthcare sector.

In the light of this situation, I would like to talk today about the challenges facing our sector and explain why I am still (very) confident about the future of companies like Roche.

But before I look ahead to the future, let me give you a brief overview of the present situation (what we have achieved so far).

## **Where is the pharmaceutical industry today?**

- **Medical progress:** Undeniably, research-based pharmaceutical companies have made enormous progress in the treatment of many illnesses, including infectious diseases, childhood diseases, some types of cancer, cardiovascular disease, diabetes and hepatitis. Looking back over the past century, it is clear that medical science has made breathtaking advances. This is shown, for instance, by the fact that life expectancy has risen enormously to

around 80 years, compared with 55 in the late nineteenth/early twentieth century when Roche was established. Even so, it is still not possible to treat the causes of most diseases.

- **Cost of research and development:** However, remaining at the cutting edge of technology in the face of such rapid advancement is becoming increasingly expensive. Despite the enormous progress that has been made, developing a new drug is still a bit like looking for a needle in a haystack: only one in 10,000 substances screened eventually becomes a fully fledged product that can be used to treat patients. And as I have said, it takes 10 to 15 years to achieve that. That costs an average of about CHF 1 billion for each drug brought onto the market (including opportunity costs and the cost of failures). Over the past 20 years the cost of developing new drugs has increased by a factor of eight. Last year Roche invested more than CHF 5 billion in research and development and spending will be a good deal higher this year.

Despite the high sums involved, there is still no guarantee of success, let alone a guarantee that prices or volume sales will be acceptable. The cost and complexity of research have increased substantially. At the same time, political pressure on prices has risen and that has evidently increased the attendant business risks. Those are the main reasons for the progressive consolidation of our industry. Fifteen years ago, the ten largest companies commanded 25% of the global market; today their market share is over 50%.

- **Geographical shift:** Another fact is that in recent years the pharmaceutical industry's "centre of gravity" has shifted from its traditional home market of Europe to America. While European companies used to dominate the "champion's league" – comprising the top ten pharmaceutical companies – the top players today are US companies.

Even so, Switzerland can boast two players in this league. Twenty years ago, the European and American pharmaceutical markets were roughly equal in size. Today the US market is twice the size of the European market and far more profitable (if price levels in the United States were the same as in Europe, it would be impossible to maintain funding of industrial research and development at the present level). This ongoing trend has serious implications for research and innovation. For some time now, European companies have been channelling more than half of their research spending to North America, whereas twenty years ago Europe accounted for two thirds of global pharmaceutical research. The United States has a clear edge both in terms of "output", in other words, the number of new active ingredients for pharmaceuticals, and in terms of "input", that is, R&D spending (USD 20 billion are spent on drug development in the United States every year).

The shift away from Europe is one outcome of years of misguided and short-sighted policies in Europe.

For pharmaceutical companies, globalisation not only means an increasingly tough race to innovate; the United States, Europe and Switzerland are also competing fiercely for jobs and investment. And it will not be long before Asian countries like China, India and Singapore narrow the gap to the global elite in the field of research. New knowledge is sourced where it is available and cost-effective, and where the general framework is right. As a consequence, at the end of last year Roche became the first pharmaceutical company to open a research centre in Shanghai.

This is a challenge to Roche's established research facilities, including those in Switzerland, to maintain the dynamism of their research work and ensure they remain internationally competitive.

Over the past 15 years, the EU has lost ground (to the US) as a centre for the pharmaceutical industry. Fortunately, this “European” trend seems to have by-passed Switzerland – indeed the importance of pharmaceuticals for the Swiss economy has grown disproportionately.

### **What will the future bring? Major trends point to a new era in medicine**

Let us look ahead to the future. Not that I have any prophetic ability .... However, there are a number of fairly clear trends that are likely to have a significant impact on the pharmaceutical industry.

