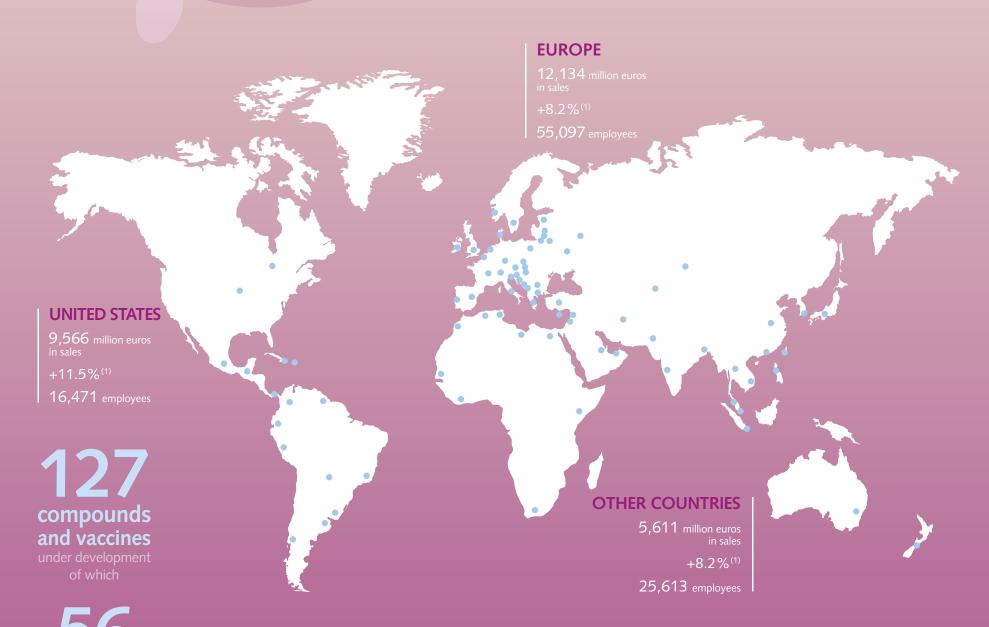
## 2005 BUSINESS REPORT



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in the pharmaceutical industry in France and Europe

N°3
Worldwide

27 billion euros consolidated sales

in 2005

97,181 people working every day to drive back disease in more than 100 countries

(phases II and III) More than billion euros

in advanced

stages

17,600 research staff\*

Budget R&D

#### 7 MAJOR THERAPEUTIC AREAS:

CARDIOVASCULAR DISEASE • THROMBOSIS • METABOLIC DISORDERS

- ONCOLOGY DISORDERS OF THE CENTRAL NERVOUS SYSTEM
- INTERNAL MEDICINE VACCINES

DISCOVERING AND DEVELOPING INNOVATIVE, EFFECTIVE AND WELL-TOLERATED TREATMENTS AND MAKING THEM AVAILABLE TO DOCTORS AND THEIR PATIENTS: THIS HAS ALWAYS BEEN THE GUIDING PRINCIPLE IN OUR BUSINESS ACTIVITIES.

CONFIDENT IN OUR EXPERTISE AND KEENLY AWARE OF THE OBLIGATIONS THAT COME WITH OUR POSITION AS EUROPEAN LEADER AND THIRD LARGEST PHARMACEUTICAL GROUP IN THE WORLD, WE DEVELOP MEDICINES AND VACCINES TO COMBAT THE MOST PREVALENT ENDEMIC DISEASES. WE ALSO CONSIDER IT OUR RESPONSIBILITY TO MEET THE NEEDS OF PATIENTS THROUGHOUT THE WORLD, WHATEVER THEIR MATERIAL CIRCUMSTANCES, FACILITATING ACCESS TO MEDICINES FOR THE GREATEST NUMBER.

WE ARE A RESPONSIBLE COMPANY; WE ARE COMMITTED TO MAKING OUR DEVELOPMENT PART OF A STRATEGY OF STRONG, SUSTAINABLE AND PROFITABLE GROWTH.

#### Chairman's message

Jean-François Dehecq, Chairman and Chief Executive Officer

all be proud of. We achieved the aim we set ourselves at the time of the merger, eighteen months ago: strong, sustainable and profitable growth. We owe our success to the motivation and dedication of our teams in getting our new Group up and running in record time.

#### Strong growth

With net sales up 9.3% on a comparable basis, our growth once again outperformed the world market<sup>(1)</sup>. This result is the reward for all our efforts in every area: our top 15 products posted growth of 14%, sales of our other products remained steady and the results for our generics business were highly encouraging. The vaccines business, which is of strategic importance to the Group, posted outstanding growth of 26.9% on a comparable basis.

Recent successes included the successful launches of Ambien CR™ in disorders of the central nervous system, Apidra® in the treatment of diabetes, and three vaccines in the United States: Menactra®, Decayac® and Adacel™.

"There are no small countries and no small products". We still hold firmly by this principle. On every continent, in every country, we have fought hard to win new market share and consolidate our performances. Our growth was superior to market in every region of operations(1), despite the impact of generics entries. Growth in Europe was 8.2% on a comparable basis. In the United States, where there is an increasingly challenging business environment, we posted growth of 11.5%\* (17.4%\* excluding the impact of generic versions of Allegra®, Amaryl®, Arava® and DDAVP® in the U.S.). We should note that a significant contribution was made by countries outside Europe and the United States. More than ever, our international presence is proving to be a key factor in our growth. We will be investing heavily over the coming years in Brazil, Russia, India and China (BRIC), four countries which together make up 43% of the world population<sup>(2)</sup>.

\* On a comparable basis.

## "OUR OBJECTIVE REMAINS UNCHANGED: STRONG, SUSTAINABLE AND PROFITABLE GROWTH."

#### Sustainable growth

We have risen to the challenge of sustainable growth by advancing on many fronts. Without any doubt, innovation is and will continue to be the key factor in our growth, which is why we reorganized our research to concentrate on innovative projects. The results to date are extremely positive: 56 products in phases II and III of development, up from 48 in 2004. Many of these products are destined to become "first-in-class"(3), i.e. the first ever developed in their therapeutic area. In other words, they will be groundbreaking innovations for the Group and for science, on a par with our medicine rimonabant which is currently under evaluation by the health authorities.

We also need to invest in our resources in the field. Much effort has gone into strengthening our sales force, for example. The considerable increase in our fourth-quarter commercial expenditure in support of the launch of Ambien CR™ and in preparation for launching Plavix® in Japan and the launch of rimonabant, as well as expanding presence in all our new markets, all bear witness to this effort. In China, for example, we have increased the number of our medical sales representatives from a few hundred to 1,600. The Group's sales force totaled almost 35,000 people in 2005. Investing in the future also means investing in our industrial facilities and running them at optimum capacity around the world. Predicting future growth is not enough in itself; we also have to implement the resources needed to make this a reality.

#### **Profitable growth**

We achieved profitable growth first and foremost by capitalizing on our synergies in record time. Within 18 months, nearly 90% of cumulative synergies were delivered by end 2005. Our profitable growth was also reflected in a reduction in debt, from 14 billion euros to under 10 billion euros, as previously announced, and in a 25.7% increase in adjusted earnings per share<sup>(4)</sup> of 4.74 euros, compared with 3.77 euros in 2004.

#### Vaccines, a strategic business

As we made clear at the time of the merger, the vaccines business is a strategic one for the Group. In terms of world public health, vaccines play a vital role in the health of millions of men, women

<sup>(1)</sup> IMS all available channels YTD at end December 2005: Pharmaceutical market: +6.1%; sanofi-aventis IMS consolidated: +8.3%.

<sup>(2)</sup> World Health Organization 2005 statistics.

<sup>(3)</sup> For definition of "first-in-class", see page 9.

<sup>(4)</sup> Adjusted earnings per share (EPS) is a specific financial indicator, which we define as adjusted net income divided by the weighted average number of share outstanding. The adjusted net income is defined on page 29 of this Report.

and children around the world. With such important issues at stake, we must strengthen our positions and organize to meet the huge existing needs, particularly in the Southern hemisphere. Sanofi pasteur employees dedicated all their efforts to this task in 2005, and will continue to do so in the future. Thanks to our industrial teams, 1.2 billion vaccine doses were produced in 2005, accompanied by sales growth of 26.9% on a comparable basis. Research teams continued their efforts to discover new vaccines. At the same time, our sales forces created a new impetus for some quality products.

#### Our responsibilities as a pharmaceutical group

By virtue of our mission, we are naturally concerned with the challenges of sustainable development. Today, 80% of the world's population does not have adequate access to medicines. As a world leader in pharmaceuticals, it is our responsibility to promote access to medicines for the greatest number, particularly in the Southern hemisphere.

In fulfillment of our responsibility, we are applying our experience where it can be used most legitimately and most effectively in developing programs to combat five diseases: malaria, leishmaniasis, sleeping sickness, tuberculosis and epilepsy. Our vaccines business also plays a crucial role in the fight against the risk of pandemic disease.

Our values of solidarity and respect also carry over into our employee relations and environmental policies, and underpin our rules on safety, ethical standards and transparency that we will continue to develop. We always keep the same aim in view: doing more and working better in the field of healthcare for the greatest number.

#### Encouraging prospects despite a challenging economic climate

Slowing growth in the United States, the intention of many countries to contain health spending, price reductions in Japan, generics—all these factors raise doubts over the future of our industry. Yet the pharmaceutical industry holds real potential, and for one simple reason: the continuing existence of huge unmet health needs. Oncology, degenerative diseases associated with an aging population, the emergence of new pandemic diseases, not to mention wider access to healthcare, particularly in our new markets, will be essential sources of market growth in the years to come.

We have ambitions, and the means to realize them: an R&D portfolio well stocked with major products and great hopes for the near and medium term; a balanced presence between the United States, Europe and other countries; powerful industrial capacity and a global sales network.

Our objective remains unchanged: strong, sustainable and profitable growth. Our strategy has proved well founded, but we must not relax our efforts. Because the world is always changing, we have to look ahead, adapt and take action. Sanofi-aventis has numerous strengths. I have every confidence in our ability to meet the challenges that await us and to live up to our commitments, for the benefit of all our patients, employees and shareholders.

Jean-François Dehecq Chairman and Chief Executive Officer



## Sanofi-aventis at the heart of major health challenges



#### the challenges www.www.www.

PREVENTION

### A global health issue:

#### in today's world, 300 million people are obese

Today, 1.7 billion people are overweight. Obesity and abdominal obesity have reached epidemic proportions and are increasing relentlessly worldwide. Abdominal obesity is associated with an increase in the risk of cardiometabolic diseases and is a heavy drain on the economy of every country.

Sanofi-aventis has decided to develop a truly innovative response to help in the fight against obesity.



#### A threat for future generations

Contrary to popular belief, obesity is due to genetic causes in only about 10 to 15% of cases. The real cause is an imbalance between excessive food intake and insufficient energy expenditure.

#### Major health risks

Even more than excess weight or obesity, what really matters is where fat is distributed around the body. The risk varies depending on whether the adipose tissue (fat) is subcutaneous (in which case it accumulates under the skin, around the waist and hips) or intra-abdominal (i.e. accumulating around the organs). Intra-abdominal fat is the biggest threat to health because the fatty tissue is near the organs, accessing the liver directly, and is itself a very active organ of secretion. The adipose cells (adipocytes)

do not simply store fat; they constitute an organ which secretes substances, such as adiponectin, which play an important role in the modulation of glucidic and lipidic metabolic processes, in inflammation and thrombosis, all of which are essential cardiometabolic risk factors. Epidemiological studies have clearly demonstrated that abdominal obesity (defined as waist size measured at the navel of more than 102 cm in men and 88 cm in women-reference: NCEP/ATP III) is accompanied by an increased risk of cardiovascular diseases such as myocardial infarction and stroke, or metabolic diseases such as diabetes. Measuring waist circumference is a simple procedure and should be systematic in every medical examination so that, if necessary, further investigations can be performed to identify those who are at greater risk for cardiometabolic diseases. Sanofi-aventis is focusing research on abdominal obesity.

#### A survey of solutions

Sanofi-aventis supports screening and awareness campaigns for abdominal obesity. An increased waist circumference is a powerful and independent predictive factor for cardiometabolic diseases. However, precise epidemiological data is not available for every country.

In the second quarter of 2005, sanofi-aventis supported a very large scale international epidemiological study, the International Day for the Evaluation of Abdominal obesity: IDEA, which was launched to evaluate

#### **•••** the commitment of sanofi-aventis

precisely the prevalence of abdominal obesity worldwide. During this international day, approximately 180,000 patients were evaluated by 6,300 primary care physicians in more than 60 countries.

This substantial database will provide precise information on the prevalence of abdominal obesity within the population as a whole and in specific subgroups, such as patients with hypertension, diabetes, lipidic anomalies, or who smoke, so as to achieve better identification of the waist circumference threshold associated with an increase of cardiometabolic risk.

#### Prevention

Experts worldwide and WHO specialists agree that the fight against obesity, abdominal obesity and excess weight generally should be global and should not concentrate solely on diet.

In other words, restricting food intake on its own is less effective than in combination with regular physical exercise. The stakes are high: losing 10 to 15% of body weight and reducing the size of your waistline makes it possible to reduce cardiovascular and metabolic risk.

#### The first selective CB1 blocker

Studies of rimonabant have shown an improvement in cardiometabolic risk factors in overweight or obese patients (the RIO program).

Constant hyperactivation of the endocannabinoid system plays a major role in the emergence of these pathologies. Rimonabant is the first selective blocker of the CB1 receptors of the endocannabinoid system.

It regulates and modulates the activity of this hyperactive system. Clinical research suggests that rimonabant acts directly on peripheral tissues, in particular the adipose tissues.

These benefits have been demonstrated during the substantial RIO phase III study program presented during the last two years in all the major international conferences on cardiology, diabetes and obesity. Rimonabant has not only demonstrated its action on weight loss and reduction of abdominal circumference, but has also shown that the improvement of glucid and lipid metabolisms (increased "good" HDL cholesterol, lowered triglycerides-blood lipid levels) with rimonabant on a 20 mg dose per day was twice as great than the effect to be expected from weight loss alone. This effect was maintained during the two-year treatment.

## Stemming the increase in diabetes

From 30 million diabetics in 1985 to 206 million in 2005: the increase is fast, furious and global. The total could reach as many as 334 million people by 2025. Sanofi-aventis is actively pursuing research.

#### An urban phenomenon

Type 2 diabetes is at the origin of this new epidemic. This is characterized by an abnormal increase in the levels of glucose in the blood. This anomaly is due to an insulin insufficiency or lowered efficacy of insulin secretion. Diabetes is a serious disease which can cause heart disease, blindness, impotence and can even lead to amputations. Causes are as evident as they are deadly: excess weight, an aging population and urban sedentary lifestyles.

Every year, 3.2 million people die of diabetic complications. Diabetes ranks fourth on the list of causes of death in developed countries.

#### Progress by sanofi-aventis

Sanofi-aventis has over 80 years' experience of innovation in the treatment of diabetes. Sanofi-aventis research, focused on the development of new therapeutic approaches, is transforming the treatment of diabetes and helping improve patients' quality of life. Launched in 2002 in the United States and in 2003 in France, Lantus® is a long-acting human basal insulin indicated for patients with type 1 and type 2 diabetes (adults, adolescents and children from the age of six). Lantus® is the first long-acting human basal insulin analog with a peakless activity profile to provide 24 hour control through a once-daily injection. Apidra®, a new quick-acting insulin analog, launched in 2005, has widened the range of therapies.

#### INBRIEF

#### THE COST OF OBESITY

2 to 8% of healthcare expenditure in Western countries. 117 billion U.S. dollars, i.e. 10% of healthcare expenditure, in the United States.

#### **SIGNS OF DIABETES**

The onset of type 2 diabetes generally occurs in those over 40 and often among those who are overweight, but children are increasingly affected. It can progress silently for several years until it is diagnosed following a glycemia test, which measures the blood sugar level).

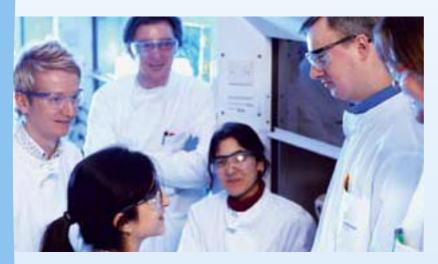


#### thechallenges .......

#### INNOVATION

## Cancer on the rise: sanofi-aventis mobilizes

With 7 million deaths a year, i.e. 12.5% of global mortality, cancer is still the leading cause of death before the age of 65. Intensifying prevention and accelerating research is more than ever a topical theme. Sanofi-aventis is in the front line.



#### A global increase

On every continent, cancer is gaining ground. In China, it is responsible for 25% of mortality. In Europe, there were 2.9 million new cases in 2004 and 1.7 million deaths. While an aging population and genetic predisposition contribute their complement of risk, tobacco, alcohol, an unbalanced diet, obesity, certain professional activities and perhaps environmental changes also play a role in this upsurge.

#### Vaccination against cancer: a promise

Helping the body to mobilize the immune system against cancer is the object of sanofi pasteur's Cancer Vaccine Program. Two vaccines are now the focus of attention: against melanoma and colorectal cancer. The team is working in close cooperation with the Group's Oncology pole, associating doctors and scientists around the world in research

and trials so that science's best efforts can be put at the service of clinical treatment. In parallel, the Cancer Vaccine Program informs patients on the progress of therapeutic vaccines and provides training at all levels *via* a dedicated web site.

#### New targeted compounds

In the last five years, research has made more progress than in the previous 20 years. Breakthroughs in our understanding of carcinogenesis mechanisms are opening the door to strategies targeting malignant cells. Sanofi-aventis has some 40 programs ongoing worldwide based on approaches adjusted for the various cellular disorders which lead to cancer. As a result, new active compounds directed at certain forms of cancer are emerging, against leukemia in particular, but also against cancer dissemination, particularly metastases.

#### Chemotherapy tomorrow

Complementing the cytotoxic substances that non-selectively destroy the so-called "chemosensitive" tumor cells, a better understanding of cellular mechanisms has led to the development of "targeted" compounds acting on specific mechanisms. This new approach which complements cytotoxic treatments, still the cornerstone of cancer therapy, has produced demonstrable improvements. Sanofi-aventis is considered to be one of the world's leading authorities on cytotoxics and is accelerating the clinical development of some twenty compounds, some of which are targeted and/or have fewer side effects.

#### INBRIEF

### THE WORLD'S FIVE MOST FREQUENT CANCERS:

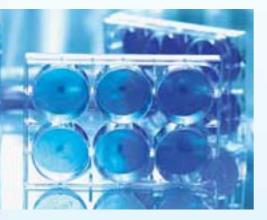
- Lung (1.2 million new cases per year),
- Breast (1 million),
- Colorectal (940,000),
- Stomach (870,000),
- Liver (560,000).

#### **KNOWLEDGE IS POWER**

A special website has been set up by sanofi-aventis to provide information to the public and researchers regarding cancers and vaccines: www.cancervaccines.com

#### EMERGENCY

## The influenza pandemic: sanofi-aventis plans ahead



In September 2005, Klaus Stöhr, coordinator of the World Health Organization's influenza program, sounded the alert. The spread of the avian flu virus H5N1 among farmed poultry birds has rekindled the threat of a pandemic. Sanofi-aventis is deploying its unique vaccines know-how.

#### Flu pandemic: the lessons of history

"15 to 35% of the world's population affected and tens of millions dead": Dr. Stöhr's warning shook the planet. With an ear permanently tuned to expert advice, sanofi-aventis is aware of the danger. Since 2002, WHO (World Health Organization) has been encouraging countries to work on their plans to fight against flu, and history bears out the danger: there is a flu pandemic every 10 to 50 years. The last was the Hong Kong flu outbreak which struck in 1968 and caused over a million deaths.

#### Level 3 alert on a scale of 6

The combination of the currently circulating H5N1 avian virus with the human influenza virus could give rise to a new, extremely virulent, virus which would be highly contagious in human-to-human transmission. If such a situation, vaccines are universally considered to be the most important medical means of preventing influenza and limiting its healthcare consequences during a pandemic.

Sanofi pasteur is committed to the effort to produce an efficacious pandemic vaccine. The Group has already supplied doses of an H5N1 candidate vaccine to some governments which

have requested it, and is preparing maximum manufacturing capacity as rapidly as possible for an adapted virus, once the pandemic strain has been isolated and provided to the industry by WHO.

#### **Emergency response**

If a pandemic is declared, a suitable vaccine will have to be developed and mass produced in record time, which will require a huge effort on the part of the vaccine industry.

#### Sanofi-aventis is prepared

More than 45% of flu vaccines used worldwide are manufactured by sanofi-aventis, which has been helping prevent influenza since 1968. An H5N1 vaccine is in the clinical study phase.

The Group is also building up maximum production capacity and, in collaboration with international organizations and with governments, it is working on priority allocation of vaccine doses and the logistics of rapid-response distribution once a pandemic is declared.

#### INBRIEF

#### VACCINES: AN URGENT NEED

27 million children worldwide still have no access to basic vaccines. Out of the 10 million children who die every year before the age of five, 3 million could have been saved by vaccination. In 2005, sanofi pasteur, the vaccines business of sanofi-aventis, sold over a billion vaccine doses, often at tiered prices, to international organizations such as UNICEF.



#### 

SYNERGIES

## Coping with an aging population: sanofi-aventis helps

With 100 billion interconnected neurons, the brain is still a mysterious organ whose complexity hinders optimal therapy for patients suffering from neurodegenerative diseases. Sanofi-aventis is stepping up research.

#### A major pole of interest for researchers

Degeneration and neuronal death are the common denominators of the "neurodegenerative" (or simply "neurological") diseases.

First on the list, Alzheimer's disease already affects 25 million people worldwide, including 5 million in Europe alone. With an aging populating, those figures might well double in the next 15 years.

Parkinson's disease affects 4 million people, mostly in industrialized countries. Of the section of the population over 65, 1.6% suffer from this disease, which is a worrying prospect in the light of constantly lengthening life expectancy.

Multiple sclerosis usually affects younger people, but the causes are similar and WHO reports 2.5 million sufferers worldwide.



Alzheimer's disease begins with impairment of the hippocampus, the nerve centre of memory, and then leads to progressive deterioration of cognition and behavior and to functional decline ending in dementia. The symptoms of Parkinson's disease are tremors and a slowing down of movement, due to the gradual and progressive destruction of a family of neurons which supply dopamine, a neurotransmitter controlling mobility. **Multiple sclerosis** is connected to the destruction of myelin which sheathes the nerves of the central nervous system. The disease generally progresses in flare-ups, followed by periods of remission, leading sooner or later to disability.

#### **Early intervention**

Sanofi-aventis is looking to curb the progress of disability by addressing the early phases of pathological degeneration. Research is focused on the development of compounds that, short of halting the process, could at least slow down disease

progression. In parallel, the Group is developing innovative pharmacological and scientific approaches to alleviating symptoms and improving patients' quality of life.

#### Sanofi-aventis: a shared dynamic process

The complexity of the brain, together with the great diversity of the disorders of the nervous system, makes the task particularly difficult. Sanofiaventis is well aware that the success of its approach depends on many other related discoveries and the development of advanced medical imagery systems. Firmly-established cooperation agreements have been set up to tackle the problem.

The "Central Nervous System" department is at the core of this organization, which involves other departments within the Group as well as major European public research institutions, and is engaged in a continuing dialogue with clinicians. Hundreds of researchers in every discipline, ranging from chemistry to molecular biology, from cell physiology to behavioral pharmacology, are contributing to sanofi-aventis' effective and innovating dynamic research program.

Sanofi-aventis is developing one of the most promising research portfolios in neurology and psychiatry, with 18 compounds in clinical development.



