



**Annual  
Report**  
*2004*



**sanofi aventis**

Because health matters

Although sanofi-aventis' management believes that the expectations reflected in this report are reasonable, investors are cautioned that forward-looking information and 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 in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include our ability to continue to maintain and expand our presence profitably in the United States; the success of our research and development programs; our ability to protect our intellectual property rights; the risks associated with reimbursement of healthcare costs and pricing reforms, particularly in the United States and Europe; and trends in the exchange rate and interest rate environments.

# Summary



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(1) IMS monthly, MIDAS all available channels, 2004.



**sanofi aventis**

Because health matters

**Active, dynamic, optimistic,  
universal, simple**

A logo which speaks to people's hearts and conveys a message of solidarity. People bearing a heart, symbolizing the gift of Research to all humanity.

# N°1 in the pharmaceutical industry in

Sales of **25 billion euros\***

**3**<sup>rd</sup> largest R&D budget worldwide

More than **17,000** research staff\*\*

**128** projects under development

**48** of which are at advanced stages (phases II and III)

and **80** in preclinical development and phase I

Creation of Sanofi by Elf Aquitaine. L'Oréal takes over Synthelabo, created in 1970 by the merger of two French pharmaceutical companies, Dausse (founded in 1834) and Robert & Carrière (founded in 1899).

Sanofi launches its first flagship product, Ticlid®. Synthelabo launches two major products, Stilnox® and Xatral®, on the French market.

Sanofi enters the U.S. market by acquiring the prescription drugs business of Sterling Winthrop, a subsidiary of Eastman Kodak. Sanofi launches its first major products on the U.S. market: Aprovel® in 1997 and Plavix® in 1998.

Creation of Hoechst Marion Roussel, the pharmaceutical division of Hoechst (founded in 1951), following several acquisitions: Roussel Uclaf, Celanese Corporation and Marion Merrel. Rhône-Poulenc, the result of the 1928 merger between two chemical companies, Frères Poulenc and Société Chimique des Usines du Rhône (founded in 1895), is first nationalized in 1982 and then privatized in 1993, but continues to refocus on its strategic businesses.

1973

1978-1988

1994

1997

\* Adjusted pro forma net sales.

\*\* Including: Vaccines, Industrial Development, Medical/Regulatory staff of subsidiaries.

# Europe and France, N°3 worldwide

**96,439** people on 300 sites in  
**80 countries**, providing high-performance industrial  
facilities and forming an exceptional sales force

## 7 major therapeutic areas

Cardiovascular Disease

Thrombosis

Oncology

Metabolic Diseases

Disorders of the Central

Nervous System

Internal Medicine

Vaccines

1998-1999

Sanofi and Synthélabo merge and the new Group refocuses on its core business: pharmaceuticals. Meanwhile, Rhône-Poulenc and Hoechst create Aventis, a world leader in life sciences within the pharmaceuticals industry.

1999-2002

Substantial growth for Group flagship products: Stilnox®, Plavix® and Aprovel® for Sanofi-Synthélabo, Lovenox®, Allegra® and Taxotere® for Aventis.

2002-2003

Sanofi-Synthélabo goes from strength to strength on the U.S. market. Sanofi-Synthélabo shares are listed on the New York Stock Exchange.

2004

Acquisition by Sanofi-Synthélabo of Aventis and subsequent merger into sanofi-aventis, the leading pharmaceutical group in Europe and the third-largest group worldwide.

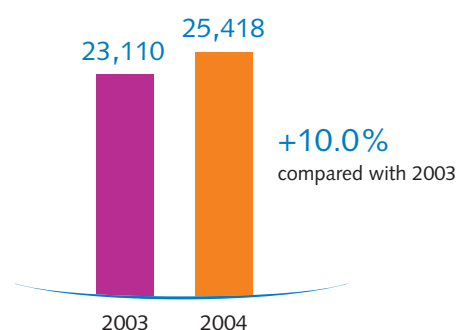
# The highest global growth rate of the leading pharmaceutical companies<sup>(1)</sup>

## Pro forma data

Sanofi-aventis financial data for the year ended December 31, 2004 include the financial statements of Aventis from August 20, 2004. As a result, financial data for the sanofi-aventis Group for the year ended December 31, 2004 are not directly comparable with published historical data. In order to give a better representation of our business performance, we have decided to present pro forma data for 2004 and 2003, which reflect the activities of the two groups as though the acquisition had occurred on January 1, 2003.