#### Trend 1: Demographic change

First, let us look at the demographic trends. The industrialised countries – in other words, Japan, Europe and the United States – will increasingly be confronted with the phenomenon of an ageing population and its consequences for all areas of life.

Today, there are about 450 million people worldwide over the age of 65 (that is 7% of the global population). This figure will

- virtually double by 2020
- more than triple by 2050 (to 17% of the global population). In the USA alone, there will be more than 80 million people over 65. Globally, about 400 million people will be over 80.

The ageing population represents a growing burden on healthcare systems (in fact, on all social security systems). Per capita healthcare spending is highest among the over-65s because the death rate is highest in this age group.

Chronic illnesses have already replaced infectious diseases as the main cause of death (in absolute terms). The older people are, the higher the (statistical) risk that they will suffer from a chronic illness. Cancer is a case in point: according to US studies, people over 65 are 17 times more likely to get cancer of the colon than younger people. Given the demographic trend, progress in medicine and disease prevention will take on a more significant role in a bid to alleviate the problems caused by rising demand for care for the elderly.

The aim of medical research is to ensure that people do not simply live longer, but that they remain healthy and independent for as long as possible so they are not dependent on care. That is also the goal for the development of innovative drugs.

One example is Alzheimer’s disease, which is a focus of Roche’s research in Switzerland. Alzheimer’s disease is one of the main reasons why many old people need care:

- Potentially, it could affect any of us. Statistically, 10 percent of the people in this room will die of Alzheimer’s. It is estimated that about 8% of over-65s in Switzerland and nearly 30% of over-85s suffer from Alzheimer’s disease. Ageing is still the only known risk factor for this disease.

Alzheimer’s is still incurable. However, innovative drugs slow the pace of development. A novel drug from Roche (a monoclonal antibody) which will shortly be entering clinical trials, could represent a major step forward in the treatment of this disease.

Prevention is an important factor, too: the most recent diagnostic studies indicate possible ways of identifying the disease before it breaks out, so preventive measures and possible methods of treatment can be considered. Such tests will have their price, but the alternative is permanent and

intensive nursing care accompanied by a reduction in the quality of life. Early diagnosis could thus prolong and improve life and also help save costs.

Healthcare economics studies show that improving the general condition of people suffering from dementia – as a result of progress in psychopharmacology, for example – can reduce the cost of care by up to EUR 10,000 per patient and year.

Emerging countries like China and India face a completely different situation. Rapid economic and population growth will drive up demand for health care. The enormous potential of the Chinese market has become something of a cliché.

One fact that is perhaps less well known is that if the recent growth rates continue, India is likely to have a larger population than China within the next 40 years. The Indian middle class is already larger than the entire population of the United States. Thanks to rising disposable incomes, 50–60 million Indians can now afford private health insurance. The industry therefore needs a presence in these growing markets.

One major reason why healthcare spending is increasing worldwide is that GDP is rising: as we become more affluent we are prepared to spend more on healthcare, and this will not change in the future.

A second major factor is the trend towards “personalised medicine”.

#### Trend 2: More individual medical treatment

One major problem is that drugs often do not have the expected effect. We all know that and most of us have probably experienced it either ourselves or in our families. The Pharmaceutical Research and Manufacturers Association of America estimates that about USD 100 billion are wasted every year in the United States alone because patients take drugs that are ineffective or have serious side effects.

There are many reasons for this. The most common is that the drugs are not taken, either because people forget, or because they are afraid of side effects. Alternatively, the medication may react with other drugs being taken at the same time.

However, there is also another possible reason. The biological make-up of everyone here in this room is different. Today, we know that that is due to genetic differences. Although 99.9 percent of genes are the same in all people, the remaining 0.1 percent can contain differences in the DNA sequences that store genetic information.

It is therefore perfectly plausible that doctors could treat you and I more effectively if the difference between us could first be determined with the aid of a lab test, enabling them to prescribe the most effective – personalised – medicine for each of us.

Is this merely a science fiction scenario? Well, yes and no.