#### INBRIEF

#### **FLAGSHIP PRODUCTS**

Over the past 38 years, Depakine® has become the reference treatment for epilepsy which affects 50 million people worldwide. It is also indicated for the treatment of bipolar disorders, characterized by alternate manic and depressive episodes.

Copaxone®\* is used to treat multiple sclerosis, an auto-immune, chronic inflammatory disease destroying the myelin sheaths in the central nervous system. By reducing the incidence of flare-ups it slows down the progression of disability.

#### SOLIDARITY

#### **Access to healthcare:**

#### sanofi-aventis acts

At a time when countries with a high standard of living seek to limit their healthcare expenses, developing countries are still trying to gain access to medicines and to vaccines. This is one of sanofi-aventis' major concerns. We are taking action to adapt our offer to local social and economic realities.



#### Coping with poverty

The 2000 WHO\* World Health Report highlighted the direct connection between poverty and health. Out of the 30 countries at the lower end of the health expenditure league table, 27 are in Africa. The continent is hard hit by epidemics such as HIV-AIDS, which kills more than two million people a year. Sierra Leone is at the very bottom of the list, ranking 191st, with health expenditure of only 4.9% of GDP (i.e. 11 U.S. dollars per head), 9.7% covered by the public health system and 90.3% paid privately.

#### Open letter to the G8

In June 2005, international organizations and 12 major pharmaceutical companies, including sanofi-aventis, sent an open letter addressed to the G8 heads of state meeting in

Gleneagles, Scotland, asking them to champion the public-private partnerships which are at the forefront of promoting access to healthcare for poor countries. Thanks to these partnerships, 45 new medicines and 50 vaccines targeting local diseases are being developed and most of them could be marketed within the next five years.

#### For sanofi-aventis, there are no small countries and no small products

In April 2005, at the Biovision World Life Sciences Forum, sanofi-aventis made a public commitment to make access to healthcare one of the pillars of its strategy. In concrete terms, the Group will make products available to developing countries on a "tiered pricing" basis, geared to the income of their inhabitants. On the

agenda: vaccines to be made available for preventive care and medicines targeting malaria, leishmaniasis, sleeping sickness, tuberculosis and epilepsy.

#### No profit, no loss

Sanofi-aventis generates profitable innovative products from its research and has massive manufacturing capacity. This enables the Group to make a commitment to the public health effort with a drug portfolio that is both pertinent and supportive. The latest item in the sanofi-aventis range: new or generic medicines sold at cost price, "no profit no loss", to facilitate access to medicines for those most in need.

#### Sanofi-aventis commitments

The sanofi-aventis "Impact malaria" program includes generics which provide effective treatment at 70 to 80% less than the usual price. The Group also partners the DNDi (Drugs for Neglected Diseases initiative) Foundation in the fight against malaria. The antimalaria drug developed jointly combines two active ingredients in a single tablet, which makes treatment easier for the patient. It will go on sale in 2006 at cost price, about 1 euro per patient, enabling over 50 million people to receive treatment.

#### **INBRIEF**

#### **ACCESS: KEY FIGURES**

80% of the world's population has little or no access to the most basic medicines.

#### FOR FURTHER INFORMATION:

"Our responsibilities as a pharmaceutical company" section of this Report.

Sanofi-aventis Sustainable Development Report 2005.

#### the challenges ••••••• the commitment of sanofi-aventis

COOPERATION

## Patients' associations: sanofi-aventis gives its support

Supporting patients in their hour of need, publicizing their cause and raising funds: patients' associations are essential healthcare participants and natural partners for sanofi-aventis.



#### Leveraging research

Patients' associations possess a fundraising capacity that puts them center-stage on today's medical scene. The AFM (Association Française contre les Myopathies-French Myopathy Association), founded in 1958 by patients suffering from neuromuscular disorders and their families, has become famous for its Telethon. In 2005, the 17th annual edition raised 104.7 million euros, which will be used to finance international research. The American Diabetes Association (ADA) is the biggest patient group in the U.S. It has a budget of 200 million U.S. dollars and financed 40 million U.S. dollars' worth of research in 2004.

#### A useful counter-weight

The ADA successfully lobbied several states in the U.S. to legalize stem cell research. In France, pressure from patient groups culminated in the passage of the law of March 4, 2002, which stated that patients should henceforth be consulted on medical decisions affecting them and should have free access to their medical records. The campaigns waged by associations defending the rights of AIDS sufferers helped increase awareness of the gravity of the pandemic and contributed to the provision of treatment by health authorities.

#### Vital support

Providing support to patients remains their primary mission. Cancer groups in countries around the world have developed a wide range of services: telephone hotlines, patient and former patient advocacy groups, campaigns to make healthcare structures more human, in support of pain management, extending support to patients' families, etc.

#### Sanofi-aventis supports their actions

Information and support are very much a part of the Group's strategy. In 2005, the sanofi-aventis "Train de la Vie" spread the message of prevention to 25 French towns over 37 days. Over 110,000 people boarded this health train in which one car was dedicated to interviews with patients' associations. In the U.S. sanofi-aventis supports CancerCare, which distributes information brochures, organizes telephone information workshops and on-line support groups for patients.

Sanofi-aventis also partners many other organizations, such as the Diabetes Care Coalition, which includes the American Diabetes Association, the Juvenile Diabetes Research Foundation and the pharmaceutical industry. This Coalition aims to change the general public's perception of diabetes.

#### INBRIEF

#### AT THE HEART OF THE SANOFI-AVENTIS ORGANIZATION

The Group has a dedicated "Access to Medicines" department and a number of operational managers are in charge of relations with patients' associations: concrete proof of sanofi-aventis' ongoing commitment.



# "VE AIM TO DEVELOP ONE OF THE MOST INNOVATIVE COMPOUND PORTFOLIOS"

INTERVIEW WITH

Gérard Le Fur, Senior Executive Vice President,

Executive Vice President, Science and Medical Affairs

# Our diversity is the source of our creativity and of our ability to innovate. It is what enables us to make a difference.

### Sanofi-aventis R&D is organized around seven major therapeutic areas. Why this choice?

The therapeutic areas we are working in are all major challenges to public health: they are the leading causes of mortality worldwide. That is why we have chosen to make them the focus of our research efforts and in so doing, we have acquired an expertise that commands worldwide recognition.

#### A year and a half after the merger, how would you describe sanofi-aventis' portfolio of compounds and vaccines in development?

The message of 2005 is simple but highly significant for the future of our Group. We currently have 127 compounds and vaccines under development, including 56 in advanced stages (phases II and III). Of these, 18 are in phase IIb and 18 in phase III, which means that we have made successful progress in the development of our most advanced products. Looking to the longer term, we have 71 products in preclinical and phase I development.

## compounds and vaccines under development including 56 in phases II and III and 71 in preclinical and phase I

More than billion euros for R&D the 3rd largest R&D budget of

the pharmaceutical industry

Over
17,600
R&D staff\*
on 28 sites in 3 continents

including 3 vaccines sites

opment, a pipeline that offers real potential for the Group's future growth.

#### What makes sanofi-aventis' R&D different?

The technology is the same for everyone, but we believe that the approach and methodology each individual brings to research are deeply rooted in specific cultural backgrounds. This is why we have always preferred an international approach and why we intend to maintain a number of research centers around the world. Our diversity is the source of our creativity and of our ability to innovate. It is what enables us to make a difference.

Our working method is a careful balance between centralization and decentralization. Above all, however, our approach is pragmatic. We believe there is more than one way to discover a new medicine: we strive for new approaches, new targets, new therapeutic classes, irrespective of the size of the potential market. Our aim is to develop first-in-class products and "first in indication", those compounds that are the first to be developed for a given target or for a therapeutic indication not previously considered.

#### Is rimonabant symbolic of the sanofi-aventis R&D policy?

Rimonabant is a landmark in the global management of the cardiometabolic risk. As we know, abdominal obesity is one of the key risk factors, and one which currently affects both Western countries and the developing world. It is a major threat to public health.

We began developing rimonabant 15 years ago without even considering its potential, but we were intrigued by the mechanisms of action that we could observe. With time, we were able to narrow down our hypotheses and today we hope to offer healthcare professionals a unique product representing a new approach to the

management of the cardiometabolic risk. The process is a compelling illustration of our approach to research.

#### What are the other major research challenges for sanofi-aventis?

As populations age, we are seeing an upsurge in diseases which may not be new but are becoming much more prevalent: Alzheimer's disease, multiple sclerosis, Parkinson's disease. These neurodegenerative diseases, as they are known, pose a serious challenge which we must confront. Then there are the problems of obesity, diabetes, viral endemics such as avian influenza, infectious diseases, cardiovascular disease, cancer... we have to contend with all these issues in our fight to drive back disease all over the world.

<sup>\*</sup> Including Vaccines, Industrial Development, Medical/Regulatory staff in affiliates.

#### **R&D** portfolio highlights in 2005:

#### Our potential equals our ambitions

#### NDAs approved in 2005

- Registration and launch of Ambien CR<sup>TM</sup> (zolpidem MR), a new, modified-release formulation for treatment of sleep continuity disorders, in the U.S.
- Marketing approval obtained in France for an "orphan" drug, Flisint® (fumagillin), a highly effective treatment for a very rare disease, microsporidiosis, in severely immunodepressed patients.
- A number of supplemental NDAs were approved in the U.S., Europe or Japan for major medicines: Taxotere®, Eloxatin®, Allegra® and Lantus®.
- Approval for Plavix® (indicated in the treatment of stroke) in Japan in January 2006, following a favorable opinion from the Bunkakai sub-committee in November 2005.

#### New Drug Applications filed in 2005

- 2 major new drug applications (NDAs) were filed in the U.S. and Europe in 2005 for rimonabant (obesity and smoking cessation) and for dronedarone (atrial fibrillation).
- A mutual recognition procedure (MRP) was also launched for a modified release formulation of zolpidem MR (insomnia) in Europe in 2005.
- A number of supplemental NDAs were filed in 2005:
- in the U.S. and in Europe for flagship products such as Actonel®, Allegra®, Aprovel®, Taxotere®, Plavix® (acute phase myocardial infarction);
- in Japan, an application for registration was filed for **Ancaron**® (amiodarone) administered intravenously, and an NDA for a new formulation of **Lantus**® was filed.

#### Significant advances in our R&D portfolio in 2005

- 11 new compounds in preclinical development, 5 of them "first-in-class": AVE 8680A (internal medicine), SAR 7226 (metabolic disorders), SAR 97276 (internal medicine), SAR 3419 (oncology), SAR 502250 (central nervous system).
- > 12 compounds entered phase I.
- 4 phase II programs and 9 phase III and IIIb programs were initiated.

#### Three new vaccines launched in 2005

- Adacel® was licensed by the FDA and released on the U.S. market. This combined vaccination against diphtheria, tetanus and pertussis was designed specially for adolescents and adults and is the first booster to address pertussis protection over a wide age range.
- Menactra® is the first conjugate vaccine effective against four serogroups of the bacterium that causes meningococcal meningitis: A, C, W-135 and Y. It received FDA approval for use in children from age 11 and in adults (to age 55) and is now marketed in the U.S.
- **Decavac®** is a preservative-free tetanus and diphtheria booster vaccine for adults, launched in the U.S. in January 2005.



LCM (Life Cycle Management) development programs for products marketed by the Group and for compounds and vaccines in phase III of development are set out in the chapter entitled "Our therapeutic responses in 7 main therapeutic areas" in this Report.

## One of the most extensive and well-balanced portfolios in the pharmaceutical industry

We have chosen to focus our research efforts on seven major therapeutic areas where the need for progress is still considerable: cardiovascular diseases, thrombotic diseases (atherothrombosis, etc.), disorders of the central nervous system (neurodegenerative diseases, depression, etc.), oncology (lung cancer, breast cancer, colorectal cancer), metabolic disorders (diabetes), internal medicine (allergies, urology, osteoporosis, etc.) and viral and bacterial diseases through our vaccines business.

These therapeutic areas are fundamental challenges to public health and represent some of the leading causes of mortality in the world today.

#### A particularly innovative portfolio of compounds

Among the many challenges facing R&D, one of the most important nowadays is to discover a compound that will be the first in its pharmacological class. Such first-in-class compounds, as they are known, represent a real therapeutic advance and are, by definition, very novel compounds. Sanofi-aventis R&D currently has some forty first-in-class compounds under development in all fields of research.

#### > First-in-class compounds

A compound or molecule is qualified as first-in-class if there is no other product with the same mechanism of action, either in preclinical or clinical development or already on the market. For example:

- cardiovascular: AVE 0118, an atrial potassium channel inhibitor, in phase II of clinical development;
- thrombosis: idraparinux, a long-acting pentasaccharide in phase III of clinical development;
- **central nervous system**: SSR 149415, a vasopressin V1b receptor antagonist in phase 1 of clinical development;
- **oncology**: SSR 128129, and FGF (Fibroblast Growth Factor) receptor antagonist, in preclinical development.

#### First-in-indication compounds

First-in-indication is another designation reflecting innovation, and refers to compounds with a therapeutic indication different from that of similar compounds with the same mechanism of action.

Our portfolio contains some 15 products of this kind. For example:

- **internal medicine**: icatibant (a bradykinin B2 receptor antagonist) in phase II of clinical development for the relief of osteoarthritic pain;
- central nervous system: SR 58611 (a Beta₃ adrenergic receptor agonist) for the treatment of depression and anxiety.



**David Williams**Senior Vice President Vaccines

#### **VACCINES: R&D STRENGTHS**

- Sanofi pasteur's R&D portfolio in 2005 contained 23 vaccines in development including two vaccines for which registration dossiers have been submitted; over the course of the year, 10 of these progressed within the portfolio and three new vaccines were launched on the North American market.
- Innovative research further consolidated sanofi pasteur's position as world leader, with new vaccines against diseases such as dengue fever, malaria and AIDS. New strategies are being explored, such as therapeutic vaccines for the treatment of HIV infection and cancer.
- As the world's leading manufacturer of influenza vaccines, sanofi pasteur is actively involved in the preparations to counter a possible pandemic, working alongside government agencies and academic institutions. Sanofi pasteur has already developed prototype vaccines against avian influenza, which have undergone clinical trials.

#### AN INNOVATIVE AND WELL-BALANCED RESEARCH AND DEVELOPMENT PORTFOLIO(1)

#### Compounds by therapeutic area and phases of clinical development

127 compounds and vaccines in development, 56 in phases II and III, 71 in preclinical and phase I

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	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Launched/LC/M
	AVE 0657 AVE 3085 AVE 4454 AVE 4890 SAR 114646	HMR 1069 AVE 1231 AVE 9488	AVE 0118 ataciguat	XRP 0038 SSR 149744 AVE 7688 SL 650472	Multaq®***	Tritace® Aprovel®
2.THROMBOSIS	AVE 6324 SSR 128428 SSR 128429 SAR 377142	AVE 3247	AVE 5026	otamixaban SR 123781 SSR 126517	idraparinux	Lovenox® Plavix®
3. METABOLIC DISORDERS	AVE 0897 SAR 7226 SAR 351034 AVE 9423	AVE 5376 SSR 162369 AVE 5530 AVE 8134	AVE 1625** AVE 0847 AVE 2268	SR 147778** AVE 0010	rimonabant***	Amaryl® Lantus® Apidra®
4. ONCOLOGY	SSR 106462 / CEP 11981 SAR 3419 AVE 1642 SSR 97225 SSR 128129 SSR 244738 SSR 250411	AVE 8062 AVE 9633 SSR 125329 CEP 7055	XRP 6258 Uvidem® AVE 0005	SR 31747	XRP 9881 tirapazamine xaliproden** alvocidib	Eloxatin® Fasturtec® Taxotere®
5. DISORDERS OF THE CENTRAL NERVOUS SYSTEM	SAR 102779 SAR 501788 SAR 502250 AVE 8112 AVE 8488 SSR 101010 SSR 103800 SSR 126374 SSR 180711 SSR 241586	AVE 9897** SSR 125543 SSR 411298 SSR 504734 SSR 180575 SSR 147778**	HP184 AVE 1625** SSR 149415	M 100907 SR 57667	teriflunomide SR 58611 xaliproden** saredutant eplivanserin rimonabant*** SSR 591813	Rilutek® Depakine® Stilnox® Ambien CR <sup>TM</sup>
6.INTERNAL MEDICINE	SAR 389644 SAR 21609 SAR 97276 AVE 8680 AVE 0675 AVE 8923	XRP 2868 AVE 9897** ferroquine SSR 126768 SSR 150106 AVE 1701	icatibant SSR 240600 pleconaril SSR 240612	SR 140333 ciclesonide / formotérol	Alvesco®*** SR 121463	Arava® Allegra® Ketek® Actonel® Xatral® Flisint® (fumagillin)

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Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Launched/LC/M
DTP-HepB-Hib* Meninge A, C, Y, W infant Pneumo Flu Cell Rabies Yellow Fever Melanoma Colorectal Malaria	Flu Pandemia Meninge B	CMV HIV Dengue Flu	DTP-HepB- Polio-Hib* Menactra® toddler (1-2 years) Flu micro-injection Flu infants (6 weeks to 6 months of age)	HIV (Thailand) DTP-HepB- Polio-Hib* Menactra®*** meningitis in 2 to 10 years Pentacel™*** D,T,C, Polio, Hib*	Pediacel® D,T,C, Polio, Hib* Menactra® Meninge A, C, Y, W Meningitis in 11 to 55 years Adacel™ DTP* booster in 11 to 64 years

#### Planned before 2008:

- 14 submissions of New Chemical Entities,
- 7 submissions of new vaccines.

#### THE PHASES OF RESEARCH AND DEVELOPMENT

#### Preclinical

Preclinical testing is designed to meet the prerequisites necessary are synthesized in sufficient quantities a pharmaceutical form suitable for human administration is developed; safety studies(toxicology and general pharmacology) are performed as well as metabolism and pharmacokinetics studies to determine what happens to the product within the body.

#### Phase I

These trials are nontherapeutic and are carried out on a small for products identified by number of healthy Discovery Research to be volunteers. The aim tested in humans. During here is to establish this phase, the products product tolerability and The aim of these trials is and to compare it to the product and, in particular, and quality controlled; as the product's pharmacokinetic and sometimes its pharmacodynamic profile (ADME and PK/PD) in humans.

#### Phase II

out on patients using trials are to confirm the compounds that have demonstrated acceptable safety in patients likely tolerability in human to benefit from the subjects during phase I. treatment being tested, further knowledge of the determine the maximum — to confirm the product's — reference treatment for — to provide essential tolerated dose, as well effectiveness (Phase IIa - the condition in question pharmacovigilance as the product's proof of concept), but in order to gather the monitoring of the also to establish the optimum dosage, i.e. the dose offering the best efficacy/tolerability often involve large ratio-Phase IIb) leading patient groups, and to Phase III studies).

#### Phase III

product's efficacy and data required to file a New Drug Application (NDA). Phase III trials also provide more information on the pharmaco-economic aspects of the product and its impact on quality of life.

#### Phase IV (Life cycle management)

These are post-marketing studies, carried out after the NDA is granted, with the object of obtaining product in everyday use. This phase may also provide opportunities for developing new pharmaceutical forms or extensions of clinical indications.

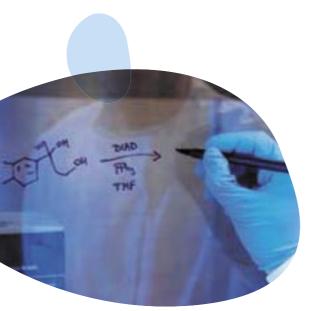
<sup>\*</sup> D = Diptheria, T = Tetanus, Hib = H influenza, HepB = Hepatitis B, P = Perfussis.

<sup>\*\*</sup> Compounds appearing in several therapeutic areas.

<sup>\*\*\*</sup> Products which have been filed for marketing approval.

#### Our R&D: project-based organization

Sanofi-aventis Research & Development is dedicated to the task of discovering, developing, registering and bringing to market innovative medicines and vaccines to satisfy major unmet medical needs around the world. In pursuit of that aim, the Group has established a project-based organization centering on two structures: Discovery Research and Development.



#### Discovering and bringing forward new compounds

Discovery Research is responsible for identifying the most promising research targets for therapeutic innovation and capitalizing on its biological and chemical experience to discover and propose new candidate compounds for development. It combines the skills and talents of 3,000 employees within a single, coherent pharmaceutical research structure with global coverage, to which each researcher contributes his or her multidisciplinary skills and distinctive culture.

#### From development to market launch

Development takes the compounds developed by Discovery Research and turns them into medicines. As soon as a compound enters development, a multidisciplinary project team is set up, with members drawn from a wide range of functions including researchers, clinicians, pharmacists, toxicologists and representatives from Regulatory Affairs and Marketing. This team is responsible for taking the compound through every stage from development all the way to marketing.

## "EXPLORING ALL THE POSSIBILITIES OF A NEW COMPOUND TO EXPLOIT EVERY THERAPEUTIC OPPORTUNITY IS A REFLEX FOR US."

Every year, Discovery Research puts forward 15 to 20 compounds potentially capable of responding to unmet treatment needs or improving existing treatments (improved efficacy/tolerability ratio for patients, etc.).

In 2005, the scientific skills of our researchers were enhanced in every one of the Group's major therapeutic areas: the Group's activities now target 12 to 16 diseases or syndromes identified by WHO as presenting unmet treatment needs.

This matrix organization allows for effective monitoring and coordination of every aspect of development activity throughout the entire procedure and is a major factor in the success of each project.

Innovation in the field of healthcare is not confined to the discovery of new compounds, however. It also means developing new formulations of existing medicines that will offer patients improved quality of life (forms that are easier to administer, require less frequent administration, minimize side effects, etc.).

#### Maximum transparency in clinical trials

In 2005, projects in development (including Life Cycle Management projects) required the organization of several hundred clinical trials in over 60 countries.

In addition to the trials required to obtain approval for its new medicines, the Group also runs major trial programs for extensions of therapeutic indications and numerous quality of life studies.

In January 2005, the principal pharmaceutical industry federations (in Europe, America and Japan) representing the world's leading pharmaceutical groups, including sanofi-aventis, signed a commitment to increased transparency on all clinical studies sponsored by their members. Doctors, patients and the general public will thus benefit from greater disclosure of clinical trial results. In accordance with this policy, the Group also undertook to publish all clinical trials it sponsors (except for exploratory trials) in a clinical trials registry accessible to the public free of charge.

## Targeted partnerships to support the development of innovative products

Through partnerships and alliances established with biotechnology firms and other pharmaceutical companies, sanofi-aventis R&D is able to access new technology and to extend or strengthen existing areas of research.

Some of the main partnerships in Discovery Research in 2005 include:

- GeneLogic (U.S.), Amphora (U.S.) and Elan (Ireland), 3 technological partnerships giving the Group access to new technologies;
- Millennium (U.S.), Immunogen (U.S.), Coley (U.S.), Mitsubishi Pharmaceutical Corp. (Japan) and Genfit (France) on novel products enabling us to explore the maximum number of new leads in our therapeutic areas;
- 3 cooperative programs as part of the "Impact Malaria" program, including one with the *Université Scientifique* et *Technique* de *Lille* to develop ferroquine, currently in phase I clinical development;
- numerous partnerships with public and university research bodies, cooperation agreements with INSERM and CNRS in France, with the University of Frankfurt in Germany and with Harvard Medical School in the United States.

In development phases, we have three major agreements in oncology with Cephalon and Regeneron Pharmaceutical Inc. in the United States and Immuno-Design Molecule in France, and two license agreements with Zealand Pharma and Ajinomoto.