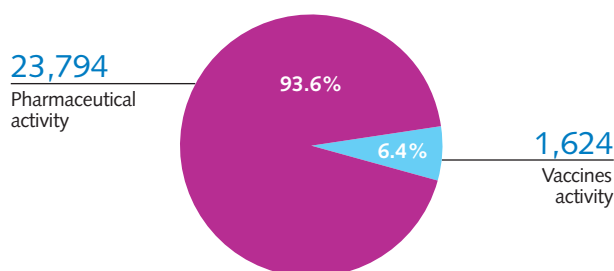
## ■ Pro forma net sales

on a comparable basis<sup>(2)</sup> (in millions of euros)



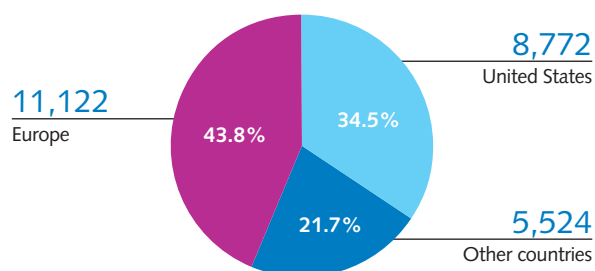
## ■ Pro forma net sales by business segment

(in millions of euros)



## ■ Prof forma net sales by geographic area

(in millions of euros)



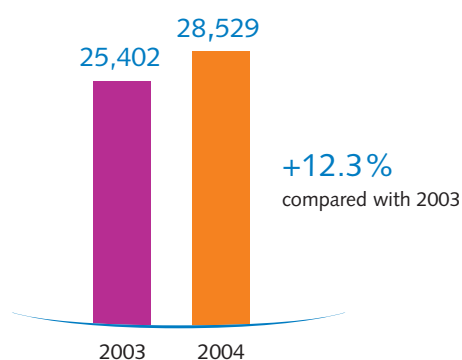
Figures according to French GAAP

<sup>(1)</sup> IMS monthly MIDAS all available channels 2004.

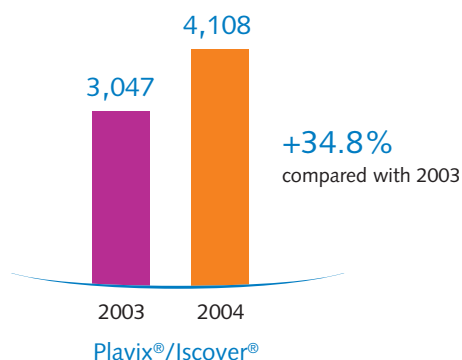
<sup>(2)</sup> At constant Group structure and exchange rates.

<sup>(3)</sup> Pro forma developed sales include pro forma sales recorded by sanofi-aventis, excluding sales of products to its alliance partners, but including sales not consolidated by sanofi-aventis and made through the alliances with Bristol-Myers Squibb on Plavix®/Iscover® (clopidogrel) and Aprovel®/Avapro®/Karvea® (irbesartan) and with Fujisawa on Stilnox®/Myslee® (zolpidem). Our alliance partners provide us with information about their sales in order to allow us to calculate developed sales. Pro forma developed sales are a useful indicator because they demonstrate trends in the overall presence of products originating from sanofi-aventis in the market.

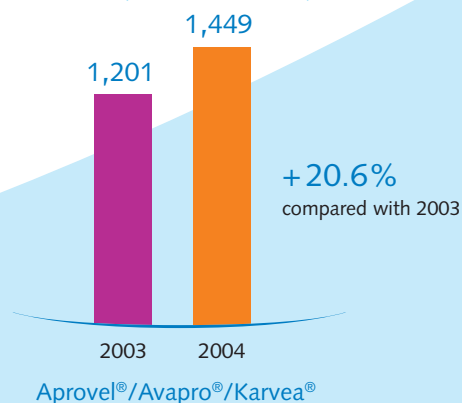
■ Pro forma developed sales<sup>(3)</sup>  
on a comparable basis<sup>(2)</sup> (in millions of euros)



■ Pro forma developed sales<sup>(3)</sup> of Plavix®  
on a comparable basis<sup>(2)</sup> (in millions of euros)



■ Pro forma developed sales<sup>(3)</sup> of Aprovel®  
on a comparable basis<sup>(2)</sup> (in millions of euros)



■ Pro forma net sales of the top 15 products  
of the pharmaceutical business  
on a comparable basis<sup>(2)</sup> (in millions of euros)