Firstly: clear advances have already been made towards personalised medicine. Roche is a leader in this sector.

A good example here is breast cancer. Breast cancer remains the most common type of cancer in women: one in ten will contract this disease sometime in her life.

We are now also aware that there are different types of breast cancer and we understand the reasons for this: for example, in one aggressive form of the disease, extremely high concentrations of an abnormal form of the growth factor Her2 are found in the malignant cells.

Together with its subsidiary Genentech, Roche has produced a genetically engineered drug (monoclonal antibody) to block the action of this growth factor. This means if this abnormality is identified before treatment, the patient can be given more specific, personalised treatment. The Roche Centre for Medical Genomics in Basel is currently conducting in-depth research into the personalised treatment of rheumatoid arthritis. This is one of the most serious forms of arthritis, affecting one percent of the population. No really satisfactory treatment is available at present. We at Roche see a chance of helping these patients with our product MabThera/Rituxan, which has been used to treat leukemia for some time now. It has been discovered that for a percentage of rheumatoid arthritis sufferers, MabThera/Rituxan is something akin to a “wonder drug”. However, this does not apply to all patients. Optimum treatment could be achieved if it were possible to test patients first to establish whether they will respond to the drug. That is the challenge facing us at present.

Roche Diagnostics recently passed a milestone on the road to personalised medicine. Last year the introduction of our first DNA chip (AmpliChip CYP450) caused a stir in Europe and the United States. As the first DNA chip test in the world to receive regulatory approval, it represents a pioneering new discovery. This test can be used to show whether people metabolise a drug faster or more slowly as a result of their genetic make-up. The chip provides information that can aid the selection and dosage of a range of medications (for example, anti-depressants, psychopharmaceuticals, painkillers and drugs to treat cardiovascular disease).

Estimates indicate that systematic use of the AmpliChip test before treatment could improve overall efficacy by 10-20% and avoid 10-15% of all serious side effects.

These molecular genetic findings open up scope for new approaches to medical research in the medium to long term.

Personalised genetic analysis enabling doctors to investigate the complete genetic make-up of their patients and then prescribe drugs and treatments specifically intended to minimise side effects is still a very distant prospect.

However, even complete genetic mapping will never enable us to answer all medical questions. Our lives are not simply dependent on genetics – environmental factors, lifestyle and our economic situation are also major causal factors of disease.

However, one thing is already clear: we are on the brink of a revolution in the diagnosis and treatment of many diseases.

A revolution that will accompany us over the next 50 years.  
This is what makes our business so fascinating.

### Trend 3: The rising importance of diagnostics – plus pharmaceuticals

A third trend is the huge progress made by modern diagnostics, especially in combination with pharmaceuticals. Diagnostic procedures will continue to gain importance, allowing the earliest possible identification of predispositions for certain diseases and, as we have just seen, more effective treatment. Increasingly, this will include disease prevention.

At present, laboratory services account for an average of just 1% of overall healthcare costs. However, these services and the information they provide have enormous potential to raise the efficiency of healthcare as a whole, allowing optimisation of the remaining 99% of spending.

This potential needs to be tapped. The prospects for patients suffering from cancer would improve considerably if diagnostics were used more widely than in the past.

More than 90 percent of cancer patients could live five, ten or more years with current methods of treatment if the disease were identified earlier. Further advances in molecular diagnostics are therefore the best way of improving the prognosis for cancer patients in the short term.

For example, in the first half of this year Roche will be launching a diagnostic chip (AmpliChip p53) to determine how aggressive a tumour is. At the end of the year we will be launching a chip to diagnose leukemia (every year 80,000 people worldwide contract leukemia). So far, eight to ten different technologies have had to be used. Diagnosis takes days and the error rate is high. The new chip will allow diagnosis in a few hours and with an accuracy of over 98 percent. This new technology will have economic as well as medical benefits: it will cost around EUR 1,500, making it far less expensive than current diagnostic costs of around EUR 2,500, even though it has significant advantages.