#### R&D at sanofi pasteur: unique research

Sanofi pasteur devotes almost 15% of its revenues to R&D and employs a team of 1,500 employees. Based at three locations—Marcy-l'Étoile (near Lyon, France), in the U.S. at Swiftwater (Pennsylvania) and in Toronto, Canada—they handle the entire process of bringing a new vaccine to market, from research laboratory to filing for marketing approval, including external alliances with biotechnology firms.

Their mission: to develop new preventive or therapeutic vaccines, to improve existing vaccines and to simplify and/or improve administration methods.

Over the past decades, advances in molecular biology have paved the way for approaches such as programming bacteria or cells to produce a vaccine or to acquire vaccine-like properties, and utilizing molecular techniques to identify protective immunogens.

Sanofi pasteur has further extended its network of partnerships and cooperation agreements with academic teams and biotechnology firms, in order to meet these new challenges and remain at the forefront of innovation in every area of vaccines research.



#### ETHICAL SAFEGUARDS AT EVERY STAGE OF R&D

- Close contacts are established with patients' associations to gain the best possible understanding of the problems posed by each disease.
- Ethics committees closely monitor research protocols.
- Independent expert committees monitor compliance with professional codes of practice (patient information, data confidentiality, etc.) when clinical trials are initiated.
- An independent Data Monitoring Committee and has the power to modify or stop the trial at any time.

# "FOR US, THERE ARE NO SMALL COUNTRIES AND NO SMALL PRODUCTS. THAT IS STILL TRUE, TODAY MORE THAN EVER"



INTERVIEW WITH

We support all our products, all over the world, whether flagship products, vaccines, traditional prescription medicines or generics. We are able to do this thanks to an industrial base that is fully integrated from start to finish and that covers the whole world. With our diversified product range, geared to specific local characteristics, we can respond to the particular needs of different populations while taking into account the economic resources they have available. This is what our strategy of "no small countries and no small products" is all about.

#### What is your assessment of the year 2005?

2005 proved our strategy well-founded. Despite a challenging environment marked by a number of our medicines coming off patent, a slowdown in the pharmaceutical market in the United States and a general tightening of healthcare policies, we posted growth in net sales of 9.3% on a comparable basis. This was driven by strong growth from our flagship products, a record performance by our vaccines business and

steady results from our traditional prescription medicines. Worldwide, we outperformed the market in all our regions, with a marked upturn in Asia and Latin America. Results like these give us an excellent platform to move into 2006.

### Do you attribute this strong performance to the organization of your teams?

Without doubt, the 35,000 members of the sanofi-aventis sales teams constitute a new and significant force. In the United States, we rank second in the pharmaceutical industry for the number of calls made by medical sales representatives. Our capacity to organize successful launches for the new products emerging from our research pipeline, products like Apidra® or Ambien CR™, bodes well for the launches of rimonabant and Multaq®.

#### How do you see your markets performing in 2006?

We expect the pattern of 2005 to continue and accelerate. In the United States, the slowdown is likely to continue. In the circumstances, however, a company like ours, with its roots in Europe, enjoys a number of advantages: we have already experienced situations of this sort, and we have long been accustomed to adapting to new regulations and budget constraints. Once again, our strategy of "no small countries and no small products" comes into its own. Our growth on so-called "intercontinental" markets, excluding Europe and the United States, currently accounts for 25% of our worldwide growth. Intercontinental markets include, for example, Brazil, Russia, India and China which currently represent 43% of world population<sup>(1)</sup> but only 3.5% of the pharmaceutical market<sup>(2)</sup>, although they are growing 2.5 times faster than the global pharmaceutical market as a whole.

We are the largest pharmaceutical company operating in these countries<sup>(3)</sup>, but our market share is still below our share of the world market, leaving considerable margin for growth.

- (1) World Health Organization 2005 Statistics (in millions).
- (2) Sales: IMS, MAT September 2005.
- (3) Market share: IMS, MAT September 2005.

35,000 sales force

members worldwide present in



#### **Outperforming forecasts**

9.3% sales growth on a comparable basis in 2005

Our medicines portfolio includes innovative medicines, vaccines, traditional prescription medicines and generics, offering a full range to cover the needs of different populations with due regard for their economic circumstances.

This diversified strategy guarantees the sustainable growth needed to ensure

Group development.

#### Innovative products...

Our innovative products, the result of sanofi-aventis R&D, are world leaders in their therapeutic areas.

In 2005, the Group's top 15 products generated 16 billion euros in sales, an increase of 14%.

The year also saw the several product launches, including Ambien®CR for the treatment of insomnia and Apidra® for the treatment of diabetes.

Another important event: marketing approval for Plavix® in Japan, with a launch planned for the second half of 2006.

Traditional prescription medicines, a unique approach to ensure a strong presence with patients, doctors and healthcare partners

Alongside the top 15 brands, there is also a range of highly diversified products which represent a significant part of our activity worldwide (36% of sales in 2005). They have been on the market for a long time and are well-known to patients and healthcare professionals for their efficacy and safety.

For several years, following a strategy unique of its kind, we have actively invested to optimize these medicines.

The top 15 sanofi-aventis medicines Change in sales figures in 2005 by geographic zone on a comparable basis (in millions of euros)

Medicines	Europe	Change	United States	Change	Other countries	Change
Lovenox®/Clexane®	647	+10.4%	1,287	+14.8%	209	+18.8%
Plavix®/Iscover®	1,480	+20.5%	210	+9.9%	336	+26.3%
Taxotere®	628	+20.1%	695	+7.3%	286	+12.2%
Eloxatin®	544	+31.4%	895	+28.0%	125	+47.1%
Stilnox®/Ambien®/ Ambien®CR™	108	-9.2%	1,331	+12.6%	80	+11.1%
Allegra®	52	-10.3%	1,001	-15.0%	292	+19.7%
Lantus®	413	+40.5%	717	+46.6%	84	+110.0%
Tritace®	576	-0.7%	8	-38.5%	425	+8.4%
Copaxone®	231	+24.9%	622	+24.9%	49	+11.4%
Aprovel®/Avapro®/Karv	ea® 727	+14.1%	_	_	165	+13.0%
Amaryl®	255	+5.8%	181	-13.4%	241	+8.6%
Actonel®	235	+22.4%	_	_	129	+26.5%
Depakine®	235	+4.0%	_	_	83	+6.4%
Xatral <sup>®</sup>	234	+6.8%	53	+120.8%	41	+20.6%
Nasacort®	38	+2.7%	212	-3.2%	28	_

Using innovative approaches for the allocation of resources, their sales can be stabilized or even revitalized, without compromising profitability

For patients and prescribers, they represent a therapeutic solution to complement innovative medicines and an advantage in terms of price; for the Group they generate stability and resources.

#### **Actively present in generics**

Today, the generics market represents 12% of the global pharmaceutical market. IMS estimates that by 2010, generics will account for 20% of the pharmaceutical industry's sales by value and 50% by volume. As a global player in the pharmaceutical industry, sanofi-aventis is naturally present in the generics market, which is a combined source of growth in value and increased volume to fill the Group's manufacturing capacity.

To fulfill this ambition, sanofi-aventis has gathered all its existing generics activity under the name of Winthrop and is focusing its strategy in three key areas:

Expanding the market presence of its own compounds when they come off patent. This policy will guarantee the "sanofi-aventis" label of quality for its generics and maintain industrial activity in its manufacturing facilities.

Supporting the competitive position of its defensive generics through the development of an extensive generic portfolio, including generics for major compounds which are no longer patent-protected.

ensure an offer which meets the needs of the main markets where healthcare authorities wish to promote generic expansion. In Europe, the Group has strengthened its presence in Germany, the United Kingdom and France. It has also become active in countries where generics are progressing such as Italy, Spain and Portugal, and in emerging markets such as the Czech Republic, Hungary and Poland.

#### The widest range of vaccines in the pharmaceutical industry

Sanofi pasteur is the largest company in the world devoted entirely to vaccines. These vaccines protect against 20 diseases, both bacterial, such as cholera, pertussis and tuberculosis, and viral, such as influenza, rabies, rubella, yellow fever and mumps. One of the strengths of the sanofi pasteur range is the sheer number of combination vaccines, which result in simplified vaccination schedules, reduced costs and improved administration.

In 2005, sanofi pasteur experienced exceptional growth of 26.9%, reflecting the successful launches of three vaccines in the United States: Decavac®, Menactra® and Adacel™.

#### Our main vaccines

Change on a comparable basis (in millions of euros)

Vaccines	2005 Sales	Change
Polio/Whooping Cough/Hib Vaccines	522	+3.2%
Adult Booster Vaccines	270	+58.8%
Influenza Vaccines	671	+28.6%
Travel Vaccines	176	+3.6%
Meningitis/Pneumonia Vaccines	256	+137.0%
Other Vaccines	167	+12.1%

#### Our sales forces: a local approach

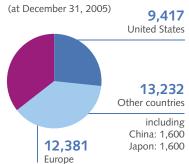
35,030 medical sales representatives, including 12,381 in Europe, 9,417 in the United States, around 1,600 in Japan and 1,600 in China, devote their recognized expertise to medical development and to product promotion and information to healthcare professionals wherever the Group is present.

To ensure strong growth, we must optimize our marketing abilities and strengthen our presence on the ground. In 2005, we recruited 4,000 medical sales representatives worldwide, particularly in markets which are likely to develop significantly over the next few years, such as China.

Whilst our sales force markets most of our medicines, we have and are continuing to set up partnerships for the joint promotion and marketing of certain products in specific areas. Main existing partnerships include: an agreement with Bristol-Myers Squibb for the cardiovascular medicines Aprovel®/Avapro®/

Karvea® and Plavix®/Iscover®; one with Procter & Gamble Pharmaceuticals for Actonel®, an osteoporosis treatment; and cooperation with Teva Pharmaceuticals on Copaxone®, a treatment for multiple sclerosis.

#### Sales force: 35,030 people



#### Mastering our production chain



Gilles Lhernould Senior Vice President Industrial Affairs

"WE HAVE CHOSEN TO INTEGRATE OUR PRODUCTION CHAIN BOTH UPSTREAM AND DOWNSTREAM, TO DEFEND ALL OUR MEDICINES AND MEET HEALTHCARE NEEDS WORLDWIDE."

#### Full integration of our production chain

For sustained growth, we must be able to meet the demand for medicines. To achieve this aim, we have a fully-integrated first class industrial tool: 86 manufacturing sites worldwide, over 30,000 employees engaged in the production of active ingredients, the manufacture and packaging of medicines and their distribution. This integrated approach is one of the main characteristics of the sanofi-aventis industrial organization.

It is designed to respond to our policy of full control over the manufacturing process, based on three key elements: optimal control of flows, benefiting from the expertise of our employees and ensuring quality worldwide.

Since it is a key sanofi-aventis strategy to continue supporting base products, this policy provides an excellent opportunity to proceed with launches and relaunches: integration is one of the components of preparedness. Manufacturing facilities must be prepared to launch production of any given medicine.

This strategic choice led to several concrete decisions being taken in 2005:

#### Locating production where expertise is found.

Matching resources and investments. This is why the merger did not give rise to the closure of any facilities. The main objective is to run all existing manufacturing facilities at full capacity.

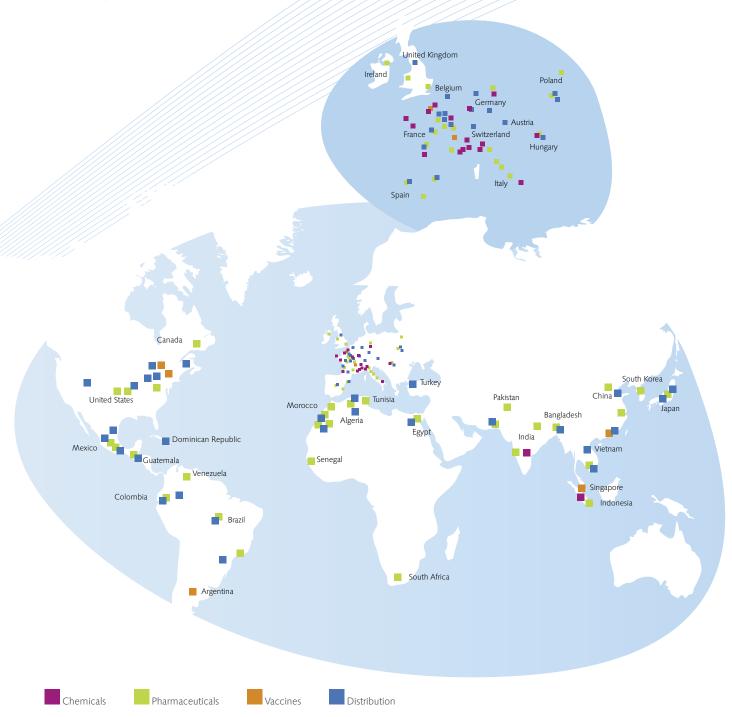
**Bringing back to Group facilities** production which had previously been outsourced.

Multisourcing, i.e. manufacturing the same compound in two or three different sites, so that the Group can respond to sudden upsurges in demand for certain medicines.

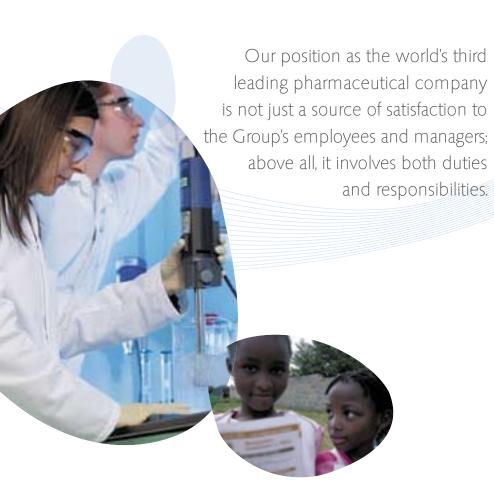
Resizing our facilities, recruiting, restructuring methods, technology transfers from one facility to another—all these decisions have improved the Group's competitiveness and its ability to satisfy demand. Another facet of our policy is to manufacture in the closest proximity possible to the focus of a disease. This has been the case, for example, with tuberculosis in South Africa or leishmaniasis in Brazil, and provides optimal response to the needs of the poorest nations or those countries which are least equipped to fight disease.

#### A TRULY INTERNATIONAL PRESENCE

#### The Group's main industrial sites



# "OUR POSITION AS THE GLOBAL Nº3 BRINGS WITH IT DUTIES AND RESPONSIBILITIES"



#### Responsibilities to the most disadvantaged

Today, 80% of the world's population have no access to medicines. As a powerful force for healthcare, it is our duty to help those who are suffering.

This is why we do our utmost to provide solutions to the resurgence or progression of neglected diseases all over the world; it is this commitment that has led sanofi pasteur to partner international organizations in campaigns to eradicate global scourges like poliomyelitis. More than ever, vaccines offer the greatest hope of better health to a world facing an onslaught of infectious diseases, and sanofi-aventis looks on vaccines as one of its strategic priorities.

As part of its strategy of support, sanofiaventis has made lower prices and increased production of basic medicines in certain countries a key component of its corporate philosophy.

## Driving back disease around the world

Mobilizing our talents around shared Values



Inspiring others with our vision, living up to our commitments and setting targets means nothing if Group employees do not feel the need for commitment.

The whole aim of our human resources policy is to encourage individual ownership of the Group's overall aims. Our active recruitment policy makes this an issue of prime importance.

#### Responsibilities to our partners

There are few industries whose demands are as exacting as those of the pharmaceutical industry, which requires scientific rigor, transparency, safety and quality. These requirements drive every aspect of our organization. We chose industrial consolidation as this also ensured consistent quality and continuity in the production chain.

The Group is constantly developing and adapting its prevention programs to provide more effective management of professional and environmental risks. Risk anticipation is the cornerstone of our HSE policy.



## Providing access to healthcare for the greatest number

Healthcare is a right and a right that all should enjoy. Yet 80% of the world's population lacks adequate access to healthcare and medicines. In 2001. in response to this fundamental challenge, we set up a structure to assess the situation and the expectations of the world's most deprived populations and to draw up action plans. This commitment is an integral part of our corporate strategy.



We have identified five neglected diseases to which our experience can be applied most legitimately and most effectively: tuberculosis, leishmaniasis, epilepsy, malaria and sleeping sickness.

#### Tuberculosis

Along with AIDS and malaria, tuberculosis is one of the world's three most deadly diseases, responsible for almost 2 million deaths a year. The Group produces rifampicine, an antibiotic central to the treatment of tuberculosis, and distributes a complete range of medicines in many countries. We have also instituted a new industrial optimization program to make these products available at the lowest possible price, and we offer training programs on tuberculosis and its treatment.

#### Leishmaniasis

Leishmaniasis is an endemic parasitic disease in 88 countries; the visceral form of the disease, known as Kala Azar, is the cause of over 200,000 deaths every year. Sanofi-aventis distributes one of the reference treatments for this neglected disease. To facilitate access to medicines, we have implemented an industrial optimization program to prioritize production in Brazil, one of the countries hardest hit by the disease. We have also introduced a tiered pricing policy, entitling the poorest patients to the lowest possible prices.

#### Epilepsy

Epilepsy strikes everywhere in the world, but is most prevalent in the southern hemisphere, in precisely those countries which are the least well equipped to manage the disease. For many years, the Group has provided one of the standard treatments for epilepsy. A pioneering program has begun to provide pharmaceutical assistance to a medical team in Mali, working with the NGO Santé Sud to offer treatment to epileptic patients in certain

rural areas. This assistance includes supplying medicines at cost price and helping to train the doctors involved.

#### > Malaria

An estimated 300 million cases and 1 to 3 million deaths worldwide are due to malaria every year; 90% of its victims live in Africa, and the majority of them are children. The Group's Impact Malaria program centers on an internal team of 17 people dedicated to fighting this killer disease. The program concentrates on four aims: research and development to find new treatments for malaria, new therapeutic strategies using compounds currently available, training and information geared to every link in the treatment chain, and the application of a tiered pricing policy.

#### Sleeping sickness

Sleeping sickness or human African trypanosomiasis is a parasite-borne disease vectored by the tsetse fly, found only in subtropical and equatorial Africa. 60 million people live in areas where the disease is endemic; around 50,000 new cases a year are recorded but only 20,000 are treated. In 2001, sanofi-aventis set up a five-year partnership with the World Health Organization to combat the disease through a monitoring and control program combined with research into new treatments. In 2005, the Group supplied over 350,000 treatment doses, which were used to treat over 40,000 patients. A new program will be drawn up and presented in 2006, aimed at eradicating this disease.

#### Vaccines programs and our role in public health

Immunization is one of the most effective ways of fighting infectious diseases and preparing to face new threats to public health such as pandemic influenza or bioterrorism.

Sanofi pasteur is working alongside international organizations on a number of far-reaching initiatives: worldwide eradication of poliomyelitis, preparedness for a possible flu pandemic, etc.

At the request of WHO, sanofi pasteur produced a monovalent poliomyelitis vaccine in record time. The new vaccine, the first in many years, will play a vital role in WHO's new strategy for the final stages of eradication of the disease in Southern Asia and in Africa. Over 60 million doses of the vaccine have already been produced at the Val-de-Reuil facility in France and distributed in Egypt and Yemen. At the beginning of 2006, WHO announced that the wild poliovirus had been eradicated in Egypt and in Niger, bringing total eradication of the disease a step nearer.

Dengue fever is the fastest-growing emerging viral disease and second leading tropical disease after malaria. The virus has now spread to all tropical countries with the exception of Africa. Dengue fever vaccine is currently one of sanofi pasteur's key projects.

Developing a vaccine effective against HIV is one of the major objectives of public health today, and also one of sanofi pasteur's main programs. The quest for a vaccine poses so many complex scientific and technical problems that sanofi pasteur has joined forces with a number of public-private partnerships, including the Global HIV Vaccine Enterprise which brings together scientists and industry members with the aim of accelerating the development of an HIV vaccine.

#### Our partnerships: a statement of our solidarity

The Group's commitment extends beyond issues of health alone. Its aim is to offer sustainable support to populations in need through programs in prevention and education, hygiene and access to healthcare, and the fight against poverty and exclusion. Such initiatives may be launched in response to humanitarian disasters in which healthcare is one of the most vital needs, as in the case of the Pakistan earthquake or Hurricane Katrina. They may also take the form of longerterm action to help the most vulnerable populations in the developed countries of the northern hemisphere, or on behalf of the populations of developing countries. Other initiatives include the "Tsunami Solidarity" program dedicated to the reconstruction of villages in South East Asia destroyed by the tsunami and to providing long-term assistance for local children, and Epivac, a vaccines and immunization training program for doctors.



## Uniting employees behind our corporate mission

For sanofi-aventis, there can be no strong, sustainable and profitable growth without the total involvement of its employees in the Group's corporate mission.

Our human resources policy is dedicated to pursuing this ambition.

#### More than 12,000 new hires in 2005

A year after the merger, the highly active recruitment policy pursued by sanofiaventis deserves special mention. In order to achieve its growth targets, the Group decided to increase its workforce wherever necessary, in particular in emerging countries like China and India. The Group's sales force has gained nearly 4,000 more medical sales representatives. R&D teams have also been expanded. In the vaccines business, some 900 new employees have been recruited to cope with rapid growth in this business activity. The industrial sector has also recruited more staff on sites scheduled for a significant upturn in activity. All in all, a total of almost 12,000 new employees joined the Group in 2005.

remuneration policy are all part of the Group's pursuit of a single objective: to create a community that shares the same ambition, strategy and values.

#### **Training and information**

Training is seen as a key component of the Group's HR policy, helping us to support the professional development of our staff and build teams around shared competencies.

Over the year, some 82.3% of staff worldwide received training, at every level of the organization.

The accent was on dialogue between training managers to promote the pooling of needs and best practices, sharing in campaigns and providing training programs geared to different audiences. In Europe, for example, an experiment with e-learn-



Jean-Claude Armbruster Senior Vice President, Human Resources

"TO MOTIVATE OUR EMPLOYEES, WE HAVE TO MAKE THEM FEEL PART OF A PROJECT, GIVE THEM CLEAR OBJECTIVES, TELL THEM WHERE THEY SHOULD BE GOING. WE MUST GIVE PEOPLE OPPORTUNITIES TO LEARN, OFFER THEM THE KEYS TO THEIR OWN PROGRESS. IN OTHER WORDS, WE NEED TO ENGAGE THEM IN THE VIRTUOUS CIRCLE OF SUCCESS."

#### An HR policy built on motivation

Sanofi-aventis has taken great care to introduce a performance management and skills development policy to ensure employee motivation. Individual interviews to establish priorities and career development paths for each employee, training, the promotion of diversity and

ing offers affiliate management teams training modules for the rapid development of specific knowledge and expertise. In the United States, awareness training in the Group's values and in the behavior expected of employees was rolled out for the entire affiliate. Training for initial levels of management in France brought teams together around shared themes.

#### Making diversity a source of wealth and performance

Sanofi-aventis has always promoted diversity as a source of creativity, innovation and performance. Diversity is the reason why our research teams are based in different countries, because we believe that their ability to discover new compounds benefits from the input of different ways of thinking. We prefer local recruitment to expatriation at every level, including managerial; our management teams come from many different backgrounds and there is no obligatory passage which guarantees a predetermined career path. We value diversity of profiles and experience, and we respect local cultures. As clearly indicated in our Social Charter, we reject all forms of discrimination.

## Recognizing and valuing individual and collective performance

As a vector for employee motivation and mobilization, our remuneration policy contributes to the Group's worldwide economic performance. Our policy recognizes and values individual performance within the bounds of respect for others, with an emphasis on team work. Recognition of collective performance, essential to guarantee our success over the long term, also plays a big part in the Group's remuneration policy. In 2005, collective performance-related remuneration systems were standardized in Fance, whilst maintaining conditions geared towards encouraging greater involvement of lower-paid employees.