In millions of euros	2003 pro forma comparable	2004 pro forma	Change on a comparable basis
<b>Products</b>			
Lovenox®/Clexane®	1,556	1,904	+22.4%
Plavix®/Iscover®	1,314	1,694	+28.9%
Allegra®	1,614	1,502	-6.9%
Taxotere®	1,290	1,436	+11.3%
Stilnox®/Ambien®/ Myslee®	1,234	1,423	+15.3%
Eloxatin®	778	1,220	+56.8%
Delix®/Tritace®/ Triatec®	1,176	972	-17.3%
Lantus®	469	843	+79.7%
Aprovel®/Avapro®/ Karvea®	677	790	+16.7%
Copaxone®	583	742	+27.3%
Amaryl®	576	684	+18.8%
Actonel®	191	305	+59.7%
Depakine®	275	303	+10.2%
Nasacort®	259	287	+10.8%
Xatral®	220	281	+27.7%
<b>Total</b>	<b>12,212</b>	<b>14,386</b>	<b>+17.8%</b>

Our results...

# Pro forma adjusted earnings per share (EPS) up by 18.2%

compared with 2003

■ Research and Development expenses  
(2004 pro forma)

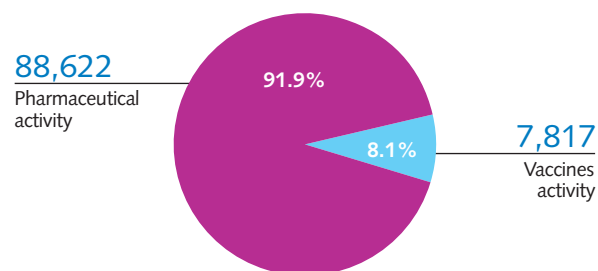
**3,961** million euros  
15.6% of pro forma net sales

**Synergies pro forma 2004:**  
220 millions of euros  
(before tax)

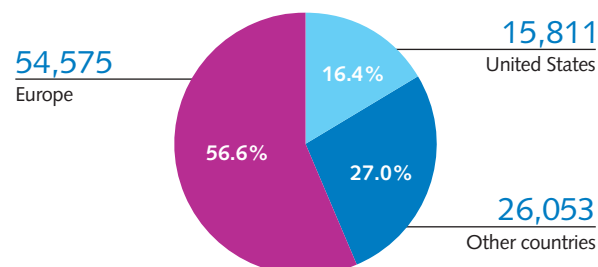
## ■ EMPLOYEES

**96,439** employees  
(at December 31, 2004)

■ Employees by business segment  
(at December 31, 2004)



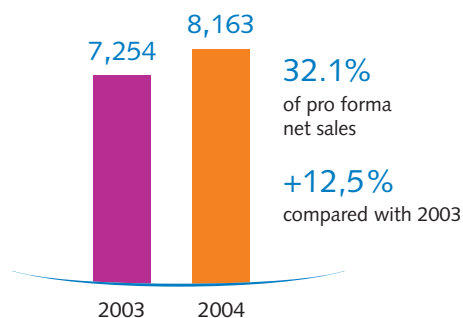
■ Employees by geographic area  
(at December 31, 2004)



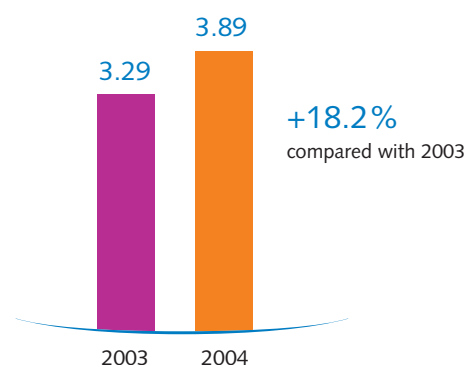


## ■ PRO FORMA EARNINGS

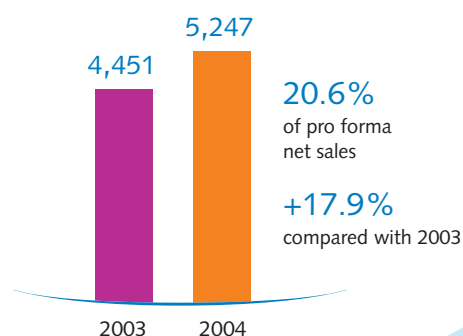
### ■ Pro forma operating profit (in millions of euros)