Diagnostic information can improve the efficiency of all aspects of medical care. Roche is the only leading healthcare company dedicated to innovation in both pharmaceuticals and diagnostics. This twin-track approach means that we can develop solutions for the entire spectrum of healthcare needs.

The fourth trend I would like to mention is biotechnology.

#### Trend 4: Biotechnology

There is no doubt that modern biotechnology is a key technology of the 21st century. Together with automation and information technology, it is starting to open up new perspectives for all areas of the life sciences, and especially for medicine.

Highly potent, selective biopharmaceuticals have already proven very successful, especially in the treatment of cancer. In future, the treatment selected will depend on the genetic pattern of the tumour.

A knowledge of the genetic differences between patients can also aid the development of new drugs. If we know which patients will not tolerate a potential new medication, or will not respond to treatment, these patients can be excluded from clinical trials at the development stage. That would enable us to pursue a number of projects that have previously had to be halted due to side effects or low average efficacy even though excellent results were obtained in specific patient groups (Herceptin; Tarceva).

These social and scientific trends indicate that research-based pharmaceutical or, to be more precise, healthcare companies like Roche should not be regarded as “part of the problem” in the healthcare sector as the Swiss media commonly do at present. Instead, they should be seen as part of the solution, helping to make healthcare more efficient.

And now I would like to say a few words about “costs versus benefits”, a central aspect of the current healthcare debate.

## **Costs versus benefits**

I have no desire to suggest that health insurance and rising premiums in particular are not a problem. Regrettably, the public debate on the cost of healthcare still concentrates primarily on drugs, and especially the cost of drugs.

Points that tend to be forgotten include:

- The (internationally) high quality of our healthcare system
- The cost savings that can be achieved – as we have seen – through innovative drugs (scientifically proven)
- Moreover, healthcare economists agree that medicines are the healthcare cost component whose cost-efficiency has been examined most rigorously. In Switzerland, they only account for only about 11% of our healthcare costs.

That is precisely why I refuse to look at medical progress and the benefits provided by our healthcare system simply from a one-sided cost viewpoint. The central issue is not whether healthcare costs are steadily rising, but what society obtains in return.

Scientific progress and economic and demographic trends have a major impact on the future of healthcare and the healthcare sector. In the end, the infrastructure and resources provided for healthcare depend to a large extent on political decisions.

## **Political and regulatory framework**

As I pointed out at the beginning, politics has a major impact on the future of our industry. Regulations on clinical trials, patent protection, parallel imports, marketing approval requirements and reimbursement prices do not only determine the pace of innovation; they also play an important role in determining the relative attractiveness of different locations.

The devastating effects of misguided industrial policy can be seen clearly in Germany. For years the leading German pharmaceutical companies were nicknamed “the pharmacy of the world”. Now they have all but disappeared.

The global success of the Swiss pharmaceutical industry is attributable to its high level of investment in research and development and the fact that so far the regulatory framework has basically been favourable.

Other European countries increasingly see the successful Swiss model, which balances the interests of industrial and healthcare policy, as exemplary.

In the international competition to attract business to a country, innovative capability is rapidly becoming more important. However, innovation is not a state, it is a highly dynamic process.

Alongside the necessary material resources, research and innovation are dependent on a framework that fosters innovation:

- through public attitudes: acceptance of new technologies and a general willingness to accept economic risk determine the extent to which a country can pursue innovative research and development.
- through political/legislative developments: in other words, providing incentives and rewards for innovation through pricing and patents to protect the fruits of innovation.

- through taxation; for example incentives to create venture capital and encourage private investment in research.

This innovation-friendly framework requires constant adaptation to new requirements.

The prospects for pharmaceutical research have never been more fascinating or more promising. Never have there been better conditions for achieving medical breakthroughs and thus commercial success.

It is up to us to determine our future.