## 14,109 United States United States 23,792 Other countries 50,582 Europe

**EMPLOYEES** 

97,181 people in 2005

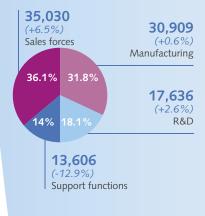
PHARMACEUTICALS:

88.483 PEOPLE

VACCINES: 8,698 PEOPLE



#### **FUNCTIONS:**



#### **TRAINING**

In 2005, almost 82 % of employees received training to help develop their business skills.



#### INVOLVING OUR COLLEAGUES

A capital increase reserved for employees was launched in December 2005, to promote a sense of belonging to the Group by giving employees a direct stake in our objective of "strong, sustainable, profitable growth". The offer was opened to almost 87,000 employees in 78 countries. Over two million shares were subscribed by 23,632 employees, with high take-up rates in South America, in Asia and also in Turkey.

## Building Health, Safety and Environment into our corporate mission

To earn and retain the trust of our stakeholders, internal and external, in our ability to meet the challenges of workplace health, safety and environment, sanofi-aventis places the highest importance on the implementation of our HSE policy.

#### **HSE** policy issues

Health, Safety and Environment policy is an integral component of the sanofiaventis Group Code of Ethics and sets out the requirements of occupational and environmental risk prevention for all employees worldwide. Its implementation is designed to respond, reliably and vigorously, to the major HSE issues currently facing the Group and to accompany the Group in its future development by identifying potential new risks.

Guaranteeing the safety of installations and surrounding areas by developing and operating the safest possible chemical processes. Pursuing clean design and development, reducing releases and emissions and disposing safely of waste, in order to protect health and the environment.

Special attention is paid to the specific challenges posed by our business activities. We must anticipate, as far as possible, the risks associated with the use of new products or with manufacturing processes for new medicines. Three specific multidisciplinary committees have been set up to evaluate and address these issues: **COVALIS** (occupational risk of exposure to chemical substances during handling and transport), **TRIBIO** (risk prevention in relation to biological agents) and **ECOVAL** (environmental impact of active ingredients developed and manufactured by the Group).



Philippe Peyre
Senior Vice President,
Corporate Affairs

"WHILE MANAGEMENT IS RESPONSIBLE FOR THE GROUP'S HSE TARGETS AND FOR THE ACTION PLANS AND PROGRAMS INTRODUCED TO MEET THEM, ITS TASK IS ALSO TO ENSURE THAT EVERY ONE OF OUR EMPLOYEES CLEARLY UNDERSTANDS THE IMPORTANCE OF HSE AND WHY ITS RULES MUST BE FOLLOWED."

- Protecting the health of every employee by rigorous control of all factors conducive to exposure to physical, chemical and biological hazards at the workstation.
- **Promoting safety** by preventing the risk of industrial accidents for each employee.
- **Curbing consumption of natural resources**, especially non-renewables, and contributing to efforts to meet the targets of the Kyoto protocol.

#### Putting our policy into action

Risk anticipation lies at the heart of the Group's HSE organization and programs, with risks systematically analyzed as the combination of a hazard and exposure to that hazard.

For the Group, this anticipation means constantly extending its knowledge in order to define the risk, and pursuing continuous development of its processes, technology, work organization and training with the aim of reducing and monitoring levels of exposure.

In the field of occupational health and hygiene, the COVALIS committee publishes recommendations on occupational exposure levels. Its standards set the Group's benchmarks. Each workstation is assessed for its degree of exposure which may, in some cases, call for the installation of appropriate protective equipment. Actual exposure levels at workstations are measured periodically and at least once a year.

In the field of safety, sanofi-aventis is keen to make its risk prevention systems even more robust. We have introduced "key safety elements" (KSE) for each workstation, i.e. the elements required to prevent a major risk which would, if an accident occurred, have irreversible effects. These elements include checking that protection systems are in good working order, testing emergency shutdown procedures and ensuring that the individual protective gear appropriate to the workstation is worn at all times.

Our industrial accident frequency rate is currently low, but we remain vigilant because we know from experience that nothing can be taken for granted where HSE is concerned.

In the field of the environment, our focus is on avoiding soil, water and air pollution. We have introduced GREEN, a new environmental assessment tool that measures the impact of our activities over the year, providing vital management information. Since it was first deployed in 2005, our results have improved as managers have been able to monitor the environmental impact of their sites.

ISO 14001 certification brings dual benefits, both in external recognition of the quality of our everyday environmental management, and as an inspiration to our teams.

27 sanofi-aventis sites worldwide already have certification. Sanofi pasteur's four main sites have embarked on the process of qualification for ISO 14001 environmental certification. This involves a farreaching program of environmental training and awareness for all employees and bears witness to sanofi pasteur's commitment to meeting international standards of environmental protection and prevention of pollution. On November 16, 2005, Toronto became the first sanofi pasteur site to be awarded this mark of international recognition. The Swiftwater site is on course for certification in early 2006.



# "EXCELLENT PERFORMANCE"



Jean-Claude Leroy Executive Vice President Chief Financial Officer

IN 2005, SANOFI-AVENTIS SALES INCREASED BY 9.3% ON A COMPARABLE BASIS, ADJUSTED EARNINGS PER SHARE (EPS) WAS UP BY 25.7%\*. DEBT WAS REDUCED BY MORE THAN 4 BILLION EUROS AND THE CROUP CONTINUED TO INVEST FOR THE FUTURE. RESEARCH WAS DEVELOPED, AND THERE WAS CONSIDERABLE INVESTMENT IN MANUFACTURING AND INTHE SALES FORCE. SO IT WAS AN EXCELLENT YEAR, WITH THE BOARD OF DIRECTORS PROPOSING AN INCREASE IN THE DIVIDEND OF 26.7% TO 1.52 EURO, UP BY 130% OVER THE LAST FIVE YEARS.

\* Pro forma change (see page 29.)

### PHARMACEUTICAL BUSINESS

(in millions of euros)

Sales for the top 15 medicines:

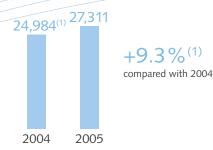
16,188 million euros in sales: : +14.0%

on a comparable basis(1)

Medicines	2005 Sales	Change on a comparable basis <sup>(1)</sup>
Loyenox®/Clexane®	2,143	+13.8%
Plavix®/lscover®	2,026	+20.2%
Taxotere®	1,609	+12.8%
Eloxatin®	1,564	+30.6%
Stilnox®/Ambien®/Ambien CR™	1,519	+10.6%
Allegra®	1,345	-9.1%
Lantus®	1,214	+47.5%
Tritace®/Delix®/Triatec®	1,009	+2.4%
Copaxone®	902	+24.1%
Aprovel®/Avapro®/Karvea®	892	+13.9%
Amaryl <sup>®</sup>	677	+0.7%
Actonel®	364	+23.8%
Depakine®	318	+4.6%
Xatral <sup>®</sup>	328	+18.4%
Nasacort®	278	-2.1%

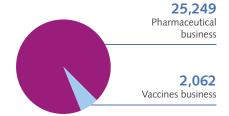
### **SALES FIGURES**

(in millions of euros)



### 2005 SALES FIGURES BY BUSINESS ACTIVITY

(in millions of euros)



### **VACCINES BUSINESS**

(in millions of euros)

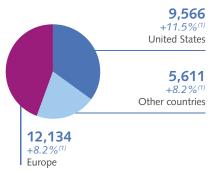
### 2,062 million euros in sales: +26.9%

on a comparable basis(1)

Vaccines	<b>2005</b> Sales	Change on a comparable basis <sup>(1)</sup>
Polio/Whooping Cough/		
Hib Vaccines	522	+3.2%
Adult Booster Vaccines	270	+58.8%
Influenza Vaccines	671	+28.6%
Travel Vaccines	176	+3.6%
Meningitis/		
Pneumonia Vaccines	256	+137.0%
Other Vaccines	167	+12.1%

(1) Comparable sales figures: when we refer to change in sales on a comparable basis, this means that we exclude the impact of changes in exchange rates and group structure (acquisitions or divestments of capital holdings, acquisitions or divestments of product rights, changes in methods of consolidation).

### 2005 SALES FIGURES BY GEOGRAPHIC AREA (in millions of euros)



# R&D expenditure in 2005

**4,044**MILLION EUROS

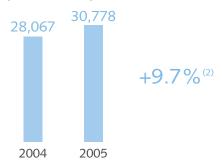
+2%
COMPARED WITH 2004

14.8%
OF SALES

### **Developed sales**

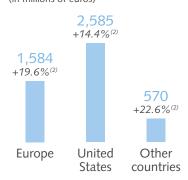
### **DEVELOPED SALES**(1)

(in millions of euros)



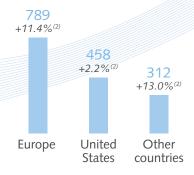
### 2005 DEVELOPED SALES<sup>(1)</sup> PLAVIX®/ISCOVER®:

**4,739 million euros**  $+17.1\%^{(2)}$  (in millions of euros)



### 2005 DEVELOPED SALES(1) APROVEL®/ AVAPRO®/KARVEA®:

**1,559** million euros  $+8.9\%^{(2)}$  (in millions of euros)



(1) **Developed sales** include sales by sanofi-aventis, excluding sales of products to alliance partners but including non-consolidated sales by our partners made through agreements with Bristol-Myers Squibb on Plavix®/Iscover®(clopidogrel) and Aprovel®/Avapro®/Karvea® (irbesartan) and with Fujisawa on Stilnox®/Myslee®, based on information provided to us by our partners. Developed sales are a useful indicator because they show the global market presence of products originating from sanofi-aventis research.

(2) On a comparable basis: i.e. at constant group structure and exchange rates.

### **Earnings**

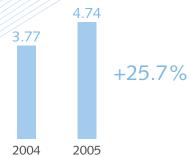
### ADJUSTED NET INCOME

(in millions of euros)



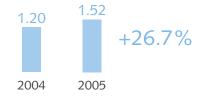
### **ADJUSTED EPS\***

(in euros)



### Dividend

(in euros)



### **INCOME**

In order to give a better representation of the Group's economic performance, we present adjusted consolidated income statements and compare them with adjusted pro forma income statements for 2004, as if the acquisition and related transactions had taken place on January 1, 2004. The 2004 pro forma financial data, determined under IFRS, are presented for illustrative purposes.

### ADJUSTED NET INCOME

This is defined as consolidated net income, determined under IFRS, adjusted to exclude the material impacts of purchase accounting for the acquisition and certain acquisition-related integration and restructuring costs. Sanofi-aventis believes that excluding these non-cash charges will enhance understanding of the Group's underlying economic performance.

The purchase-accounting effects on net income primarily relate to:

- charges resulting from the workdown of acquired Aventis inventory, net of tax;
- charges related to the impairment of the goodwill arising from the acquisition of Aventis;
- amortization and impairment charges related to the revaluation of Aventis intangible assets, net of tax and minority interests.

Sanofi-aventis also eliminates from adjusted net income integration and restructuring costs net of tax to the extent that they are specific to the operation.

<sup>\*</sup> Earnings per share.

# Stock exchange information

# Ranked second in the CAC 40 by market capitalization

### Trend in share price

### SANOFI-AVENTIS ON THE EURONEXT EUROLIST COMPARTMENT A IN PARIS



### SANOFI-AVENTIS IN PARIS ON THE EUROLIST COMPARTMENT A AND IN NEW YORK ON THE NYSE



### Indices

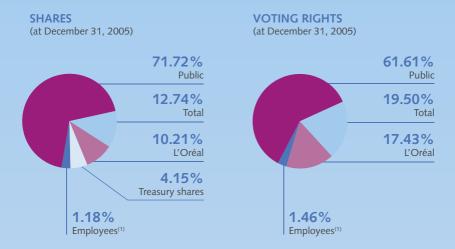
Sanofi-aventis shares are included in the following benchmark indices:

- French pan-sector index CAC 40
- European pan-sector indices Dow Jones Euro Stoxx 50, FTS Eurofirst 100, FTS Eurofirst 80
- European pharmaceutical index Dow Jones Stoxx Pharma
- American pan-sector indices NYSE International 100, NYSE World Leaders

### Share Particulars

- Par value of share: 2 euros
- Traded on
  - Eurolist Compartment A Euronext Paris (code SAN)
  - New York Stock Exchange (Ticker SNY)
- ISIN Code: FR0000120578
- Trading
  - continuous in Paris, eligible for the SRD and PEA
  - continuous in New York

# Sanofi-aventis share ownership at December 31, 2005



(1) Shares held through sanofi-aventis company share savings plan mutual fund.

### Shareholder information at a glance

			2005
Number of shares as of December 31 73	2,848,072	1,411,404,317	1,401,306,569
Dividend (in euros)	1.02	1.20	1.52*
Share price in euros			
High	60.00	63.25	76.70
Low	41.50	49.42	56.40
Latest	59.70	58.80	74.00
Market capitalization			
as of December 31 (in millions of euros	3) 43,751	82,990	103,697
Ranking in CAC 40			
by market capitalization	6	2	2

<sup>\*</sup> Conditional to shareholder approval

# 7 ANAJOR THERAPEUTIC AREAS TO ADDRESS THE HEALTH NEEDS OF THE GREATEST NUMBER

Cardiovascular Disease	p.32
Thrombotic	
Diseases	p.38
Metabolic	- 44
Disorders	p.44
Oncology	p.50
Disorders of the Central	
Nervous System	p.56
Internal medicine	p.64
Vaccines	p.72

# CARDIOVASCULAR DISEASES

# The single leading cause of death worldwide

Every year, over 17 million people throughout the world die as a result of cardiovascular diseases (CVDs)—over 30% of all human mortality. Contributory factors include smoking, high cholesterol levels, diabetes, stress, sedentary lifestyle and an aging population. While CVDs are more prevalent in the developed countries, there are clear signs of converging trends around the world in response to rising standards of living and changes in lifestyle.

Every year, 10 million myocardial infarctions are recorded around the world. Men are at greater risk than pre-menopausal women but 5 to 10 years after the menopause, women are at equal risk with men.

Cardiovascular diseases are the leading cause of disability and premature death, especially in men.

Over the last 30 years, progress in terms of healthier lifestyles and preventive treatment has led to a reduction in these risk factors, and in morbidity and mortality.

# Diseases targeted by sanofi-aventis

- > Arterial hypertension
- > Atrial fibrillation
- > Peripheral arterial disease
- > Heart failure
- > Venous and arterial thrombosis
- Angina



### **Arterial hypertension**

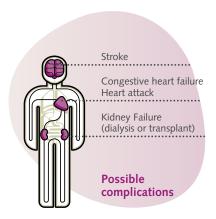
Arterial hypertension is the most frequent CVD, affecting 25% of the world population. An insidious, asymptomatic disease, it poses a serious threat to public health through the many complications to which it gives rise.

### The root cause of serious complications

Arterial hypertension can cause severe complications in the brain, heart, blood vessels, kidneys and eyes. Hypertension is defined as blood pressure above the normal level of 140/90 mmHg. The threshold figures are lower, however, when associated diseases increase the risk of cerebral, cardiac and renal complications. Diabetes, for example, doubles the risk of complications so blood pressure must be lower than 130/80 mmHg. The WHO recommends a full risk profile evaluation for each hypertensive patient to establish individual treatment protocols.

### AIIRAs, the most innovative class of the latest generation of anti-hypertensives

The Angiotensin II Receptor Antagonists (AIIRA) class is particularly recommended for hypertensive patients with type 2 diabetes. The American Diabetes Association (ADA) recommends that diabetics undergo annual screening for early signs of renal impairment followed, if confirmed, by treatment with an AIIRA, the new reference class in the treatment of hypertension. There are currently over 190 million diabetics worldwide, forecast to rise to 300 million by 2025.



25% of the world's adult population affected

cardiovascular risk factor, but prevention is particularly effective

# Our therapeutic response in the treatment of arterial hypertension



A powerful Angiotensin II Receptor Antagonist (AIIRA), a leader in the treatment of hypertension, with documented renal protective effects

Irbesartan belongs to the fastest-growing class of anti-hypertensive medicines: the angiotensin II receptor antagonists. These are indicated in the first-line treatment of hypertension, and are extremely effective. They work by impeding the effects of angiotensin II, the hormone respon-

sible for vasoconstriction, allowing arterial blood pressure to return to normal. Alongside Aprovel®/Avapro®/Karvea® in monotherapy, the Group markets **CoAprovel®/**Avalide®/Karvezide®, a fixed-dose combination of irbesartan and a diuretic, hydrochlorothiazide (HCTZ), which increases the rate at which water is excreted by the kidneys and thus augments the anti-hypertensive effect. Both



MILLION EUROS
2005 SALES
+13.9 %
ON A COMPARABLE BASIS

1,559
MILLION EUROS
IN DEVELOPED SALES
+8.9 %
ON A COMPARABLE BASIS



### LIFECYCLEMANAGEMENT

irbesartan

Two major clinical studies with planned enrolment of 14,100 patients. Results expected in 2007.

I-PRESERVE evaluates the efficacy of Aprovel® in the treatment of a specific but frequent form of heart failure known as diastolic heart failure.

The study was launched in 2002 with the aim of recruiting 4,100 patients.

ACTIVE-I evaluates the efficacy of Aprovel® in combination with clopidogrel (the active ingredient of Plavix®) in preventing vascular complications in patients with atrial fibrillation. The clinical program began in 2003 and the recruitment of 10,000 patients is under way.

products restore normal blood pressure in over 80% of patients and are extremely well tolerated.

A major clinical development program guaranteeing continued growth and success in the hypertension market

Avapro®/Aprovel® was approved for a new indication, the treatment of diabetic nephropathy in hypertensive patients, in the United States and Europe in 2002, after the PRIME clinical program demonstrated that it prevents renal impairment in hypertensive diabetic patients in both the early and late stages.

In 2005, the INCLUSIVE study involving hypertensive patients failing to achieve blood pressure goal on monotherapy demonstrated that Avalide®/CoAprovel® enabled patients to achieve blood pressure goal with good tolerability. Given

that less than a third of patients treated for hypertension manage to attain blood pressure control to internationally recommended levels, these results hold out great hope for improved management of the condition.

A number of clinical studies were launched or completed in 2005 in order to continue demonstrating the protective effect of irbesartan in addition to its efficacy as an anti-hypertensive:

- A broad-based international survey, i-SEARCH, was launched to evaluate the prevalence of microalbuminuria, a recognized marker for cardiovascular risk, in hypertensive patients with and without CVD. The survey will recruit 23,000 patients from 33 different countries. Results of this study are expected in 2006.
- A new clinical study involving 400 hypertensive patients with metabolic syndrome was launched in 2005, with the aim of studying the metabolic effects of Aprovel® in this patient population. Results of this study are expected in 2007.

### Main markets

Irbesartan is marketed in over 80 countries, including the United States, through a partnership with Bristol-Myers Squibb. Irbesartan is in the process of registration in Japan.

# Our therapeutic response treatment of hypertension or congestive heart failure after myocardial infarction



### Tritace®/Triatec®/Delix®/Altace®

ramipril

Tritace® (ramipril) is an angiotensin converting enzyme (ACE) inhibitor for the treatment of hypertension, congestive heart failure following myocardial infarction and nephropathy.

Its use has increased widely since the initial publication in 2000 of the HOPE (Heart Outcomes Prevention Evaluation) study showed it to be effective in reducing the incidence of stroke, myocardial infarction and cardiovascular-related death in high-risk patients.

### **Cumulative benefits**

The results of an extension to the HOPE study, HOPE-TOO, published in the journal *Circulation* in September 2005, demonstrated sustained vascular and metabolic benefits obtained from treatment with Tritace® 10 mg.

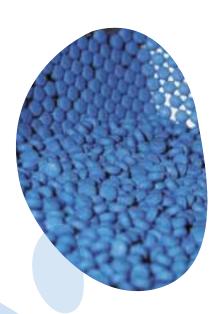
### Main markets

Tritace<sup>®</sup> in 2005 figured among the market leaders in Canada, France and Spain and ranked no. 1 in Italy.

Although its market exclusivity expired in Germany in January 2004, Tritace® (marketed as Delix®) remains the market leader in its class, with demand continuing to grow. Marketing rights in the United States were sold to King Pharmaceuticals in 1998. (Source: IMS end 2005, except GERS for France. ACE Inhibitors).

1,009 MILLION EUROS 2005 SALES

+2.4%
ON A COMPARABLE BASIS



# OUR OTHER THERAPEUTIC RESPONSES Cardiovascular

Sanofi-aventis continues to market a number of classic cardiovascular products in many parts of the world.

**Lasilix** (furosemide) is still a diuretic treatment of reference. With sales of over 60 million packs a year, it is one of the Group's best-selling products by volume.

35 years after it was first marketed, **Cordarone**® (amiodarone®) is still an anti-arrhythmic of choice, enjoying steady growth worldwide.

**Tildiem®** (diltazem), used in the treatment of angina and hypertension, is marketed in 54 countries in Europe, Asia, Africa, the Middle East and Latin America. Antihypertensive **Selectol®** (celiprolol), cholesterol-lowering **Lipanor®** (ciprofibrate) and anti-angina medicine **Ikorel®** (nicorandil) are also successfully marketed in a number of European countries.

RESEARCH & DEVELOPMENT

# Meeting tomorrow's needs

Sanofi-aventis is pursuing its efforts in this therapeutic area to develop new treatments for cardiac arrhythmia, one of our fields of excellence.

Atrial fibrillation: Cardiac arrhythmia affects the cardiac muscle's electrical system, causing irregular contractions and leading to diminished cardiac function, which in turn limits the quantity of blood pumped to the brain and other vital organs and can also induce the formation of clots. The condition can impact significantly on patients' quality of life and, in the most severe case, lead to sudden death. Atrial fibrillation (AF) is the most frequent form of cardiac arrhythmia.

### Submitted to the European and U.S. health authorities in 2005

Multaq® (dronedarone)

A new anti-arrhythmic agent, potentially offering a high degree of efficacy and tolerability.

Dronedarone is a new multichannel blocker for the prevention and treatment of atrial fibrillation. Whilst it is similar in structure to amiodarone, it does not contain an iodine radical and thus should benefit from better tolerance.

The first indication developed for dronedarone is preventing recurrence of atrial fibrillation, the most common cardiac rhythm disorder.

The aim in treating AF is to restore and maintain the heart's normal sinusal rhythm and control ventricular rate. The usual treatment for persistent AF is initial electrical cardioversion, generally followed by treatment with anti-arrhythmics to avoid what would otherwise be frequent recurrences.

Two phase III clinical trials, EURIDIS (Europe) and ADONIS (North and South America, Australia and South Africa) involving a total of 1,245 patients with atrial fibrillation, have shown good efficacy and safety—absence of toxic effects on vital organs—of dronedarone as an anti-arrhythmic, and particularly the absence of any pro-arrhythmic effect in patients with atrial fibrillation.

A more recent study, ERATO, demonstrated the benefits of dronedarone in maintaining ventricular rate control in patients suffering from permanent AF

On the strength of these results, a New Drug Application has been submitted to the European and U.S. regulatory authorities and is currently under review.

### Phase IIb Atrial fibrillation SSR 149744C

As well as offering improved tolerability, SSR 149744C has a different metabolic profile from amiodarone and should thus be free of the drug interactions frequently observed with amiodarone. In addition, SSR 149744C should provide ease of administration with once-daily dosage. The target indication for SSR 149744C is atrial fibrillation. SSR 149744C entered phase IIb in December 2004.

Critical leg ischemia: this is the most severe stage of obliterating peripheral arterial disease. It is a common disorder, in which narrowing of the arteries leads to a restricted flow of blood to the lower limbs, and is accompanied by an increased risk of myocardial infarction or stroke. Critical lower-limb ischemia may be the origin of severe leg pain at rest, and may make skin ulcers on the leg slow to heal. It may also be a frequent cause of amputation and even death.