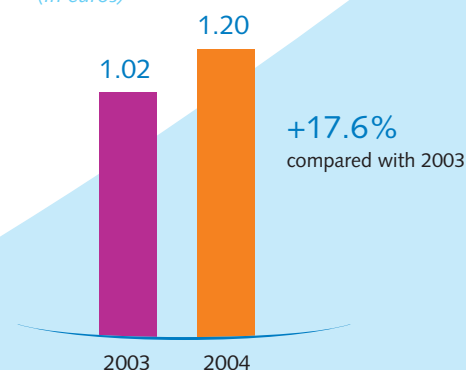
### ■ Adjusted pro forma EPS (in euros)



### ■ Adjusted pro forma net income (in millions of euros)



### ■ Dividend (in euros)



## Adjusted net income

We have also decided to present an adjusted net income. Adjusted net income is defined as net income adjusted for the material impacts of applying purchase accounting to the Aventis acquisition, and for certain costs associated with the deal. Adjusted net income will be used as an internal performance indicator, as a significant factor in calculating the variable portion of employee remuneration, and as the basis for determining the dividend policy of the new entity.

Our results...

# Doing more, working better and moving faster in healthcare to serve everyone

■ *The pharmaceutical industry is today facing new challenges. Across the world, healthcare needs are growing. At the same time, healthcare systems are weakened, intellectual property rights to medicines are under threat, and pharmaceutical research is faced with serious productivity and profitability problems. To continue delivering solutions to the world's healthcare needs, the industry must change. This imperative was the driving force behind the creation of sanofi-aventis in 2004.*



**W**ith the creation of sanofi-aventis, we now have one of the richest and most innovative research pipelines in the world pharmaceutical industry. We are present in seven major therapeutic fields (cardiovascular, thrombosis, oncology, disorders of the central nervous system, metabolic disorders, internal medicine and vaccines), and offer a wide range of medicines. Building on our European base, our Group now has a major presence in the United States and solid positions throughout the world. We also have highly efficient industrial and sales operations.

## Growth outperforming the market from year one

Already in 2004, our results show that we have made the right strategic choices, and that we have the ability to carry through a large-scale merger while continuing to improve our business performance.

With pro forma sales up 10% on a comparable basis, we have achieved growth which outperforms the market. Our top 15 products posted growth of 17.8% on a comparable basis. They include no fewer than eight flagship products: Lovenox®, Plavix® and Aprovel® in cardiovascular and thrombosis, Taxotere® and Eloxatin® in oncology, Ambien® in disorders of the central nervous system, and Allegra® and Actonel® in internal medicine. Apart from Allegra®, all our flagship products reported very strong sales growth. Of the other products in our top 15, two

more are poised for flagship product status: Lantus®, now the biggest-selling insulin brand in the United States, and Copaxone®, the first non-interferon treatment for multiple sclerosis. As regards our base portfolio, a targeted strategy has enabled us to keep sales steady, in line with our "no small products" philosophy.

In vaccines, a business for the Group, pro forma net sales rose by 7.5%, driven mainly by influenza and meningitis vaccines.

2004 also saw the launch of a generics division, trading under the name of Winthrop® Pharmaceuticals.

In all regions where we operate, we achieved sales growth which outperformed the market, living up to our "no small countries" philosophy.

In Europe, against a backdrop of even tighter control over healthcare spending we confirmed our ability to outpace market growth, with sales up 5.9% on a comparable basis (pro forma).

In the United States, despite an increasingly challenging business environment, we delivered growth well above that of the market for the fourth consecutive year, with developed sales rising by 20.2% on a comparable basis. In Asia, where the merger between the two groups gave us strong market positions, we achieved robust growth, this was also the case in South America.

Our fine sales performance was reflected in a 12.5% increase in pro forma operating profit. In 2004, we generated 220 million euros of pre-tax synergies, compared with the 160 million euros we predicted at the time of the deal. Adjusted pro forma net income rose by 17.9%, while pro forma earnings per share advanced by 18.2% to 3.89 euros, against 3.29 euros in 2003. This too was one of the strongest performances in the world pharmaceutical industry.

We have combined our many different headquarters operations onto a single site in Paris, and, as announced, the new Group has been up and running since January 1, 2005.



**Jean-François Dehecq**

Chairman and  
Chief Executive Officer



## Our R&D is driving ahead

During the last quarter of 2004, the R&D teams carried out a complete review of the portfolio of compounds under development. This review has led us to focus on seven major therapeutic fields where medical needs are huge and therapeutic responses critical. In each of these fields, we have selected the best and most promising projects from the two teams.