### Phase IIb Non-viral gene therapy

NV1-FGF (XRP 0038)

NV1-FGF is an approach based on gene therapy involving the injection of non-viral plasmid DNA to induce angiogenesis in patients suffering from obliterating peripheral arterial disease (OPAD).

Following the encouraging results obtained from the phase IIb TALISMAN study (significant reduction in the risk of amputation in patients presenting with critical leg ischemia) the development of NV1-FGF will move into phase III in this indication in 2006.

### Phase IIb ACE-NEP Inhibitor

**AVE 7688** 

AVE 7688 has demonstrated its efficacy in patients suffering from hypertension. A randomized, dose-ranging trial (phase IIb) was recently launched in 1,730 patients to establish the long-term tolerability over one year.





# THROMBOTIC DISEASES

# One of the main causes of mortality worldwide

Thrombotic diseases, with their venous and arterial repercussions, are now one of the world's leading causes of mortality.

### Deep venous thrombosis (DVT) and its complication, pulmonary embolism

Deep venous thrombosis, also called thrombophlebitis, and its main complication, pulmonary embolism, are the cause of more deaths every year in Europe than breast cancer, prostate cancer, HIV contamination and road accidents combined.

It is estimated that 1.5 million Europeans are affected and over 500,000 of them die annually.

### Arterial thrombosis or atherothrombosis

Atherothrombosis is the underlying cause of heart attack and stroke which together represent a third of all deaths. An increase in the number of heart attacks and strokes is expected in the future. Estimates forecast over 20 million deaths in 2020 and over 24 million in 2030. Today, one man in four and one woman in three still die as a result of their first heart attack, even in countries with advanced healthcare systems.

# Diseases targeted by sanofi-aventis

- Deep venous thrombosis, complicated or not by pulmonary embolism
- > Atherothrombosis
- Acute coronary syndromes (angina, myocardial infarction)

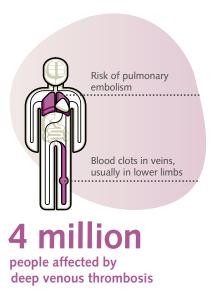


### Venous thromboembolism

A mostly avoidable disease

### Deep venous thrombosis or thrombophlebitis

DVT occurs when a blood clot is formed in the deep veins of the leg. Prolonged bed rest, heart failure, some tumors and reduced mobility are all causative factors of deep venous thrombosis. Without treatment, the blood clot may cause pulmonary embolism, which is frequently fatal. A third of all cases occur outside a hospital environment.



### Our therapeutic response

venous thrombosis, and prophylactic treatment for ischemic complications of unstable angina and non-Q wave myocardial infarction



### The world's leading\* Low Molecular Weight Heparin (LMWH)

Lovenox®/Clexane® is the world's most widely studied and prescribed low molecular weight heparin. Since it was launched, Lovenox® has been used to treat approximately 170 million patients in 96 countries. Lovenox® has the broadest spectrum of approved indications of any LMWH.

A number of studies have demonstrated its efficacy in reducing the risk of deep venous thrombosis.

Similarly, in arterial thrombosis, Lovenox® has proved effective in preventing ischemic complications of unstable angina and non-Q wave myocardial infarction, when administered in combination with a platelet antiaggregation treatment.

More recently (September 2005) the results of the STEEPLE study demonstrated that for patients who had undergone percutaneous coronary interventions (PCI) or coronary angioplasty, enoxaparin alone was as effective as the traditional treatment (unfractionated heparin), but with a significantly reduced risk of major hemorrhage and more easily regulated anticoagulation levels.

### Main markets

Lovenox<sup>®</sup> is the leader on all the major markets, including the United States, Germany, France, Italy, Spain and the United Kingdom. (Source: IMS end 2005, except GERS for France).

2,143
MILLION EUROS
2005 SALES

+13.8%
ON A COMPARABLE BASIS

### LIFECYCLEMANAGEMENT

### enoxaparin sodium

Three studies to demonstrate the efficacy of Lovenox® in other indications are in progress.

Two major studies to demonstrate the efficacy of Lovenox® for the prevention of venous thromboembolic events:

- EXCLAIM: a trial on the **optimal length of treatment** in approximately 4,000 patients at risk of thrombosis due to temporarily restricted mobility as a result of various medical conditions.
- PREVAIL: a trial to establish the efficacy of Lovenox® administered once a day compared to unfractionated heparin twice a day in the prevention of thromboembolic events in patients after acute ischemic stroke...

<sup>\*</sup> Source IMS.

### ...LIFECYCLEMANAGEMENT

A major study of the severe repercussions of arterial thrombosis:

• EXTRACT-TIMI25: a trial on the use of Lovenox® in the treatment of 20,500 patients with myocardial infarction receiving concomitant thrombolytic treatment. The results were presented in 2006, demonstrating the superiority of Lovenox® over the usual treatment worldwide.

Heart attack

Peripheral Arterial

Disease (PAD)

# Unstable angina and non-Q wave myocardial infarction

Unstable angina is an acute aggravation of angina pectoris. This occurs when the blood flow into the arteries feeding the heart is slowed down by blood clots to the extent that the heart's oxygen supply is reduced. The main risk is myocardial infarction. Angina pectoris is the second most frequent cardiovascular disease worldwide.

### **Atherothrombosis**

Some 17 million people suffer from atherothrombosis-related conditions, which are responsible for over a million deaths every year in Europe and the United States.

### A single disease, many forms

Acute coronary syndrome, myocardial infarction, stroke, transient ischemic attack and peripheral arterial disease are all variations of a single disease: atherothrombosis, itself a consequence of atherosclerosis.

Atherosclerosis occurs as a result of the thickening and hardening of the arterial wall where fatty and calcification deposits, called plaque, build up. When the atherothrombotic plaque breaks up or ruptures, a clot is formed on the damaged artery, reducing flow or even completely obstructing a blood vessel, which is known as atherothrombosis.

# Our therapeutic response prevention of ischemic events caused by atherothrombosis

2,026
MILLION EUROS
2005 SALES

+20.2%
ON A COMPARABLE BASIS

4,739
MILLION EUROS
2005 DEVELOPED SALES

+17.1%
ON A COMPARABLE BASIS



Plavix® (clopidogrel) is a platelet antiaggregation inhibitor and an antagonist of adenosine disphosphate (ADP) receptors. It is indicated for the prevention of atherothrombotic complications in patients with a recent history of myocardial intarction, recent stroke, or established peripheral arterial disease.

Plavix® is currently the only medicine indicated for the secondary prevention of atherothrombosis regardless of the location of the primary arterial damage.

This indication is supported by the decisive results of the CAPRIE study on nearly 20,000 patients which demonstrated the superior efficacy of Plavix®

compared to acetylsalicylic acid (ASA, the active ingredient of aspirin) with equivalent tolerability.

Following the impressive results obtained in the CURE study in 2002, Plavix  $^{\circ}$ 

obtained an extended indication for the treatment of acute coronary syndrome (non-Q myocardial infarction and unstable angina) in combination with aspirin. This indication was included in the recommendations of the American Heart Association, the American College of Cardiology and the European Society of Cardiology. On top of standard therapy, including aspirin, Plavix® reduced by 20% the relative risk of atherothrombotic events with a 1% increase of major bleeding occurrences.

# The beneficial effects of Plavix® demonstrated by an extensive clinical study program.

The results of the CREDO study published in November 2002 confirmed the therapeutic benefits of Plavix® in the short and long term prevention of atherothrombotic events in patients who had undergone coronary angioplasty, with or without a stent.

The results of the MATCH study demonstrate that aspirin does not contribute any added therapeutic value when combined with Plavix® in patients with a history of recent stroke or transient ischemic attack.

The CLARITY-TIMI 28 study showed that Plavix® added to standard therapy including fibrinolytics and aspirin reduced the odds of acute myocardial infarction patients having another occluded artery, or a second heart attack or death after one week of hospitalization.

The COMMIT/CCS-2 study, one of the most extensive studies worldwide, involving over 46,000 patients, demonstrated that Plavix<sup>®</sup> in combination with standard treatments, aspirin in particular, reduces the high incidence of death 28 days after an acute myocardial infarction.

In the last two studies, the incidence of severe bleeding was similar in the Plavix® and placebo groups, thereby demonstrating a favorable benefit/risk ratio for Plavix®. On the basis of these results, the US Food and Drug Administration decided on January 18, 2006, to grant Plavix® a priority review for a supplemental new drug application (sNDA) in a new indication: acute phase myocardial infarction.

On March 12, 2006, the results of the **CHARISMA study** were presented at the American College of Cardiology (ACC) conference. Although results for the study as a whole did not verify the initial hypothesis, an analysis of the various populations suggests that:

- patients presenting with multiple risk factors but no previous cardiovascular event did not benefit from combining the two antiplatelet agents;
- however, for patients with established atherothrombosis (previous cardiovascular event), the combination of clopidogrel and aspirin produced a statistically significant reduction of 12.5% in the relative risk of myocardial infarction or stroke recurrence, or of cardiovascular-related death, compared to aspirin alone. Improvement was not associated with any significant increase in severe bleeding. These patients represented close to 80% of the total CHARISMA population.

### Main markets

Plavix® was launched in 1998. It is currently marketed in over 80 countries, including the United States, through an alliance with Bristol-Myers Squibb (BMS). In Japan, an application for marketing approval was accepted in January 2006 and launch is planned for this year. Plavix® sales in Japan are not covered by our alliance with BMS.

### LIFECYCLEMANAGEMENT clopidogrel

The Plavix® clinical trial program is one of the largest. It will eventually include over 100,000 patients.

The CASPAR study will assess the benefits of Plavix® in patients presenting with peripheral arterial disease (PAD) after bypass surgery.

The ACTIVE trial is evaluating the efficacy of Plavix® in the prevention of cardiovascular events in patients presenting with atrial fibrillation. The study will include 14,000 patients. Results are expected in 2007 or 2008.

One of the study arms (ACTIVE W) was stopped prematurely. The other two (ACTIVE A and ACTIVE I) are continuing.

# OVER 41 MILLION PATIENTS WORLDWIDE HAVE BEEN TREATED WITH PLAVIX® SINCE LAUNCH



RESEARCH AND DEVELOPMENT

# Meeting tomorrow's needs

The formation of a blood clot is a process in which coagulation of the blood and platelet aggregation are closely intermeshed. In this field, sanofi-aventis aims to develop new compounds capable of specifically inhibiting factors involved in blood coagulation, in particular factors Xa and IIa.

Phase III Long-term treatment of thromboembolic events.

Prevention of thromboembolic events associated with atrial fibrillation

Idraparinux sodium (SR 34006)

Idraparinux sodium is a selective indirect inhibitor of coagulation factor Xa with a long duration of action. It is a synthetic pentasaccharide. The VAN GOGH phase III program is investigating the efficacy and safety of idraparinux sodium in the long-term treatment of thromboembolic events in patients suffering from deep-vein thrombosis or pulmonary embolism and is progressing as planned. In the AMADEUS program studying idraparinux sodium in comparison to Vitamin K antagonists in the prevention of thromboembolic events associated with atrial fibrillation, a substantially lower incidence of events than initially expected was observed. As a result, sanofi-aventis has decided in agreement with the Steering Committee and the Drug Safety Monitoring Board, to make no further recruitments in the AMADEUS program. The principal reason was the very large number of patients that would be required in order to show statistical significance.

### Phase IIb Thromboembolic diseases SSR126517

SSR126517 is a neutralizable selective inhibitor of coagulation Factor Xa. It has the same pentasaccharidic structure as idraparinux, with the addition of a biotin "hook" to allow quick and efficient "fishing" by its specific neutralizing agent, avidin. It demonstrated similar anticoagulant, pharmacokinetics and antithrombotic properties to idraparinux. Because of this similarity to idraparinux we have started an abridged clinical development based on idraparinux clinical studies. It includes in particular a phase III program in patients with pulmonary embolism and deep vein thrombosis due to start in the second quarter of 2006.

# Phase IIb Prevention of major cardiovascular events in acute coronary syndrome

SR 123781

SR 123781A is a synthetic hexadecasaccharide. It includes two functional domains, an antithrombin binding domain, and a thrombin binding domain, responsible for its dual anticoagulant activity via indirect inhibition of coagulation factors Xa and IIa. Based on its demonstrated potent antithrombotic activity in animal models, it is currently being studied in phase IIb in patients with acute coronary syndromes treated with an invasive strategy.

### Phase IIb Acute coronary syndrome

Otamixaban (XRP 0673)

Otamixaban is an injectable non-saccharidic synthetic direct inhibitor of coagulation factor Xa. It is fast-acting and has a short half-life. It is being investigated in patients undergoing cardiac catheterization.





# METABOLIC DISORDERS

### Diabetes rates soaring

Millions of people around the world suffer from diabetes and its complications. Diabetes currently affects nearly 200 million people worldwide and WHO statistics forecast that more than 300 million will be affected by the year 2025.

### Cardiometabolic risk

Cardiometabolic risk is a term that refers to the overall risk of developing type 2 diabetes or cardiovascular disease. It is linked to the presence of traditional risk factors such as hypercholesterolemia (a high rate of LDL or "bad" cholesterol in the blood), hypertension, type 2 diabetes and smoking, as well as to a cluster of emerging insulin resistance markers that are often present in patients with abdominal obesity (an excess of high-risk abdominal fat). Research has shown that adipose tissue does not simply store fat; it also functions as an organ in its own right, releasing substances that can contribute to the development of cardiometabolic risk factors such as high levels of triglycerides and hyperglycemia, thus compounding the risk of diabetes and cardiovascular disease. In the United States, around 46% of men and women over the age of 20 suffer from abdominal obesity.



### **Diabetes**

Diabetes is a chronic disease in which the body fails to produce or properly utilize insulin, a hormone that enables cells to absorb glucose and convert it into energy. In people with diabetes, the system functions inadequately or not at all, leading to a high level of glucose in the blood known as hyperglycemia.

### A chronic disease

In type 1 diabetes, the body fails to secrete any insulin at all because the beta cells in the pancreas that produce insulin have been destroyed by the body's own immune system. People with type 2 suffer from a progressive form of the disease in which the pancreas continues to secrete insulin, but not in sufficient quantities to keep blood glucose levels under adequate control. In addition, insulin secretion by the pancreas tends to diminish over time. In some cases, insulin is produced in large quantities but fails to ensure normal glucose absorption by the body's tissues, or to regulate the production of sugar by the liver. This condition, in which insulin is secreted normally but remains ineffective, is known as insulin resistance.

### Controlling diabetes to limit the risks

Diabetes cannot be cured but it can be treated or controlled very effectively. The monitoring factors for diabetes are:

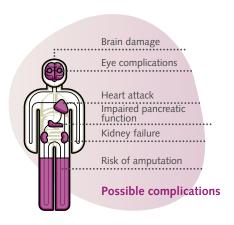
- measuring blood glucose levels, which should be maintained as close to normal as possible;
- measuring glycated hemoglobin or HbA1C (A1C), which gives an indication of average glycemia over the past 2 or 3 months. Non-diabetics automatically maintain an A1C concentration of between 4 and 6%, while diabetics should aim to keep their level of A1C at or below 7%.

### Uncontrolled diabetes carries a high risk of severe complications

A person suffering from diabetes with A1C levels constantly above normal (uncontrolled diabetes) runs a high risk of developing severe short and long term complications, including blindness, kidney failure, amputation of the lower limbs, heart disease, stroke or impotence.

### A rampant epidemic

200 million people around the world currently suffer from diabetes and its complications, and WHO statistics predict that over 300 million people will be affected by 2025.



200 million



# 1,214 MILLION EUROS 2005 SALES

+47.5 %
ON A COMPARABLE BASIS

### LIFECYCLEMANAGEMENT insulin glargine

Many studies carried out since the launch of Lantus® have demonstrated that it represents a simple method for initiating routine basal insulin treatment in type 2 diabetics.

- The 2003 TREAT-TO-TARGET study showed that, compared to NPH insulin, a significantly higher number of people with type 2 diabetes treated with Lantus® attained a target A1C control of 7% or less, without episodes of nocturnal hypoglycemia.
- Results of the LANMET study in 2006 demonstrated that symptomatic hypoglycemia was 44% more frequent with isophane insulin (NPH) than with Lantus® in people with type 2 diabetes. In addition, dinnertime glycemic control was improved with Lantus®.
- The LAPTOP 2005 study showed that the combination of Lantus® once daily with an oral antidiabetic (OAD) restored glycemic control more effectively than conventional treatment, without causing episodes of nocturnal hypoglycemia.
- A meta-analysis of four studies involving Lantus® demonstrated that the reduced risk of hypoglycemia is lasting and significant with Lantus® in people with type 2 diabetes who are no longer able to achieve glycemic control with an oral antidiabetic alone.
- The AT-LANTUS 2005 study found that people with diabetes using a simple self-directed titration algorithm with Lantus® achieved a significant improvement in glycemic control accompanied by reduced frequency of episodes of severe hypoglycemia compared to physician-directed titration.

After receiving marketing approvals from the appropriate regulatory authorities, **OptiClik®** was launched in the U.S. and Japan in 2005. OptiClik® is a reusable insulin pen that offers people with diabetes a new, easy-to-use insulin delivery option.

# Our therapeutic response Treatment of type 1 and type 2 diabetes



### LANTUS® HAS BEEN THE WORLD'S BEST-SELLING INSULIN\*

In 2005, Lantus® posted net sales in excess of 1 billion of euros and outstanding growth of 46.5% over 2004.

### **Lantus®** (insulin glargine)

Lantus® (insulin glargine) is a long-acting insulin analog administered in a single once-daily subcutaneous injection, and is indicated for the treatment of adults with type 2 diabetes and of adults and children over the age of 6 with type 1 diabetes.

Lantus® (insulin glargine) is the first basal insulin with a 24-hour peakless activity profile, and so can be administered in a single dose at any time of the day. It allows self-directed titration of doses by patients under optimum safety conditions and is less prone than isophane insulin (NPH) to cause hypoglycemia. Lantus® represents a revolution in the therapeutic options available to patients, who can now be treated more effectively and attain their target A1C control while enjoying a better quality of life.

The simplicity of a single daily injectable dose of insulin may also encourage earlier initiation of insulin therapy in primary medical care.

### A dynamic market

Lantus® has consistently outperformed the insulin market since it was first launched in Germany in 2000, then in the U. S. in 2001, in the U.K. in 2002 and in France in 2003. Lantus® is now marketed in more than 70 countries.

After the U.S., the biggest market for insulin is Germany, followed by Japan. Since December 2003, Lantus® has been the world's most frequently prescribed insulin. Net sales exceeded one billion euros in 2005. The three main markets for Lantus® are the U.S., Germany and the U.K. (Source: IMS, Sales at end 2005. Pharmacy sales only, except for the U.S.: total insulin market, pharmacy and hospital).

\* Source IMS/MAT July 2004.

### Apidra®

A NOVEL FAST-ACTING INSULIN ANALOG FOR THE TREATMENT OF ADULTS WITH TYPE 1 AND TYPE 2 DIABETES.

Apidra<sup>®</sup> used with the OptiClik<sup>®</sup> injection pen delivery system can be associated with longer-acting insulins such as Lantus<sup>®</sup> for supplementary glycemic control.

Apidra® has a more rapid onset and shorter duration of action than fast-acting human insulin. In addition, Apidra® is equally effective in adult diabetics ranging from lean to obese and offers patients greater flexibility of administration, either before or just after a meal.

Apidra® is scheduled for launch in a number of countries in 2006.

# Our therapeutic response the oral treatment of type 2 diabetes



### Amaryl®/Amarel®/Solosa®

glimepiride

Amaryl® (glimepiride) is an orally administered once-daily hypoglycemic sulfonylurea indicated in the treatment of type 2 diabetes, in association with exercise and a controlled diet.

Studies show:

- the efficacy of Amaryl® in combination with Lantus®, when treatment with an OAD alone fails to provide adequate glycemic control;
- reduction in glycemic level with Amaryl® thanks to a dual mechanism of action, helping the body to produce more insulin both at mealtimes and between meals, and reducing insulin resistance:
- very good levels of glycemic control with Amaryl® and a low risk of hypoglycemia.

Amaryl® was first launched in 1995 and now has product license approval in around 100 countries. The three main markets for Amaryl® are Japan, Germany and Poland.

The European patent on Amaryl® expired in December 2005.

Following expiry of the U.S. patent, sanofiaventis launched an authorized generics partnership with Prasco. At the end of December 2005, within a week of their launch, authorized generics accounted for a 29.6% share of the market for prescriptions of generic glimepiride.

677 MILLION EUROS 2005 SALES

+0.7 % ON A COMPARABLE BASIS

# OUR OTHER THERAPEUTIC RESPONSES Metabolic disorders

Sanofi-aventis pays particular attention to traditional therapies for the of type 1 and type 2 diabetes management. The Group is well placed to address a significant proportion of the needs of patients and healthcare professionals, while responding to the economic constraints of developing countries, thanks to its Insuman® range of human insulins and its extensive portfolio of oral anti-diabetics (including the sulfonylurea Daonil®). These products, with their tried and tested efficacy and tolerability, are irreplaceable in the management of diabetes.



RESEARCH AND DEVELOPMENT

# Meeting tomorrow's needs

Some of our developments in the field of metabolic disorders are aimed at producing new insulin analogs, optimized in terms of rapidity of action and methods of administration. Other developments target the mechanisms regulating glycemia: Na+/glucose cotransporter inhibitor, glycogen phosphorylase inhibitor, PPAR agonist. Others aim at regulating the endocannabinoid system.

### Obesity and cardiometabolic risk

Rimonabant (SR 141716) in the process of registration

Rimonabant is the first of a new therapeutic class known as the  $CB_1$  receptor antagonists.  $CB_1$  receptors were first identified in the brain and subsequently in several other human tissues including the adipocytes (fatty tissues). These receptors are part of the endocannabinoid system which plays a crucial role in the regulation of body mass and weight, lipid metabolism and insulin resistance. The system is also involved in sensitivity to positive reinforcers such as nicotine.

Rimonabant has been investigated in two major phase III trial programs, one evaluating the product in obesity and associated disorders such as type 2 diabetes and dyslipidemia (RIO program: Rimonabant in Obesity), and the second in smoking cessation (STRATUS program). NDAs for the respective indications were filed with the U.S. and European authorities in 2005 and are currently under review.

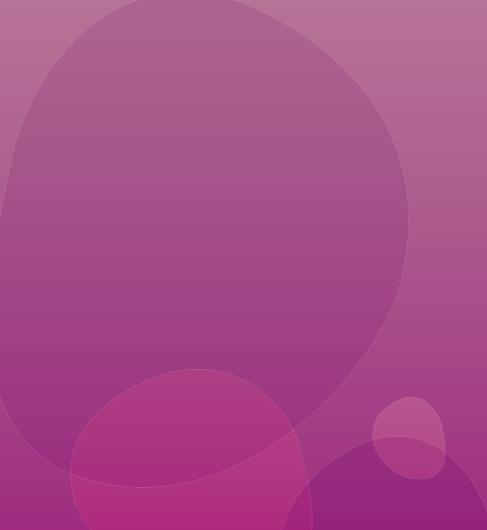
# Phase IIb Obesity SR 147778\*

# Phase IIb Type 2 Diabetes mellitus AVE 0010

This injectable GLP-1 receptor agonist entered phase IIb for patients with type 2 diabetes. Compounds which increase the circulating levels of GLP-1 can not only lower glycemia but also restore the ability of pancreatic beta cells to produce insulin.

The rights to AVE 0010 were acquired under a license agreement with Zealand

Pharma.







# ONCOLOGY

# The leading cause of mortality among the under-65s

Cancers are insidious diseases that can strike anyone and take many different forms. Cancer incidence is on the rise everywhere, in both industrialized and developing countries and could increase by as much as 50% by 2020 as a result of an aging population.

An estimated 10 million people worldwide are diagnosed with cancer every year. Because of their high life expectancies, industrialized countries are particularly hard hit: in the United States and Europe, cancer has become the second most common cause of death after cardiovascular disease. Lung cancer is the first cancer-related cause of death for both men and women. Breast cancer in women and prostate cancer in men follow close behind. Head and neck (ENT) cancers rank fifth but affect men disproportionately: 9 men for every 1 woman, especially between the ages of 50 and 60.

Colorectal cancer, which is also more prevalent in Western countries, is the third most common type of cancer worldwide and the second leading cause of cancer-related mortality in the United States.

# Cancers targeted by sanofi-aventis

- > Colorectal cancer
- Breast cancer
- Non-small cell lung cancer (NSCLC)
- > Prostate cancer
- → Gastric cancer
- Cancer of the head and neck (ENT)
- Malignant hemopathies (leukemias)
- > Melanoma



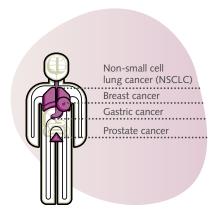
### Solid tumors

Breast cancer, colorectal cancer, lung cancer, prostate cancer and cancers of the head and neck are responsible for high levels of morbidity and mortality.

### Cancer is a disease involving multiple factors

Just as the body is made up of hundreds of different types of cells, so cancer is not a single disease but exists in many forms.

Cancer develops as a result of the uncontrolled proliferation of abnormal cells leading to the formation of a malignant cell mass. Cancer is described as metastatic when the presence of malignant cells is not confined to the initial site of the disease but has spread to other parts of the body. How the cancer develops depends on its type and its sensitivity to existing forms of treatment. The initial anomaly that makes a cell cancerous is genetic in origin. One of the many theories advanced to explain tumor development is that of a series of genetic mutations that may be influenced by behavior and environment (tobacco, over-exposure to sunlight, fatty foods, pollution, etc.), and in some cases hereditary factors may be identified.



### 10 million

people are diagnosed with cancer every year worldwide

The **earlier** a tumor is detected, while still localized, the greater the likelihood that treatment will be effective

# Our therapeutic response solid tumors



# A reference chemotherapeutic agent indicated in a large number of solid tumors

Taxotere® (docetaxel) is a drug in the taxoid class, which inhibits cancer cell division by essentially "freezing" the cell's internal skeleton, comprised of microtubules which assemble and disassemble during a cell cycle. Taxotere® promotes assembly and blocks disassembly, thereby preventing cancer cells from dividing and resulting in their death.

Taxotere® was first approved in 1995 and is currently marketed in over 100 countries in eight indications for four major forms of cancer.

Taxotere® is indicated for the treatment of breast cancer in both the early stages (adjuvant treatment) and in the metastatic phase, as well as in the HER2/neu positive forms for which prognosis is very poor.

Taxotere® is also indicated for the treatment of stage IV non-small cell lung cancer and for metastatic hormone-refractory prostate cancer. In March 2006, Taxotere® received approval in the U.S. and Europe for the treatment of patients with metastatic gastric cancer.

The clinical development of Taxotere® continues, including diseases for which Taxotere® is already licensed, to give patients the benefit of Taxotere®'s efficacy at every stage of disease.



1,609 MILLION EUROS 2005 NET SALES

+12.8 %
ON A COMPARABLE BASIS

### LIFECYCLEMANAGEMENT

docetaxel

Taxotere® is being studied extensively for safety and efficacy in cancers of the head and neck (ENT).

A supplemental New Drug Application (sNDA) for a new indication in induction chemotherapy for patients with locally advanced and inoperable epidemoid adenocarcinoma of the head and neck will be filed in Europe and in the United States in the second quarter of 2006.

In breast cancer, as an adjuvant treatment and in metastatic forms, intermediate analysis of a phase III study has shown that Herceptin® (trastuzumab) combined with a Taxotere®-based regimen in HER 2-positive diseases significantly improved treatment efficacy.

Results also suggest that, again in adjuvant therapy, a Taxotere®-based regimen (Taxotere®-carboplatin/Taxotere®-cyclophosphamide) could successfully replace anthracyclines, thereby reducing the cardiac toxicity of chemotherapy while maintaining efficacy.

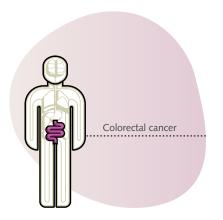
In non-small cell lung cancer, the SWOG 9504 study (South Western Oncology Group), presented at the American Society of Clinical Oncology (ASCO) congress in 2005, showed that Taxotere® used as consolidation chemotherapy achieved a 29% five-year survival rate, a result so far unique to Taxotere® in this setting.

Studies are ongoing in all settings (adjuvant, metastatic, HER 2-positive) to optimize therapeutic regimens with Taxotere®, such as sequential regimens which could offer an improved tolerability profile.

In prostate cancer, in view of Taxotere®'s recognized efficacy in the metastatic phase of the hormone-refractory form, studies are investigating its use in early hormone-sensitive stages of the disease, in conjunction with hormone therapy.

### In advanced metastatic gastric cancer,

Taxotere® has demonstrated its superiority over the standard regimen in terms of survival, while Eloxatin® has proved to be better tolerated than cisplatin in the same indication, for equivalent efficacy. As a result, development in gastric cancer is being pursued with a regimen combining Taxotere® and Eloxatin®.



# 1 million people affected every year worldwide

3rd
most common
Cancer
worldwide

### Colorectal cancer

Colorectal cancer is the third most common form of cancer worldwide, and is particularly prevalent in Western countries. In the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, more than 500,000 new cases are diagnosed every year.

### 80% of colorectal cancers diagnosed in the over-60 age-group

Colorectal cancer is relatively rare before the age of 45, but its frequency increases with age. In most cases, it is the result of a benign tumor, or polyp, becoming malignant. If undiagnosed and untreated, the tumor initially develops by invading the wall of the rectum or colon and then produces distant metastases, generally in the liver. 5 to 10% of colorectal cancers are hereditary in origin but behavioral factors such as diet, overeating and sedentary lifestyle can also be contributory.

### Treatment by a combination of surgery and chemotherapy

Treatment depends on the staging of the disease. In localized forms, the primary curative treatment is surgery, i.e. removal of the tumor and adjacent lymph nodes. Adjuvant chemotherapy is often recommended, however, to avoid the risk of recurrence. In more advanced metastatic forms of the disease, chemotherapy has demonstrated its efficacy and ability to prolong patient survival.

## Our therapeutic response colorectal cancer



## Reference treatment for colorectal cancer

Eloxatin® (oxaliplatin) is a new-generation platinum salt and currently the only treatment indicated for both metastatic colorectal cancer and early stage colon cancer.

The development of Eloxatin® in the treatment of colorectal cancer has led to major breakthroughs:

- An extension in median survival rate in patients in the metastatic stage receiving Eloxatin® as first-line treatment.
- Optimized surgical excision of liver metastases after Eloxatin®-based treatment, making it possible to treat more patients with initially unresectable liver metastases.

• A 21% to 23% reduction in the risk of recurrence in early stage colon cancer (stages II and III).

This remarkable efficacy coupled with a good safety profile makes Eloxatin® the agent of choice in the treatment of colon cancer at every stage of the disease.

Eloxatin®- a cornerstone chemotherapy for combination with the new "targeted" therapies

In the hope of further increasing survival rates, a development program is under way to study the association of Eloxatin® with targeted therapies based on new compounds; initial results are encouraging.

#### Main markets

Eloxatin® is in-licensed from Debiopharm and is marketed in almost 75 countries worldwide.



1,564
MILLION EUROS
2005 NET SALES

+30.6%
ON A COMPARABLE BASIS

## LIFECYCLEMANAGEMENT oxaliplatin

In accordance with its activity profile as determined by preclinical trials, Eloxatin® is under clinical investigation for other types of malignant tumors, in particular gastrointestinal tumors such as pancreatic or gastric cancer, but also in lung cancer, ovarian cancer, breast cancer and certain malignant hemopathies.

## OUR OTHER THERAPEUTIC RESPONSES Oncology

#### Fasturtec®/Elitek®

Prevention and treatment of tumor lysis syndrome

> Need to prevent and control the side effects of chemotherapy. The rapid and massive destruction of malignant cells during chemotherapy may give rise to serious and potentially fatal side effects, one of which is tumor lysis syndrome. Certain cancers, mainly certain forms of leukemia or lymphoma, are particularly sensitive to chemotherapy and are rapidly destroyed once treatment is initiated. This triggers a massive release of residual materials and cellular waste that may overwhelm the kidneys' capacity to eliminate them. One of the waste products, uric acid, is relatively insoluble and may precipitate as crystals in the kidneys, where it can lead to kidney failure and the need for dialysis. The situation can become immediately life-threatening and the successful completion of the anticancer regimen may be compromised.

> Fasturtec® is administered prior to and during chemotherapy to prevent tumor lysis syndrome.

Fasturtec® is a recombinant enzyme produced by genetic engineering. In less than four hours, it converts uric acid

into highly soluble allantoin which is easily eliminated in the urine, thereby preventing tumor lysis syndrome.

Sanofi-aventis 2005 Business Report

RESEARCH AND DEVELOPMENT

# Meeting tomorrow's needs

Cytotoxics are still considered by the scientific community as the cornerstone of cancer treatment. Sanofi-aventis is a leader in this field, and continues to focus research and development efforts on cytotoxic and anti-mitotic agents. The sanofi-aventis oncology portfolio also contains a broad spectrum of novel, "targeted" agents with a variety of mechanisms of action for treating cancer and/or cancer side effects, including bioreductive agents, anti-angiogenic and anti-vascular agents, receptor antagonists, monoclonal antibodies and cancer vaccines, as well as supportive care therapies.

### Phase III Head and neck cancer (ENT)

Tirapazamine (SR 259075)

Tirapazamine is an anti-cancer agent activated under hypoxic conditions to promote the destruction of resistant hypoxic cells. This innovative approach could lower the rate of recurrence in tumors associated with hypoxia. Phase III trials are evaluating tirapazamine in combination with cisplatin and radiotherapy for cancer of the head and neck. Exploratory studies in other tumors associated with hypoxia are also ongoing.

## Phase III Metastatic breast cancer after failure of taxane therapy XRP 9881

XRP 9881 is a new taxane derivative that has been designed to overcome resistance to the existing taxanes, docetaxel and paclitaxel. In phase II, XRP 9881 has proved to be active on metastatic breast tumors continuing to progress after taxane therapy. XRP 9881 has also been shown to cross the blood-brain barrier and could therefore be effective in the treatment of

## Phase III Chronic leukocytic leukemia

Alvocidib (HMR 1275)

Alvocidib is a novel cyclin-dependent kinase inhibitor (CDK). Development was interrupted by Aventis in 2004 due to lack of clinical efficacy of the tested

regimen.
A phase I/II study carried out under an agreement with the U.S. National Cancer Institute in patients with refractory chronic leukocytic leukemia in third-line treatment demonstrated a 43% partial response rate and overall survival of over 12 months when alvocidib was administered using a novel dosing regimen. Based on these results, development was reinitiated using the novel regimen in homotopical malignancies.

## Phase III Chemotherapy-induced neuropathy Xaliproden

Xaliproden is an orally administered neurotrophic agent whose activity in the prevention of oxaliplatin-induced neuropathy has been demonstrated chemotherapy-induced neuropathy and also in Alzheimer's disease.

### Phase IIb Prostate cancer SR 31747

SR 31747 is the first of a new family of anticancer agents called the sigma ligands. SR 31747 has a high affinity for sigma receptors (which are overexpressed by cancer cells) and has cytostatic and anti-proliferative properties. A phase II study is investigating its performance in the treatment of non-metastatic hormone-refractory prostate cancer.





# CENTRAL NERVOUS SYSTEM

## A group of complex diseases

Millions of people suffer from central nervous system (CNS) disorders. With an aging population, this figure is likely to increase.

Insomnia is without a doubt the most frequent of all CNS disorders. It afflicts some 150 million people worldwide and a large proportion of cases go untreated (73% in the United States, 65% in France).

Alzheimer's disease is now one of the most frequent severe cerebral disorders. Over 8 million people are reported to be suffering from some form of dementia in the world's seven leading markets (U.S., Japan, France, Germany, U.K., Italy, Spain). The risk increases with age, with Alzheimer's affecting 1% of the population in the 65-69 age group and 15% of people over-85. Clearly, with increasing life expectancy, the number of people affected will be rising in proportion.

Multiple sclerosis (MS) is characterized by the destruction of the myelin sheaths that surround the nerves of the central nervous system. The WHO estimates that it affects 2.5 million people worldwide.

**Schizophrenia**, a habitually chronic disease characterized by delirium and hallucinations or withdrawal and an inability to act. Schizophrenia affects some 1% of the world's population.

And also anxiety, Parkinson's disease and many other conditions.

## Diseases targeted by sanofi-aventis

- > Insomnia
- **E**pilepsy
- Multiple sclerosis
- Depression
- Anxiety
- > Alzheimer's disease
- > Smoking cessation
- > Parkinson's disease
- > Spinal cord injury
- Schizophrenia

## Insomnia

Insomnia is by far the most frequent sleep disorder, affecting between 20 and 30% of the population.

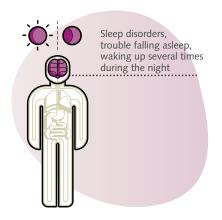
#### Consequences can be dramatic

They include: mood, attention, vigilance, and memory disorders as well as difficulty in concentrating. The consequences of insomnia are numerous and affect the quality of life of sufferers. They can also be the cause of serious events such as car crashes or industrial accidents in which insomniacs are two or three times more likely to be involved.

#### Occasional, transitory and chronic insomnia

Sleep regulating mechanisms are complex and the factors that may affect them are numerous. There are several types of insomnia.

Occasional or transitory insomnia has reversible causes, such as poor quality lifestyle, noise, setbacks or grief, and can last for several days or up to two or three weeks. It disappears with the cause that brought it on. Chronic insomnia persists after the cause has disappeared. The cause may be somatic (sleep apnea, ingestion of certain substances, psychosis or anxiety disorders). Left untreated, occasional or transitory insomnia may become chronic, which significantly increases the risk of developing a state of depression.



Nearly
150 MILLION
people suffer from insomnia

A significant number of them are not treated: 73% in the US

65% in France

64% in Japan

(Harris Medical International study 2003)

## Our therapeutic response the treatment of insomnia



Ambien®/Myslee®/Stilnox®

zolpidem

#### The world's leading hypnotic\*

Zolpidem is quick to act and produces a quality of sleep that is close to natural sleep without the side effects which generally characterize hypnotics. Its effects persist for a minimum of six hours and it is usually well-tolerated. In addition, the risk of dependency is low when the recommended doses and treatment times are followed.

Today, zolpidem is the only hypnotic to have demonstrated its efficacy when

used "as needed" through a program of eight studies involving 6,000 patients. The major advantage of this mode of administration is that patients suffering occasional insomnia can avoid taking a hypnotic on a regular basis.

Since its launch in 1988, zolpidem has been investigated in 160 studies involving 80,000 patients to demonstrate its efficacy and tolerance.



1,519 MILLION EUROS 2005 SALES

+10.6%
ON A COMPARABLE BASIS

<sup>\*</sup> Source: IMS

## LIFECYCLEMANAGEMENT zolpidem

In adults, a study involving chronically insomniac patients treated with zolpidem MR for approximately 6 months, 3-7 days per week, has just been completed and results will be available at the end of the year.

Several studies are also ongoing in the United States to demonstrate the product's efficacy for patients suffering from insomnia as a result of depression or generalized anxiety. A clinical trial was also launched this year for children suffering from insomnia linked to hyperactivity disorders. Results are expected by the end of 2006.

It has been better studied than any other hypnotic in the world and the experience and feedback provided by 14 billion nights of treatment is exceptional.

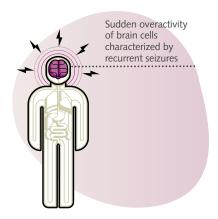
#### A better quality of sleep

In order to improve sleep continuity without residual effects upon wakening, sanofi-aventis has developed a modified-release formulation for zolpidem. The two main studies of zolpidem MR have demonstrated the compound's sleep continuity properties during the second part of the night, thus ensuring excellent sleep quality throughout the night. These results have been the basis for launching the drug in the United States in September 2005 under the brand name of Ambien CR™. A clinical development program has also been initiated in Japan and results are expected in 2008.



#### Main markets

Zolpidem is now sold in over 100 countries. Zolpidem is the market leader in France, in the United States where it is marketed as Ambien®, and in Japan, where it is sold under the brand name Myslee®. (Source: IMS, Sales at end 2005. GERS for France).



Approximately 1% of the world's population is concerned

## **Epilepsy**

Epilepsy is a frequent, chronic neurological disorder affecting approximately 1% of the world's population, particularly children under the age of 10 and adults over 65.

#### A better understanding of the disorder

Epilepsy has always caused curiosity or alarm. Thanks to progress in genetics and new functional cerebral imaging techniques, a better understanding of the disease is emerging. Today, in 70% to 80% of newly diagnosed cases, epileptic seizures can be kept under control.

#### Considerable physical, psychological and social repercussions

Epilepsy is characterized by repeated spontaneous seizures resulting from abnormally high neuronal discharge. Patients and their families suffer from considerable physical, psychological and social consequences due to repeated seizures which make daily life difficult. Early diagnosis and appropriate care are the keys to avoiding distress and enabling patients to lead normal lives.

# Our therapeutic response treatment of epilepsy and bipolar disorders\*



## Depakine®/Ergenyl®/Epilim®/ Deprakine®

sodium valproate

## The reference treatment for the past 38 years

Prescribed for over 38 years, sodium valproate is a broad-spectrum anti-epileptic viewed as a reference treatment throughout the world. Numerous clinical studies and many years of experience have demonstrated its efficacy for all kinds of epileptic seizures and syndromes. Generally well-tolerated, it does not cause paradoxical aggravation of seizures, unlike other anti-epileptics.

## A broad range of formulations for all types of patients

Sodium valproate is available in a large variety of formulations (syrups, soluble drinks, injections, gastro-resistant tablets and Chrono®, an extended-release tablet) in order to cover the full range of patient needs.

Depakine® Chronosphere®, a new sustained-release sachet formulation, has been approved in several European countries. It was launched in Austria in October 2004 and in France and Germany in 2005. This new formulation is easier to use for children (it was the first extended-release pediatric form of Depakine®) and

for the elderly or adults who have difficulty swallowing. Product launches are planned in most European countries.

#### Treatment of bipolar disorders

Sanofi-aventis has also demonstrated the role this medicine can play in bipolar disorders\* which affect approximately 2% of the world's population and are characterized by alternate manic and depressive episodes. In 2005, Depakine® Chrono® and Chronosphere® were approved for this indication in several European countries.

#### Main markets

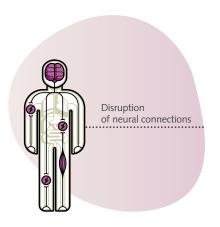
Sodium valproate is marketed in over 100 countries, including the United States, where Abbott holds the license.

318
MILLION EUROS
2005 SALES

+4.6%
ON A COMPARABLE BASIS

<sup>\*</sup> The bipolar disorders indication has been obtained for most countries.





2.5 million people affected worldwide

## Multiple sclerosis

An insidious disease, multiple sclerosis evolves over a period of several decades and can culminate in a total loss of autonomy. The WHO estimates global prevalence at 2.5 million people.

#### Young adults are the main sufferers

Multiple sclerosis is a chronic inflammatory disease that affects the white matter in the central nervous system. The main symptoms are motor, sensory and visual. Onset is typically in early adulthood (on average around the age of 30) and the disease is much more common in women. It evolves over several decades and is characterized by the gradual development of disability, varying from one patient to another, but possibly culminating in a total loss of autonomy.

#### An insidious disease

The exact causes of multiple sclerosis are still largely unknown. There is progressive destruction of myelin, leading to the appearance of demyelinated plaques on certain neurons and subsequent degeneration. Multiple sclerosis evolves insidiously either as a series of relapses punctuated by almost complete recovery episodes, which is the relapsing-remitting form of MS, or in phases of primary or secondary continuous progression from onset.

## Our therapeutic response

A reduction in the frequency of relapses in ambulatory (able to walk unaided) patients with relapsing-remitting multiple sclerosis characterized by at least two relapses in the last two years

902 MILLION EUROS 2005 SALES

+24.1%
ON A COMPARABLE BASIS

Copaxone®

glatiramer acetate

Copaxone® (glatiramer acetate) is an immunomodulator indicated for reducing the frequency of exacerbations in patients with relapsing-remitting multiple sclerosis (RRMS). This intercritical treatment is characterized by an original and specific action on RRMS. Studies have demonstrated that Copaxone®'s efficacy against relapses is twice that of placebo after a two-year period of treatment. Clinical efficacy over ten years has also been evidenced regarding the reduction of relapses and

the progression of disability. A significant effect on lesions was confirmed by magnetic resonance imaging (MRI).

Copaxone® was launched in the United States in 1997 and in Europe between 2000 and 2002. It is licensed by Teva to sanofi-aventis and commercialized through an alliance with Teva.

In 2004, in Europe, the two marketing partners launched the prefilled syringe, a new formulation that offers easier administration and improved patient comfort.

#### Main markets

Over 90,000 patients around the world are treated with Copaxone®. The three leading markets for Copaxone® are the United States, Germany and Canada. (Source: IMS, Sales at end 2005).

A phase III clinical trial, PreCise, is ongoing for early-stage multiple sclerosis.



## OUR OTHER RESPONSES therapeutic

The sanofi-aventis portfolio of medicines for the central nervous system also includes some established treatments such as **Solian®** (amisulpride), an anti-psychotic indicated for schizophrenia, **Rilutek®** (riluzole), the only drug indicated for amyotrophic lateral sclerosis (ALS) and **Tranxene®** (lorazepate), a reference anxiolytic.

**Solian®** is marketed in the main European markets and 60 countries worldwide. **Solian®** continues to be launched in new markets around the world.

RESEARCH AND DEVELOPMENT

# Meeting tomorrow's need

Sanofi-aventis has one of the most extensive and promising portfolios in this particularly complex therapeutic area where intervention must take place very early in the pathological process if it is to influence disease progression and at least slow it down if it cannot be halted. To this end, sanofi-aventis is multiplying and diversifying its pharmacological and scientific approach in two major areas: psychiatric disorders and neurodegenerative diseases.

## Phase III Depression SR 58611

SR 58611 is a beta-3 adrenergic receptor agonist. This substance stimulates neuronal activity in a specific region of the prefrontal cortex and could give rise to a new class of anti-depressants. In a phase II trial in patients suffering from severe depression with melancholic features, SR 58611 was observed to be superior to fluoxetine, a reference treatment, and was well tolerated. A phase III program in depression is ongoing and a phase III clinical program in general anxiety disorder started in 2005.

## Phase III Depression

Saredutant (SR 48968)

Saredutant is an NK2 receptor antagonist developed for the treatment of major depressive disorders. Patient inclusion for the two first phase III clinical trials has been completed.

## Phase III Multiple sclerosis

Triflunomide (HMR 1726)

Teriflunomide is a dihydro-orotate dehydrogenase inhibitor effective when administered orally. An international phase III development program is ongoing.

## Phase III Alzheimer's disease Xaliproden (SR 57746)

Xaliproden is a non-peptide compound that activates the synthesis of endogenous neurotrophins. Two phase III studies in Alzheimer's disease are ongoing. Xaliproden is also studied in the oncology area (see oncology).