In 2005, we will learn the results of around a dozen trials in late stages of clinical investigation in major fields like cardiovascular and disorders of the central nervous system. A number of new medicine applications will be filed, including Acomplia™ (rimonabant), a medicine to combat obesity (and its cardiovascular and metabolic effects) and assist smoking cessation; dronedarone, a treatment for atrial fibrillation; and the pediatric vaccine Pentacel™. New indications and formulations for Allegra®, Aprovel®, Plavix®, Taxotere® and Stilnoxium™ (the

successor to Stilnox® in Europe) will also be submitted to the healthcare authorities for approval.

With 128 compounds in development—48 in phases II or III, and 80 in the pre-clinical phase or phase I—the sanofi-aventis Group now has one of the most promising pipelines in the industry, featuring some highly innovative pharmacological classes. After a flood of innovations in the cardiovascular, thrombosis and metabolism fields, we have high hopes for our pipeline of compounds in disorders of the central nervous system, oncology, vaccines and internal medicine.

## Strong, sustainable and profitable growth

Our business consists of finding innovative medicines and vaccines that offer new therapeutic solutions for patients. Our strategy for achieving this has been consistent for over 30 years, and involves strong, sustainable and profitable growth.

Thanks to the motivation and commitment of our people, we have lost no time in getting the Group up to speed, so that we can continue to record strong growth. Our 2004 results speak for themselves.

To achieve sustainable growth, we must be able to produce new medicines, and fast. From this year, we will be stepping up investment to accelerate the clinical development of compounds. We will consolidate our base portfolio, on which the growth of our flagship products and new products will be built. And we will strengthen our sales teams and improve our industrial facilities in as many countries as possible.

This approach will deliver the profitable growth needed to fund research, outpace our rivals and reward our shareholders.

### Our responsibility as a pharmaceuticals group

Now that we are one of the world's leading pharmaceuticals groups, we feel our sense of responsibility more keenly than ever. We will continue to tighten our rules on safety, ethical standards and transparency.

We also have a duty to help provide access to medicines to the greatest number. One initiative which gives us particular satisfaction is "Impact malaria", a program which aims to combat one of the most widespread diseases in the developing world, enabling as many people as possible to gain access to effective medicines. We are also developing programs to combat sleeping sickness, tuberculosis and leishmaniasis.

The tragic events in South-East Asia have only served to strengthen our determination to do more and better for the greatest number in the field of healthcare.

### Encouraging prospects

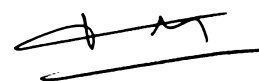
With eight flagship products, a stable base portfolio and one of the best R&D profiles in the sector, our growth prospects are highly encouraging.

In 2005, we are set to achieve sales growth in line with 2004. We will also meet our stated target for synergies. Whilst affirming the need to increase investment in R&D and in promoting our entire range of products, which guarantee current and future growth, we predict that in 2005 (barring adverse events) we will again record

comparable-basis sales growth above that of the world pharmaceutical market, coupled with growth in adjusted earnings per share in line with 2004, assuming an exchange rate of 1.25 U.S. dollar to the euro.

In 2004, we aimed high and we succeeded. We can therefore look forward to 2005 with confidence, convinced of our ability to continue delivering on our commitment to strong, sustainable and profitable growth, for the benefit of all—patients, employees and shareholders alike.

Jean-François Dehecq  
Chairman and Chief Executive Officer



# ➤ Management Committee



**Jean-François Dehecq**  
Chairman and Chief  
Executive Officer



**Gérard Le Fur**  
Senior Executive  
Vice President



**Gérard Le Fur**  
Executive Vice President,  
Science and  
Medical Affairs



**Hanspeter Spek**  
Executive Vice President,  
Pharmaceutical  
Operations



**Jean-Claude Armbruster**  
Senior Vice President,  
Human Resources



**Gilles Brisson**  
Senior Vice President,  
Pharmaceutical  
Operations Europe



**Pierre Chancel**  
Senior Vice President,  
Global Marketing



**Jean-Claude Leroy**  
Senior Vice President,  
Finance



**Gilles Lhernould**  
Senior Vice President,  
Industrial Affairs



**Heinz-Werner Meier**  
Senior Vice President,  
Pharmaceutical  
Operations Germany



**James Mitchum**  
Senior Vice President,  
Pharmaceutical  
Operations Japan



**Dirk Oldenburg**  
Senior Vice President,  
Legal Affairs  
& General Counsel





**Christian Lajoux**  
Senior Vice President,  
Pharmaceutical  
Operations France



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



**Jean-Pierre Kerjouan**  
Senior Vice President,  
Advisor  
to the Chairman



**Olivier Jacquesson**  
Senior Vice President,  
Business Development



**Nicole Cranois**  
Senior Vice President,  
Communications



**David Williams**  
Senior Vice President,  
Vaccines



**Pascal Soriot**  
Senior Vice President,  
Commercial Operations  
United States



**Tim Rothwell**  
Senior Vice President,  
Pharmaceutical  
Operations United  
States and Canada



**Philippe Peyre**  
Senior Vice President,  
Corporate Affairs




**Antoine Ortoli**  
Senior Vice President,  
Pharmaceutical  
Operations  
Intercontinental  
*as of January 2005*



**sanofi aventis**

Because health matters

# The choice of continuity

- 
- *In 2004, sanofi-aventis adapted its corporate governance policy to the new company structure and continued implementing systems which correspond to changed requirements in this area in France and the United States.*

## Key events in 2004

- **In January 2004** Sanofi-Synthélabo announced a share and cash offer on Aventis's shares. When the offering period expired definitively on September 6, 2004, Sanofi-Synthélabo held 98.03% of Aventis shares.
- **The General Meeting of Shareholders on June 23, 2004** decided to change the name of the company from Sanofi-Synthélabo to sanofi-aventis, and proceeded to appoint new directors, with effect from August 20, 2004.
- **As regards the results of the offer**, putting into practice the highly positive response to this project, sanofi-aventis and Aventis began a merger process. The aim was to simplify the legal structures of the new entity and facilitate the integration of the two groups. The merger of Aventis into sanofi-aventis was approved by the General Meeting held on December 23, 2004. This merger took legal effect as of December 31, 2004.

## Board of Directors

The company is managed by a Board of Directors composed of 17 members, 10 of whom are independent. Members of our Board of Directors are appointed for a maximum term of 4 years. No more than one-third of the serving members of our Board of Directors may be aged more than 70.

The age limit for holding office as Chairman or Chief Executive Officer is 68 years.

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.

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.

At December 31, 2004, non-corporate members of the Board of Directors collectively held a total of 273,293 sanofi-aventis shares.



# Composition of the Board of Directors at December 31, 2004

## **Jean-François Dehecq, aged 65**

*Chairman and Chief Executive Officer of sanofi-aventis from May 1999 to 2008*

- Director of Air France
- Chairman and Director of Sanofi-Synthelabo Daiichi Pharmaceuticals Co Ltd (Japan)
- Director of Sanofi-Synthelabo Inc. (United States) and Fujisawa Sanofi-Synthelabo (Japan)

## **Jürgen Dormann, aged 65**

*Vice Chairman and Director\* from August 2004 to 2008*

- Chairman of ABB Ltd (Switzerland)
- Director of Adecco (Switzerland)

## **René Barbier de la Serre, aged 64**

*Director\* from May 1999 to 2008*

- Member of the Supervisory Boards of La Compagnie Financière Edmond de Rothschild Banque
- Director of Calyon and Schneider Electric
- Member of the Supervisory Boards of Compagnie Financière Saint-Honoré, Pinault-Printemps-Redoute and Euronext NV (Netherlands)
- Delegated Director of Harwanne Compagnie de Participations Industrielles et Financières SA (Switzerland)

## **Jean-Marc Bruel, aged 69**

*Director\* from August 2004 to 2008*

- Chairman of La Fondation Villette-Entreprises and Firmenich
- Director of Rhodia, Institut Curie and the Ecole Centrale

## **Robert Castaigne, aged 58**

*Director from February 2000 to 2008*

- Chief Financial Officer of Total SA
- Chairman and Chief Executive Officer of Total Chimie and Total Nucléaire
- Director of Arkema, Elf Aquitaine, Hutchinson, Total Gestion Filiales, Omnium Insurance & Reinsurance Company Ltd (Bermuda), Petrofina (Belgium), Total Holdings UK (United Kingdom) and Total Gabon (Gabon)

## **Thierry Desmarest, aged 59**

*Director from February 2000 to 2008*

- Chairman and Chief Executive Officer of Total SA and Elf Aquitaine
- Member of the Supervisory Boards of Areva and L'Air Liquide

## **Lord Douro, aged 59**

*Director\* from May 2002 to 2006*

- Chairman of Richemont Holdings UK (United Kingdom)
- Chairman of Framlington Group (United Kingdom)
- Director of La Compagnie Financière Richemont AG (Switzerland) and GAM Worldwide (United Kingdom)

## **Jean-René Fourtou, aged 65**

*Director\* from August 2004 to 2008*

- Chairman and Chief Executive Officer of Vivendi Universal
- Chairman of the Supervisory Board of Canal +
- Vice-Chairman of the Supervisory Board of Axa
- Director of Cap Gemini

## **Serge Kampf, aged 70**

*Director\* from August 2004 to 2008*

- Chairman of the Board of Directors of Cap Gemini SA, Chairman of Cap Gemini Service and Cap Gemini Suisse
- Director of Sogeti-Transiciel and Cap Gemini North America Inc.