## Phase IIb Alzheimer's disease, Parkinson's disease SR 57667

SR 57667, like xaliproden, is a non-peptide compound that activates the synthesis of endogenous neurotrophins. One phase II study is ongoing in Alzheimer's disease. Two phase II studies are ongoing in Parkinson's disease.

## Phase III Smoking cessation SSR 591813

This nicotinic partial agonist is being developed for smoking cessation. Phase IIb results of showed a clear evidence of a dose response effect. Treatment with SSR 591813 was associated with a greater percentage of subjects who achieved the primary efficacy endpoint (4-week prolonged abstinence) compared to placebo.

### Phase III Sleep disorders

Eplivanserin (SR 46349) 5HT<sub>2A</sub> receptor antagonist

The drug is being developed for the treatment of insomnia characterized by difficulties maintaining sleep (sleep maintenance insomnia). A worldwide phase III program started in November 2005 in patients with chronic primary insomnia.

## Phase IIb Sleep disorders

M 100907 5HT<sub>2A</sub> receptor antagonist

This second 5HT<sub>2A</sub> receptor antagonist is being developed for the treatment of sleep maintenance insomnia. The phase IIb program is now completed.

## Phase IIa Spinal cord injury HP 184

HP 184 is a potassium channel and use-dependent sodium channel blocker. A first phase II study showed improvement in ASIA Total Motor Score (a measure of sensory and motor function impairment developed by the American Spinal Injury Association) and confirmed the tolerability in patients with spinal cord injury. A second phase II study is ongoing aiming to treat 240 patients worldwide.





# INTERNAL MEDICINE

## Very diverse and common diseases

#### **Asthma**

100 to 150 million people around the world suffer from asthma, and the numbers continue to rise. Worldwide, the costs associated with asthma are estimated to outstrip those of tuberculosis and AIDS combined. In France, asthma affects over 2.5 billion people, one third of them children<sup>(1)</sup>.

### **Respiratory tract infections**

Upper respiratory tract infections (RTIs) such as sinusitis, tonsillitis and pharyngitis and lower RTIs such as bronchitis or community-acquired pneumonia are the most common infectious diseases.

The pathogens responsible for most of these infections, *Streptococcus pneumoniae* and *Haemophilus influenzae*, have developed resistance to many antibiotics.

#### Rheumatoid arthritis

Rheumatoid arthritis (RA) is an autoimmune disease, a common form of arthritis that causes inflammation of the synovial membrane in joints and/or other internal organs. An estimated 1% of the world population is affected by RA, and one in three patients will probably suffer severe functional disability after 20 years of the disease.

Estimated prevalence in Europe is 1.75 million patients in 2008<sup>(2)</sup>.

## Urology: benign prostatic hyperplasia (BPH)

Benign prostatic hyperplasia (non-cancerous enlargement of the prostate gland) is responsible for significant disruption of everyday life, frequent waking at night, fatigue and depressive moods. The pathology may also be complicated by urinary infections, sexual dysfunction and acute urinary retention.

### **Osteoporosis**

Osteoporosis is a diffuse skeletal disease, characterized by decreased bone mass and changes in the microarchitecture of bone tissue, increasing bone fragility and the risk of fracture<sup>(3)</sup>.

## Diseases targeted by sanofi-aventis

- > Bacterial, viral and parasitic infections
- > Rheumatoid arthritis
- Osteoporosis
- Pain
- **Urology**
- Chronic obstructive pulmonary disease (COPD)
- Allergy
- > Inflammation
- > Urinary incontinence

<sup>(1)</sup> La Fondation pour la Recherche médicale.

<sup>(2)</sup> Data Monitor report.

<sup>(3)</sup> Consensus Development Conference. Diagnosis, prophylaxis and treatment of osteoporosis. Am J Med, 1993; 94:646-50.

Nasal congestion

## **Allergy**

Allergies are some of the most common disorders in the world, affecting around 500 million sufferers. Allergies are found all over the world, but observers nonetheless note a more rapid increase in the number of cases in emerging countries.

These disorders, whether chronic or allergic, often have an adverse effect on the everyday life of sufferers. In children, there is also evidence of diminished learning capacity and academic attainments.

The economic impact of these disorders is too substantial to be overlooked.



Allergy is an excessive reaction or hypersensitivity of the body's immune system to certain specific substances (allergens) such as pollen, molds, house dust mites, animal fur/dander and insect stings. When an allergic subject is exposed to a specific allergen, the immune system produces antibodies (lgE or immunoglobulin E antibodies) which act as a signal to the body's defenses.

This inflammatory reaction produces a number of symptoms: sneezing, stuffy nose, cough, watery eyes, itching skin or rash.

#### Changing lifestyles implicated

While the causes are many, no single cause stands out. Pollution is often cited, but so too is excessive hygiene, unwarranted use of antibiotics, new eating habits, etc. Numerous studies have underlined the fact that asthma and allergic disorders are more prevalent in heavily industrialized western countries than in developing countries with predominantly rural populations.

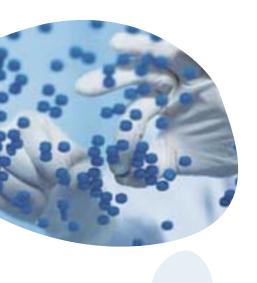


# Our therapeutic response treatment of symptoms associated with seasonal allergic rhinitis (SAR) and chronic idiopathic urticaria (CIU)



Allegra® (fexofenadine hydrochloride) is a powerful, effective and non-sedating long-lasting prescription antihistamine (to be taken once or twice daily) for the treatment of seasonal allergic rhinitis (hay fever) and chronic idiopathic urticaria (a skin disorder familiarly known as hives). It provides effective allergy relief without inducing drowsiness. 1,345 MILLION EUROS 2005 SALES

**-9.1%**ON A COMPARABLE BASIS



Our three main markets for Allegra® in 2005 were the United States (number 1), Japan (number 1) and Australia (number 1).

(Source: IMS, sales through all distribution channels, December 2005). Sanofi-aventis also markets Allegra-D® 12 Hour, a combination of Allegra® and an extended-release decongestant, for effective, non-sedating relief of seasonal allergy symptoms including nasal congestion.

July 2005 saw the launch of Allegra-D® 24 Hour, another association of Allegra® and a decongestant but to be taken in a single, once-daily dose.

In September 2005, the FDA approved an NDA filed for a 180 mg once-daily dosage for the treatment of chronic idiopathic urticaria in adults. An NDA for the pediatric indication was filed in Japan in February 2004 and two new

pediatric forms are also under development: a 30 mg orodispersible tablet and a 6 mg/ml oral suspension. An NDA for the pediatric suspension in the United States was filed in December 2005.

The three main markets for Allegra-D<sup>®</sup> 12 Hour and Allegra-D<sup>®</sup> 24 Hour are the United States, Brazil and Mexico.

(Source: IMS, sales through all distribution channels, December 2005).

In September 2005, Barr Laboratories and Teva Pharmaceuticals jointly launched a generic version of fexofenadine hydrochloride in 180 mg, 60 mg and 30 mg doses, in competition with Allegra®. Sanofi-aventis responded by authorizing Prasco Pharmaceuticals to launch an approved generic version of fexofenadine. In December 2005, the generic product marketed by Prasco represented over 30% of fexofenadine prescriptions for the month (IMS NPA).

# Our therapeutic response treatment of the symptoms associated with seasonal and perennial allergic rhinitis in adults and children 6 years of age and older



## Nasacort®

triamcinolone acetonide

278
MILLION EUROS
2005 SALES

-2.1%
ON A COMPARABLE BASIS

Nasacort® (triamcinolone acetonide)
AQ Spray is a nasal spray containing
an unscented aqueous solution, and
is indicated in the treatment of the
nasal symptoms of seasonal (intermittent) and perennial (persistent)
allergic rhinitis in adults and children of six years of age and over.

In April 2004, the FDA approved Nasacort® HFA, the first intranasal corticoid dry-aerosol formulation approved in the United States to contain hydrofluoroalkane (HFA) rather than chlorofluorocarbons (CFCs).

Nasacort® HFA Aerosol offers a new option for physicians and patients seeking a dry-aerosol formulation for the management of nasal allergy symptoms.

#### Main markets

Nasacort® AQ Spray is available in 44 countries around the world. Its main markets are the United States, France and Canada.

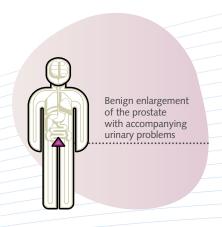
# Benign prostatic hyperplasia

Benign prostatic hyperplasia is the most frequent disorder affecting men over 50. As the name implies, it is benign and should not be confused with prostate cancer.

Benign prostatic hyperplasia leads to an enlargement in the volume of the prostate, a small gland lying below the bladder, close to the male urinary and genital systems. As it grows in size, the prostate compresses the urethra, the canal that evacuates urine out of the bladder, impeding the flow. Left untreated, the condition may worsen and in the long term cause severe complications such as acute urinary retention, a complete and extremely painful blockage of the urethra for which urinary catherization is required, and frequently surgery.

#### The disorder is under-diagnosed and under-treated.

An inescapable consequence of aging, this condition causes considerable urinary discomfort to 20% of men in their fifties and over 40% of men after the age of 70. However, it is still under-diagnosed and under-treated. A recent survey involving 14,000 men over the age of 50 in seven countries revealed that only 19% of men with moderate symptoms were being treated and only 43% of those with severe symptoms. In addition, men over 50 suffering from symptomatic benign prostatic hyperplasia are four times more at risk of developing sexual dysfunction, an area in which there is growing demand for treatment.



55 million people affected

1 of every 2 men over 70

# Our therapeutic response treatment of benign prostatic hyperplasia and of acute urinary retention



Xatral<sup>®</sup>/Uroxatral<sup>®</sup>/Benestan<sup>®</sup>/Dalfaz<sup>®</sup>

alfuzosin

#### **Immediate efficacy**

Xatral® (alfuzosin) belongs to the alpha1-blocker class of medications, and was the first product of the class to be indicated solely and specifically for treatment of the symptoms of benign prostatic hyperplasia (BPH), as well as the first marketed product capable of acting selectively on the urinary system. Active from the first dose,

it provides rapid and lasting symptom relief, improving patient quality of life. It has also demonstrated good cardiovascular tolerability in particular in elderly and hypertensive patients. Xatral®'s good cardiovascular safety profile was also confirmed in combination with a phosphodiesterase type 5 inhibitor (PDE5), a specific treatment

328
MILLION EUROS
2005 SALES

+18.4%
ON A COMPARABLE BASIS

for erectile dysfunction (results communicated in 2005 and now in the process of publication).

#### **New indications**

Xatral® has demonstrated a beneficial effect on the clinical progression of benign prostatic hyperplasia in a two-year controlled study *versus* placebo which has just been published.

Benign prostatic hyperplasia is known to be linked with sexual dysfunction (erectile and ejaculatory dysfunction). Xatral® does not impair sexual function in patients with urinary symptoms and is well-tolerated when used in combination with specific treatment for erectile dysfunction.

#### **Optimizing formulations**

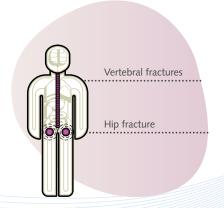
Since Xatral® was launched in 1988, sanofi-aventis has worked constantly on developing new formulations.

The new once-daily formulation of Xatral® (branded Uroxatral® in the United States) has now been registered in over 90 countries.

Phase IIb clinical trials of the once-daily formulation are under way for the treatment of BPH in Japan and phase III trials will begin in 2006.

#### Main markets

Most of Xatral® sales are in Europe where it is constantly reinforcing its second ranking position on the market for alpha-blockers. Xatral® leads in France with a 25.7% share of the market (IMS MATDec05) and ranks second in Italy. Launched more recently in the United States, it now holds fourth place.



# (1) World Health Organization. Prevention and management of osteoporosis. WHO Technical Report Series 921. Geneva: World Health Organization 2003.

- (2) World Health Organization. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: technical report series 843. Geneva: World Health Organization, 1994.
- (3) Tosteson A, Solomon D, King A et al. (1078) Projections of Osteoporosis Fractures and Costs by Skeletal Site in the USA. Abstracts of the 27th Business Meeting of the American Society for Bone and Mineral Research.
- (4) Melton L.J, Chrischilles E.A, Cooper C, et al. *Perspective. How many women have osteoporosis?* J Bone Miner Res 1992; 7: 1005-10.
- (5) Kanis J.A. *Diagnosis of osteoporosis and assessment of fracture risk*. Lancet 2002; 359: 1929-36.

## Osteoporosis

In Europe, the United States and Japan, some 75 million people suffer from osteoporosis<sup>(1)</sup>, a condition characterized by a reduction in bone density and quality weakening the skeleton and increasing the risk of fracture<sup>(2)</sup>.

Osteoporosis is often described as a silent disease. There are no visible symptoms until a bone is fractured. The fact that bones become thinner and more fragile goes unnoticed. The frequency of osteoporosis-related fractures increases with age. This type of fracture is less frequent in men since they naturally have greater bone mass and the process of age-linked osteopenia (bone loss) is slower in men<sup>(1)</sup>.

In the United States alone, 73% of osteoporosis fractures diagnosed in women over 50 affect non-vertebral sites and represent 94% of total expenditure<sup>(3)</sup> linked to osteoporosis fracture.

In fact, the risk for a 50 year old woman of falling victim to osteoporosis fracture at some time in her life is approximately 40%<sup>(4)</sup>—identical to the risk a woman has of developing cardiovascular disease<sup>(5)</sup> in the course of her lifetime.

# Our therapeutic response treatment and prevention of postmenopausal osteoporosis, treatment of Paget's disease

364 MILLION EUROS 2005 SALES

+23.8%
ON A COMPARABLE BASIS



Actonel® belongs to a class of medicines called bisphosphonates. Bone is made up of constantly renewed living tissue, older bone being replaced by new bone. In osteoporosis, the cells responsible for bone resorption become more numerous than those ensuring bone renewal. As a result, with time bones become less solid and more fragile and more vulnerable to fracture. Actonel® makes bones less fracture-prone by inhibiting the action of cells involved in bone degradation and loss. Actonel® is also known as Optinate® in Italy and Scandinavia and Acrel® in Spain.

Actonel® 35 mg once-a-week is indicated for:

- the treatment of post-menopausal osteoporosis to reduce the risk of vertebral fracture;
- the treatment of established post-menopausal osteoporosis to reduce the risk of hip fracture.

With the same indications as Actonel<sup>®</sup> 35 mg, daily Actonel<sup>®</sup> 5 mg is also indicated for:

- the prevention of osteoporosis in postmenopausal women at increased risk;
- maintaining or increasing bone mass in post-menopausal women continuing systemic and prolonged (over 3 months) glucocorticoid treatment (daily dosage of 7.5 mg or more of prednisone or equivalent).

#### Main markets

Currently approved in over 90 countries worldwide, Actonel® is marketed by The Alliance for Better Bone Health, created in May 1997 by Procter & Gamble and sanofi-aventis. The Alliance promotes bone health and increased patient awareness of the risk of disease through a number of activities designed to help doctors and patients the world over.

In July 2005, The Alliance for Better Bone Health announced that the Food and Drug Administration (FDA) had approved the use of Actonel® with calcium (combining risedronate sodium and calcium carbonate tablets) the first prescription medicine to combine Actonel® tablets and calcium tablets in the same package. This formulation is also available in several other countries, for example Germany, Sweden and the Netherlands.

## OUR OTHER THERAPEUTIC

## responses

Sanofi-aventis has been involved in antibiotics research and development from the outset and offers a vast range of solutions to medical problems. The range of classic antibiotics includes products as varied as Claforan®, Ketek®, Oflocet®/ Tarivid®, Pyostacin®, Rovamycin®, Targocid® and Tavanic®.

Sanofi-aventis also plays a role in the fight against tuberculosis, one of the major public health problems in some emerging markets with **Rifadin®**, **Rifater®** and **Rifinah®**.

As regards pain relief, sanofi-aventis has a very complete range of analgesics represented by **Doliprane®**, **Profenid®**, **Novalgine®**, and **Aspegic®** or again **NoSpa®**, an antispasmodic much in demand in Central and Eastern Europe.

The Group has a range of products for gastroenterological treatment, for example **Ercefuryl®** in Europe, Africa, Asia and the Middle East, **Enterogermina®**, **Magnesia San Pellegrino®** in Italy and **Pepsamar®** in Latin America.

In the field of respiratory conditions, Rhinathiol® is particularly prominent on the market for expectorants in Europe, Africa, the Middle East and Asia. Also noteworthy are Maxilase® in France, Portugal and some African countries, Histiacil® in Mexico, Pax® in Columbia and Physiomer® in France and Italy.

Finally, sanofi-aventis sells a large number of medicines and products for the management of family health such as **Lactacyd®** (gynecology), **Mitosyl®** (dermatology) and vitamins and minerals, for example **Magné B6®** and **Omnivit®**.

RESEARCH AND DEVELOPMENT

# Meeting tomorrow's needs

Sanofi-aventis R&D is developing innovative approaches in the field of inflammation, with compounds targeting a vast range of mechanisms: immunomodulators, chemical mediator receptor antagonists, cytokine inhibitors, etc.

#### TREATMENT FOR ASTHMA

### Submitted in the United States

Alvesco® (ciclesonide, XRP 1526)

The Alvesco® metered-dose inhaler is being developed jointly with our partner Altana Pharma.

Sanofi-aventis is conducting clinical studies to respond to the FDA's questions from review of the Alvesco® NDA, and a response to the approvable letter is planned for submission in the first quarter of 2007.

#### Phase IIb

AVE 2635 (ciclesonide/formoterol)

Clinical studies are ongoing with the dry-powder inhaler combination of ciclesonide and formoterol. Phase IIb studies will be completed in the second quarter of 2006.

## Phase III Dilutional hyponatremia

Satavaptan (SR 121463, vasopressin V2 receptor antagonist)

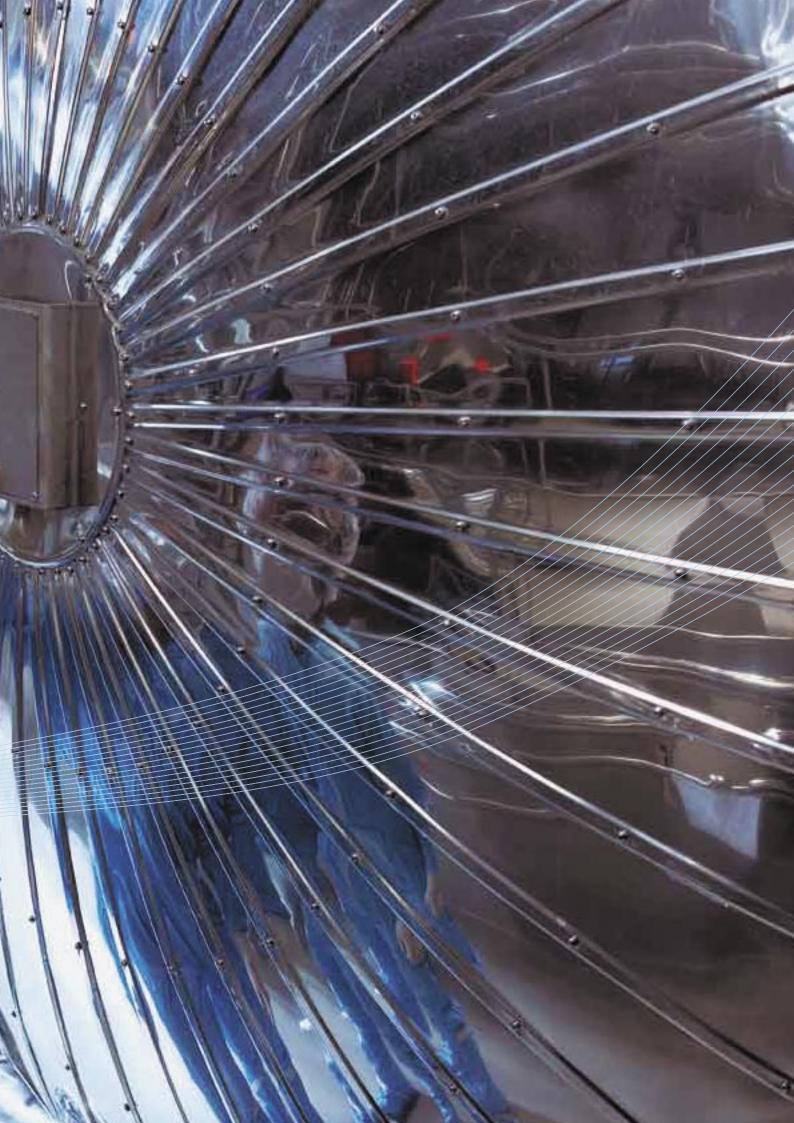
This compound is a pure aquaretic developed for the treatment of dilutional hyponatremia.

The double blind part of the phase III program in patients with the syndrome of inappropriate antidiuretic hormone secretion (SIADH), showing a rapid, statistically significant and clinically relevant correction of hyponatremia has now been completed.

In addition, based on the positive results of the phase IIb program in cirrhotic patients which indicated that the product in association with a standard treatment produced a better control of ascites, through a decrease in weight or a reduction in paracentesis (removal of fluid), a phase III program is to be implemented in 2006.







# VACCINES

## **Every year vaccines:**

- save the lives of 3 million children across the world,
- protect 750,000 children from the devastating consequences of disease.

Vaccines are our best weapons in the fight against infectious disease. According to the World Health Organization, vaccines annually save 3 million lives worldwide and protect three-quarters of a million others from the destructive consequences of disease. Mass vaccination programs have led to the eradication of smallpox and have reduced the incidence of typhoid and diphtheria in much of the world. Vaccination campaigns against poliomyelitis have reduced its incidence by 99.9% since 1988 and the eradication of wild poliovirus may soon be at hand. However, infectious diseases are still responsible for almost a third of all deaths worldwide. Two million children under five years of age die every year from vaccinepreventable diseases because they do not have access to vaccines.

Vaccination can currently protect against 26 infectious diseases. However, we do not yet have vaccines against major diseases such as AIDS, dengue fever or malaria. That is why hundreds of research projects are underway throughout the world to develop vaccines against deadly viruses, bacteria and parasites.



## **Vaccination**

#### Long lasting protection

Vaccination consists of exposing the body to a live, attenuated (i.e. killed or inactivated) pathogen in order to stimulate a specific immune response and induce protection against a disease.

#### New avenues of research

Developments in molecular biology have provided new tools to identify novel antigens for inclusion in vaccines and created new production methods. For example, antigens can be produced in recombinant bacteria or yeast (e.g. Hepatitis B vaccine) and harmless viruses or bacteria can be used as antigenic vectors.

Additionally, new ways to administer vaccines are being studied that could result in the end of injections resulting in less patient discomfort and potentially increasing vaccine efficacy.



## Our vaccine solutions

Sanofi pasteur, the vaccines division of the sanofi-aventis Group, offers the largest range of vaccines in the world, protecting more than 500 million people every year from 20 infectious diseases.

2,062 MILLION EUROS 2005 SALES

+26.9% ON A COMPARABLE BASIS



## Fluzone® and Vaxigrip®/Mutagrip®

Influenza vaccines

Sanofi pasteur is the world leader with more than 45% market share. The worldwide demand for vaccines is expected to increase as government policies become more focused on increasing immunization rates.

In 2005, sanofi-aventis significantly invested to increase its global flu vaccine production capacity. The U.S. facility has doubled in size to respond to the everincreasing demand in the U.S., and the capacity of the Val-de-Reuil facility in France has been increased thanks to a new packaging unit.

Over the last few years, countries such as China, Korea and Mexico have experienced strong growth, which is expected to continue. In April 2005, sanofi pasteur signed a five-year contract with the U.S. Government to accelerate the development of a new production process based on cell culture, including developing plans for a cell culture flu vaccine production unit in the U.S.