## **Igor Landau, aged 60**

*Director from August 2004 to 2008*

- Director of Thomson, Essilor, CCF and INSEAD
- Member of the Supervisory Boards of Dresdner Bank, Allianz and Adidas-Salomon

## **Hubert Markl, aged 66**

*Director\* from August 2004 to 2008*

- Member of the Supervisory Boards of BMW AG, Münchener Rückversicherungs-Gesellschaft, Royal Dutch Shell

## **Christian Mulliez, aged 44**

*Director from June 2004 to 2008*

- Vice-President, General Management, Administration and Finance of L'Oréal
- Chairman and Director of Regefi
- Director of DG 17 Invest and L'Oréal USA Inc.

## **Lindsay Owen-Jones, aged 59**

*Director from May 1999 to 2008*

- Chairman and Chief Executive Officer of L'Oréal
- Director of BNP Paribas
- Vice-Chairman and member of the Supervisory Board of L'Air Liquide

## **Klaus Pohle, aged 67**

*Director\* from August 2004 to 2008*

- Chairman of the German Accounting Standards Board (GASB)
- Director of Coty Inc. (United States)
- Member of the Supervisory Board of DWS Investment GmbH (Germany)
- Vice-Chairman of the Supervisory Board of Hypo Real Estate Holding AG (Germany)

## **Hermann Scholl, aged 69**

*Director\* from August 2004 to 2008*

- Chairman of the Supervisory Board of Robert Bosch GmbH (Germany)
- Member of the Supervisory Boards of Allianz AG (Germany) and BASF AG (Germany)

## **Gérard Van Kemmel, aged 65**

*Director\* from May 2003 to 2007*

- President of Novell for Europe, the Middle East and Africa

## **Bruno Weymuller, 56**

*Director from May 1999 to 2008*

- Executive Vice-President, Strategy and Risk Assessment of Total SA
- Director of Elf Aquitaine and Technip-Coflexip

\* Independent Director.

## Activities of the Board of Directors in 2004

During 2004, the Board of Directors met 12 times, with an overall attendance rate among Board members of 83%. The main items included on the agendas for these meetings were:

### January 25, 2004

- approval of a credit agreement,
- approval of a guarantee,
- approval of the filing of the public offers for the shares of Aventis in France, the United States and Germany, and of the related documentation,
- approval of the engagement letters entered into with BNP Paribas,
- calling of an Extraordinary General Meeting of the shareholders:
  - report of the Board of Directors
  - proposed resolutions.

### February 13, 2004

- review and adoption of consolidated and parent company financial statements for 2003,
- appropriation of profits,
- calling of a Combined General Meeting:
  - Management Report and Report of the Chairman (as required under the French Financial Security Law),
  - Report of the Board of Directors,
  - proposed resolutions,
- setting of Directors' attendance fees,
- unrestricted and restricted related party agreements,
- review of projected statement of income and statement of cash flows for 2004,
- progress report on the public offer for Aventis.

### April 14, 2004

- confirmation of the interim dividend and payment date,
- information on the offer for Aventis.

### April 24, 2004

- approval of a credit agreement to finance the improved offer,
- approval of a guarantee,
- approval of the filing of an improved offer over and above the offers initially filed for the shares of Aventis in France, the United States and Germany, and of the related documentation,
- approval of the engagement letter entered into with BNP Paribas relating to the improved offer,
- additions to the agenda and proposed resolutions for the Combined General Meeting of May 24, 2004 to insert a resolution concerning the consideration for the offers,
- additions to the report of the Board of Directors,
- powers.

### May 3, 2004

- adjournment of the Combined General Meeting of May 24, 2004,
- powers.

### May 13, 2004

- calling of a Combined General Meeting:
  - report of the Board of Directors,
  - proposed resolutions,
- progress report on the offer for Aventis.

### May 24, 2004

- reappointment and appointment of members of the Board of Directors,
- Directors' attendance fees.