Sanofi pasteur offers the first and only quadrivalent, conjugated vaccine available against invasive meningococcal disease in the U.S. This vaccine, Menactra®, protects against the four most common serogroups (A, C, Y, W-135) of *Neisseria meningitidis*, the bacteria responsible for the most serious forms of meningitis. Menactra® offers enhanced protection via the conjugation technique: antigenic bacteria are linked to a protein, which is recognized more easily by the immune system and allows for a stronger response.

In January 2005, the FDA licensed Menactra® for use in people 11 to 55 years of age. One month later, the ACIP

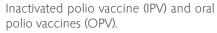
(Advisory Committee on Immunization Practices) recommended the vaccination of pre-adolescents aged 11-12 years, adolescents entering high school and college freshmen living in dormitories. Sanofi pasteur has made an additional submission to the FDA to expand the use of the vaccine to children aged 2 to 10 years. In 2005, it also submitted a registration request in Canada and similar requests are expected to be made in various parts of the world.

Meningococcal meningitis vaccines are expected to contribute significantly to the growth of sanofi pasteur, as recommendations for their use is extended to new segments of the population.



## IPOL® and Imovax® Polio

Poliomyelitis vaccines



Sanofi pasteur is one of the world's leading producers of injectable polio vaccines and is a privileged partner in the WHO and UNICEF's worldwide polio eradication program. In March 2005, sanofi pasteur developed a new monovalent polio vaccine against

type 1 polio, which is the remaining wild-type virus circulating in a handful of countries, as part of a new WHO strategy for eradication. The French and Egyptian regulatory agencies (AFSSAPS and NODCAR) licensed this vaccine, M-OPV1, for use in vaccination campaigns in Egypt, which was declared polio-free less than a year later.





## Daptacel®, Pentacel™, Pediacel®

Pediatric combination vaccines

These vaccines are designed to meet the needs of a wide range of vaccination programs in place across the world. These products all contain an acellular pertussis valence. Daptacel® is a trivalent vaccine that protects against pertussis (whooping cough), diphtheria and tetanus. It was launched in the U.S. in 2002. Pentacel<sup>TM</sup>, which protects

against five diseases (pertussis, diphtheria, tetanus, poliomyelitis and *Haemophilus influenzae* type b, sometimes called Hib disease), is currently licensed in nine countries. In Canada, where it has been available since 1997, it forms part of the routine childhood immunization program. Pediacel® has been licensed in the U.K. since 2004 and in several other European countries since 2005.



## Adacel™, Decavac®

Booster vaccines for adults and adolescents

There has been a worldwide resurgence of pertussis, affecting both adolescents and adults. This has been accompanied by an increased awareness of the dangers inherent in diseases which can be prevented by vaccination, and has driven sales of this product category over recent years

Adacel<sup>TM</sup>, the first trivalent booster vaccine protecting against diphtheria, tetanus and pertussis, has become the reference for booster vaccination against pertussis in Canada, where the majority of provinces have initiated systematic vaccination

programs for adolescents. This vaccine not only prevents disease in adults and adolescents, but also reduces the risk of transmission to newborn babies, who have not yet reached the age for vaccination or who have not yet completed the full vaccination program and are more at risk of contracting the disease. Adacel™ was licensed in the U.S. in 2005. Moreover, Decavac®, a preservative-free booster vaccine for diphtheria and tetanus has experienced strong growth on the U.S. market.





## Vaccines against hepatitis A, typhoid, rabies, yellow fever, Japanese encephalitis, cholera, and anti-venoms

Vaccines for travelers and for endemic areas

Thanks to a wide range of vaccines for travelers and people living in countries where these diseases are endemic, sanofi pasteur is the leader in most market segments in a sector that shows sustained growth.

The distribution of these vaccines in endemic areas in developing countries is ensured in partnership with international organizations such as UNICEF.

## **MAIN MARKETS**

Sanofi pasteur is present in more than 150 countries, enabling it to address the health needs of 80% of the world's population:

- North America (Canada & U.S.),
- Europe: presence in 19 countries through sanofi pasteur MSD,
   a joint venture with Merck & Co., Inc.,
- Internationally funded public markets,
- Emerging markets.

RESEARCH AND DEVELOPMENT

# Meeting tomorrow's needs

Sanofi pasteur is focused on vaccines for every stage of life, working in two key research areas: new vaccine combinations that will protect against several diseases simultaneously, thus reducing the number of injections, and continuous efforts to improve the effectiveness and tolerability of existing vaccines.

### World leader in influenza vaccines

Sanofi pasteur has developed a new pediatric flu vaccine which does not contain a preservative. Other vaccine formulations, designed to increase their effectiveness in the elderly, will go into phase III trials in 2006. A microinjection technique developed by Becton Dickinson has been adapted for use with influenza vaccine, with phase III trials beginning in 2006.

The company has also been exploring new production techniques for influenza vaccine, which traditionally has been produced with egg embryos, using cell cultures. The first clinical trials of the cell culture vaccine candidate will begin in 2006.

## A major role in flu pandemic preparedness

Sanofi pasteur has taken a leadership role in pandemic influenza vaccine development, developing the first prototype H5N1 vaccines produced in the U.S. and Europe. In 2005, a clinical trial conducted in France comparing pre-pandemic H5N1 vaccine candidates with and without adjuvants, demonstrated safety and an immune response in a significant number of volunteers, consistent with requirements of regulatory agencies for licensure of seasonal influenza vaccine.

for licensure of seasonal influenza vaccine.

This research will continue in 2006, using vaccine produced on an industrial scale, with the goal of determining the optimal dosage to provide protection and allow the greatest number of doses to be produced, should a pandemic be declared. The data will be submitted as part of the company's core prototype vaccine dossier to the European Medicines Agency (EMEA.)

The core dossier has been developed in strict accordance with the EMEA guidelines. This process is expected to reduce the time necessary for approval of a pandemic vaccine in Europe once a strain is identified and a pandemic is declared.

## Meningitis and Pneumococcal disease

#### Meningococcal meningitis

Sanofi pasteur is seeking to expand the indications for Menactra®, its quadrivalent (A, C, Y, W-135) vaccine. The Group is developing new formulations for the administration of this conjugated vaccine to infants. In addition, clinical trials began in 2005 for a candidate vaccine, using an innovative approach against Neisseria meningitidis serogroup B.

#### Pneumococcal disease

Streptococcus pneumoniae is the leading etiological agent of severe infections such as pneumonia, septicemia, meningitis and otitis media, and causes over three million deaths per year worldwide, of which one million are children. Sanofi pasteur has two projects in its pneumococcal program, both of which are expected to enter the clinic before the end of 2006.

## Pediatric combination vaccines and booster vaccines for adults and adolescents

Phase II clinical trials have been completed with a hexavalent pediatric vaccine, which will protect against diphtheria, tetanus, pertussis, hepatitis B (with improved efficacy), poliomyelitis and *Haemophilus influenza* type B. Moreover, Adacel™, a trivalent booster vaccine against diphtheria, tetanus and pertussis has recently been licensed in U.S.

#### **Travel/Endemic vaccines**

#### **Dengue Fever**

Several approaches are being explored to develop a vaccine to protect against the four main viral serotypes responsible for dengue fever and its serious complications (hemorrhagic fever). This disease is found mainly in Asia, Africa and Latin America. A vaccine for residents of endemic countries, as well as visitors to these regions, is currently undergoing phase IIa clinical trials.

#### Malaria

The sanofi pasteur malaria vaccine project is in the pre-clinical stage and will benefit from the malaria partnership network and vaccine adjuvant technology developed in-house.

### New vaccine targets

#### HΙV

Sanofi pasteur is one of the pioneers in the search for a vaccine against HIV, and continues to work in partnership with international agencies and other pharmaceutical companies. Sanofi pasteur is currently exploring several avenues of research for both preventive and therapeutic vaccines to combat HIV.

#### Cancer

Research is being carried out on colorectal cancer and malignant melanoma, seeking to develop vaccines which specifically activate the immune system to destroy cancerous cells. A vaccine based on the ALVAC vector has demonstrated a good safety profile in phase I clinical trials in patients suffering from melanomas and colorectal cancers.

#### Chlamydia trachomatis

Chlamydia trachomatis is the most commonly reported sexually transmitted bacterial pathogen and produces serious morbidity and long term sequelae, especially in women. The Chlamydia trachomatis project goal is to develop a preventive recombinant protein vaccine, with a target population of pre-sexually active young women, 11 to 14 years of age. Currently, the project is in the exploratory stage.







Jean-François Dehecq Chairman and Chief Executive Officer



**Gérard Le Fur**Senior Executive Vice President
Executive Vice President
Scientific and Medical Affairs



Hanspeter Spek Executive Vice President Pharmaceutical Operations



Jean-Claude Leroy Executive Vice President Chief Financial Officer



Jean-Claude Armbruster Senior Vice President Human Resources



Nicole Cranois Senior Vice President Communications



Olivier Jacquesson Senior Vice President Business Development



Jean-Pierre Kerjouan Senior Vice President Legal Affairs & General Counsel Advisor to the Chairman



Gilles Brisson
Senior Vice President
Pharmaceutical Operations
Europe (excluding France
and Germany)



Pierre Chancel Senior Vice President Global Marketing



Olivier Charmeil Senior Vice President Pharmaceutical Operations Asia/Pacific



Philippe Fauchet Senior Vice President Pharmaceutical Operations Japan

## **Management Committee**



Gilles Lhernould Senior Vice President Industrial Affairs



Philippe Peyre Senior Vice President Corporate Affairs



**David Williams**Senior Vice President Vaccines



Marie-Hélène Laimay Senior Vice President Audit and Internal Control Assessment



Heinz-Werner Meier Senior Vice President Pharmaceutical Operations Germany



Antoine Ortoli Senior Vice President Pharmaceutical Operations Intercontinental



Timothy Rothwell
Senior Vice President
Pharmaceutical Operations
United States

Christian Lajoux Senior Vice President Pharmaceutical Operations

## **Our Corporate Governance**

Adapting the rules of corporate governance to ensure transparency and shareholder information

In 2005, the company decided to introduce a Board appraisal procedure to monitor and improve the functioning of the Board of Directors as regards the principles of good corporate governance.

## Chairman and Chief Executive Officer

• Jean-François Dehecq, aged 66 Date appointed: May 1999 Term of office ends: 2008

## Senior Executive Vice President

• **Gérard Le Fur**, aged 55 Non-Board member Date appointed: December 2002 Term of office ends: 2008

#### The Board of Directors

Subject to the authority expressly reserved by law to the General Meetings of shareholders, and within the scope of the corporate objects, the Board of Directors deals with and takes decisions upon issues relating to the proper management of the company and other matters concerning the Board.

In 2005, the Board of Directors met seven times.

#### Specialist committees

In 1999, the Board of Directors set up specialist committees charged with providing input to assist the Board in its decision-making.

Members of these committees are chosen by the Board from amongst its members on the strength of their experience. Each committee is chaired by an independent director.

#### Audit Committee

Klaus Pohle, Chairman, René Barbier de la Serre, Jean-Marc Bruel, Gérard Van Kemmel. The Audit Committee is composed of four independent directors, one of whom qualifies as a financial expert within the terms of the Sarbanes-Oxley Act. It is responsible for keeping under constant review the existence and effectiveness of the company's financial control and risk management procedures. The Audit Committee met eight times in 2005.

## • The Compensation, Appointments and Governance Committee

René Barbier de la Serre, Chairman, Thierry Desmarest, Jürgen Dormann, Jean-René Fourtou, Serge Kampf, Lindsay Owen-Jones.

This committee is composed of six directors, four of whom are independent directors. Its roles are: to issue recommendations and proposals concerning the various forms of compensation paid to corporate officers; to select new directors; to oversee implementation of structures and procedures ensuring the application of good corporate governance practices within the Group; to implement the Board of Directors appraisal procedure.

The Compensation, Appointments and Governance Committee met twice during 2005.

Further information regarding the Board of Directors, corporate officers and specialist committees is provided in the 20-F Document on our website: www.sanofi-aventis.com.



## COMPOSITION OF THE BOARD OF DIRECTORS

The Board of Directors is made up of 17 directors, 10 of whom are independent. An independent director is one who has no material association whatsoever with the company, group or its management that might compromise the independent exercise of the director's best judgment. It is the responsibility of the Board of Directors to draw up the list of its members who meet these criteria. Members of the Board of Directors are appointed for a maximum term of four years, renewable on a rolling basis. No more than one third of the serving members of the Board of Directors may be aged over 70. The age limit for holding office as Chairman or Chief Executive Officer is 68. Under our statutes, each member of the Board of Directors must be the direct legal owner of at least one of our shares throughout his or her term of office.

Jean-François Dehecq, aged 66 Chairman and Chief Executive Officer Date appointed: May 1999 Term of office ends: 2008

Jürgen Dormann\*, aged 66 Vice Chairman Date appointed: August 2004 Term of office ends: 2008

René Barbier de la Serre\*, aged 65 Date appointed: May 1999 Term of office ends: 2008

**Jean-Marc Bruel\***, aged 70 Date appointed: August 2004 Term of office ends: 2008

**Robert Castaigne**, aged 59 Date appointed: February 2000 Term of office ends: 2008 **Thierry Desmarest**, aged 60 Date appointed: February 2000 Term of office ends: 2008

**Lord Douro\***, aged 60 Date appointed: May 2002 Term of office ends: 2006

**Jean-René Fourtou\***, aged 66 Date appointed: August 2004 Term of office ends: 2008

Serge Kampf\*, aged 71 Date appointed: August 2004 Term of office ends: 2008

**Igor Landau**, aged 61 Date appointed: August 2004 Term of office ends: 2008

**Hubert Markl\***, aged 67 Date appointed: August 2004 Term of office ends: 2008 **Christian Mulliez**, aged 45 Date appointed: June 2004 Term of office ends: 2008

**Lindsay Owen-Jones**, aged 60 Date appointed: May 1999 Term of office ends: 2008

Klaus Pohle\*, aged 68 Date appointed: August 2004 Term of office ends: 2008

Hermann Scholl\*, aged 70 Date appointed: August 2004 Term of office ends: 2008

**Gérard Van Kemmel\***, aged 66 Date appointed: May 2003 Term of office ends: 2007

**Bruno Weymuller**, aged 57 Date appointed: May 1999 Term of office ends: 2008

<sup>\*</sup> Independant director.

## **Shareholder information**

The relationship between sanofi-aventis and its shareholders is based on trust. To maintain and strengthen this trust, the Group has set itself three priorities: informing, listening and meeting.





### **Informing**

Sanofi-aventis provides its shareholders with a wide range of tools to ensure a regular flow of comprehensive, transparent and accessible information on the Group, its business activities and its results.

The Group's corporate Internet site, www.sanofi-aventis.com, features a dedicated area for individual shareholders within the Investors section, offering real-time access to all the available information: financial documents, Letters to Shareholders, press releases, financial calendar, sanofi-aventis current stock quotes, information about Annual General Meetings, etc.

Every year, sanofi-aventis publishes a wide range of documents which are specifically intended for both individual shareholders and the financial community. Downloads of all these documents are available from the Group's corporate website (en.sanofi-aventis.com/investors).

#### • The Business Report

This is a widely circulated document, also available on request, which gives an illustrated account of the Group's strategy, business activity and key facts and figures. It is accompanied by the Sustainable Development Report which sets out the Group's commitments and its achievements

- Regulatory filings provide still more financial and legal details: these include the annual Reference Document filed with the French financial markets authority, the *Autorité des Marchés Financiers* (AMF), and Form 20-F filed with the U.S. financial regulator, the Securities and Exchange Commission (SEC).
- **Financial Notices** enable shareholders to monitor Group quarterly results.

- The **Letter to Shareholders** is a vital link between the Group and its shareholders. Issued at least four times a year, this features all the latest financial news and events relating to the Group's products, research and strategy. It also contains regular updates on the stock markets and provides practical information for sanofiaventis shareholders, giving them the clearest possible picture of the challenges and opportunities the Group faces.
- Shareholders Guide. Since 2005, sanofiaventis has also published an Individual Shareholders Guide, designed to give current and potential sanofi-aventis shareholders a better understanding of the Group and its activities. The Guide contains all the relevant information on the Group, its responsibilities and activities, on the sanofi-aventis stock and on the Group's commitment to its shareholders.

#### Listening

A **team of advisors** is also on hand to answer any questions shareholders might have. A call from any telephone to the relevant shareholder voicemail server will provide, all the latest key information on sanofi-aventis in a few minutes: a current stock quote, the latest CAC 40 index figures and stock movements over the day, financial news including the latest published results, and the dates of upcoming financial events and shareholder meetings.

The sanofi-aventis Individual Shareholders Committee is a consultative body made up of twelve members drawn from different geographical and professional backgrounds to represent individual shareholders. Members of the Committee are in regular communication with the Investor Relations Department through working sessions and frequent informal contacts.

Through these contacts, the committee keeps sanofi-aventis management teams informed of investor viewpoints

and their main concerns and expectations. The committee also plays its part in developing quality communication for individual shareholders, participating in strategic planning for future projects and in the production of shareholder documents and information published on the website, and attending regional shareholder meetings.

### Meeting

The **Annual General Meeting** of shareholders is a privileged opportunity to present to shareholders the results and activity of their Group. It is also the occasion for submitting a number of resolutions for the shareholders' approval that will govern the life of the company, and also proposing for their approval the amount of the yearly dividend to be paid.

Sanofi-aventis' commitment to dialogue and information is reflected at the local level in **shareholder information meetings** held in cities around France, at which the Investor Relations Department presents the Group, its business activities and latest news, and answers shareholders' questions.

Sanofi-aventis regularly attends the annual French **Actionaria** shareholder fair in order to strengthen its links with individual shareholders.

At the 2005 fair, held on November 18-19, 2005, nearly 5,000 people visited the sanofi-aventis stand.

## Shareholder meetings in France for 2006:

March 20	Toulon
April 6	Montpellier
April 11	Nancy
May 23	Annecy
September 11	Clermont-Ferrand
October 9	Biarritz
October 10	Toulouse
November 20	Strasbourg
December 4	Lyon
December 18	Perpignan

## Financial communications calendar for 2006

• January 30, 2006

Fourth-quarter and full-year 2005 sales

• February 24, 2006 2005 full-year results—Analysts/

Investors Meeting in Paris

• March 22, 2006

Analysts/Investors Meeting in New York

• May 5, 2006

2006 first-quarter sales and results

• May 31, 2006

Annual General Meeting of shareholders

• August 2, 2006

2006 second-quarter sales and results

• October 31, 2006

2006 third-quarter sales and results

## **CONTACTS**

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## **Consolidated balance sheet**

## Simplified

## **ASSETS**

In millions of euros	31.12.2005	31.12.2004*	
Property, plant and equipment	6,184	5,892	
Intangible assets (including goodwill)	60,463	61,567	
Non-current financial assets, investments in associates and deferred taxes	6,890	5,985	
Non-current assets	73,537	73,444	
Inventories, accounts receivable & current financial assets	11,872	10,123	
Cash and equivalents, short-term investments & deposits	1,249	1,840	
Current assets	13,121	11,963	
TOTAL ASSETS	86,658	85,407	

<sup>\*</sup>As allowed under IFRS 3, sanofi-aventis has reviewed some aspects of the Aventis purchase price allocation within the permitted 12-month period.

## LIABILITIES & EQUITY

In millions of euros	31.12.2005	31.12.2004*
Shareholder's equity	46,637	41,061
Minority interests	189	462
Total equity	46,826	41,523
Long-term debt – part due over one year	4,750	8,654
Provisions & other non-current liabilities	7,454	6,929
Deferred taxes	12,208	13,123
Non-current liabilities	24,412	28,706
Accounts payable & other current liabilities	8,995	7,790
Short-term debt	6,425	7,388
Current liabilities	15,420	15,178
TOTAL LIABILITIES & EQUITY	86,658	85,407

## Adjusted consolidated income statement(1)

In millions of euros	2005 full-year Adjusted consolidated come statement (unaudited)	As % of net sales	004 full-year Adjusted pro forma income statement (unaudited)	As % of net sales	% change
Net sales	27,311	100%	25,199	100%	+8.4%
Other revenues	1,202	4.4%	1,109	4.4%	+8.4%
Cost of sales	(7,172)	(26.3%)	(6,918)	(27.5%)	+3.7%
Gross profit	21,341	78.1%	19,390	76.9%	+10.1%
Research & development expenses	(4,044)	(14.8%)	(3,964)	(15.7%)	+2.0%
Selling & general expenses	(8,250)	(30.2%)	(7,888)	(31.3%)	+4.6%
Other current operating income	261	_	314	_	+13.1%
Other current operating expenses	(124)	_	(98)	_	-10.7%
Amortization of intangibles	(112)	_	(114)	_	-1.8%
Operating income - current	9,072	33.2%	7,640	30.3%	+18.7%
Restructuring costs	(25)	_	(141)	-	-82.3%
Impairments of PP&E and intangibles	(7)	-	_	-	-
Other operating income and expenses	79	-	181	-	- //
Operating income	9,119	33.4%	7,680	30.5%	+18.7%
Financial expenses	(532)	_	(848)	-///	-37.3%
Financial income	287	-	109	<u></u>	-
Income before tax and associates	8,874	32.5%	6,941	27.5%	+27.8%
Income tax expense	(2,774)	(10.1%)	(2,146)	(8.5%)	+29.3%
Effective tax rate	31.3%	<u>-</u>	30.9%	-	_
Share of profit/loss of associates	584	_	535	_	+9.2%
Net income before minority interests	6,684	24.5%	5,330	21.2%	+25.4%
Minority interests	(349)	_	(305)	_	+14.4%
Net income <sup>(2)</sup>	6,335	23.2%	5,025	19.9%	+26.1%
Average number of shares outstanding (million)	1,336.5	_	1,333.4	_	-
Earnings per share (in euros)	4.74	_	3.77	_	+25.7%

<sup>(1)</sup> See definition of adjusted net income on page 29.

<sup>(2)</sup> Consolidated net earnings – Group share (audited): 2,258 million euros in 2005 and 1,986 million euros in 2004.

## Simplified statement of cash flows

In millions of euros	2005 (unaudited)
Adjusted consolidated net income <sup>(1)</sup>	6,335
Depreciation, amortization & impairment of property, plant & equipment and intangibles	983
Impact of restructuring costs, net of tax	(530)
Other items	(151)
Operating cash flow before changes in working capital	6,637
Changes in working capital	(239)
Net cash provided by operating activities	6,398
Acquisitions of property, plant & equipment and intangibles	(1,143)
Acquisitions of consolidated investments, net of acquired cash	(692)
Proceeds from disposals of property, plant & equipment and intangibles	734
Net cash used in investing activities	(1,101)
Issuance of sanofi-aventis shares	314
Proceeds from sale of shares on exercice of stock options	105
Dividends	(1,614)
Other items	174
Change in net debt	4,276

<sup>(1)</sup> See definition of adjusted net income on page 29.

This report contains projections and other forward-looking statements that are not historical facts. Although the management of sanofi-aventis believes that these projections and forward-looking statements, and their underlying assumptions, are reasonable as of the date of this report, investors are cautioned that such projections, assumptions and forward-looking statements are subject to various risks and uncertainties (many of which are difficult to predict and generally beyond the control of sanofi-aventis) that could cause actual results and developments to differ materially from those expressed or implied. These risks and uncertainties include those discussed elsewhere in this report, as well as in the filings of sanofi-aventis with the U.S. Securities and Exchange Commission (SEC) and the French Autorité des marchés financiers (AMP), notably under the caption "Risk Factors" in the companys Annual Report on Form 20-F. Other than as required by applicable law, sanofi-aventis does not undertake any obligation to update any statement that is not a historical fact.

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