#### June 23, 2004

- reappointment of the Chairman and Chief Executive Officer, and the Senior Executive Vice President,
- powers of the Chairman and Chief Executive Officer and Senior Executive Vice President,
- decision on and delegation of powers to the Chairman and Chief Executive Officer to trade in the company's shares,
- delegation of powers to the Chairman and Chief Executive Officer to formally record the quantity and par value of shares issued on the exercise of options to subscribe for shares and of composite securities giving access to the share capital,
- authorizations in respect of guarantees,
- progress report on the offer for Aventis,
- delegation of powers to the Chairman and Chief Executive Officer to set the definitive amount of the capital increase in the light of the notice of the result of the offer as published by the *Autorité des Marchés Financiers* (or the notice of the reopened offer, if appropriate) and, with authority to subdelegate, to carry out the formalities necessary for completing the capital increase,
- review of the company's operations.

#### August 30, 2004

- appointment of the Vice-Chairman of the Board of Directors,
- review of the interim financial statements to June 30, 2004, and draft report on the consolidated interim financial statements to that date,
- review of projected statement of income and statement of net realizable, liquid assets as of June 30, 2004 as required under French company law (Law 84.148 of March 1, 1984),
- review of the company's operations,
- share repurchase program, delegation of powers to the Chairman and Chief Executive Officer,
- authorizations in respect of guarantees,
- progress report on the offer for Aventis and matters arising,
- appointments to Committees, working procedures of the Board of Directors.

#### October 14, 2004

- review of the interim accounts to August 31, 2004,
- review and approval of the proposed merger of Aventis into sanofi-aventis and related transactions, powers,
- review and approval of information documents as currently drafted, powers,
- powers for miscellaneous formalities associated with the merger,
- calling of an Extraordinary General Meeting:
  - report of the Board of Directors,
  - proposed resolutions,
- working procedures of the Board of Directors – Committees.

#### December 16, 2004

- review of the company's operations,
- report of the Compensation and Appointments Committee:
  - compensation of the Chairman and Chief Executive Officer and the Senior Executive Vice President,
  - principles for the allocation of Directors' attendance fees for the year ending December 31, 2004,
- composition of Committees,
- mandatory offer for Hoechst,
- offering for sale of shares unclaimed following the merger.

#### December 23, 2004

- replies to written questions submitted by shareholders.

## Senior Executive Vice President

The Senior Executive Vice President, who is not a Board member, attended all the Board meetings in 2004:

### Gérard Le Fur, aged 54

*Senior Executive Vice President from December 2002 to 2008*

- Executive Vice President, Science and Medical Affairs, sanofi-aventis
- Director of Sanofi-Synthelabo Inc. (United States)

## Specialist Committees

In 1999, our Board of Directors set up three specialist Committees tasked with providing specialist input to assist the Board in its decision-making.

Members of these Committees are chosen by the Board from among its members.

### ■ Audit Committee

**At December 31, 2004**, the Audit Committee is composed of four Board members, one of whom qualifies as a financial expert within the terms of the Sarbanes Oxley Act:

- Klaus Pohle, Chairman
- René Barbier de la Serre
- Jean-Marc Bruel
- Gérard Van Kemmel

The Audit Committee is responsible for evaluating the existence and effectiveness of our financial controls and risk management procedures. Its responsibilities include reviewing:

- the scope of consolidation,
- the interim and annual parent company and consolidated financial statements,
- control procedures,
- internal audit work programs,
- appropriateness of elective accounting treatments,
- significant risks and material off balance sheet commitments,

- any issue liable to have a material financial or accounting impact,
- major litigation on an annual basis.

The Committee may visit or interview persons responsible for our operations or involved in the preparation of our financial statements. It may interview the statutory auditors with or without management present, and may consult external experts.

It directs selection procedures for statutory auditors when their mandates are due for renewal; it also monitors fees paid to the statutory auditors and compliance with auditor independence rules.

*During 2004, the Audit Committee met six times. The main items on the agendas of these meetings were:*

### February 12, 2004

- comments on the consolidated financial statements for the year ended December 31, 2003,
- update on specific issues relating to the year ended December 31, 2003:
  - management of market risk,
  - draft Report of the Chairman (as required under article 117 of the French Financial Security Law),
- comments and opinion of the statutory auditors,
- parent company financial statements for the year ended December 31, 2003,
- proposed dividend,
- draft press release,
- proposed request for assistance from the statutory auditors in connection with the Internal Control Project pursuant to the Sarbanes Oxley Act and the French Financial Security Law.

### May 5, 2004

- pharmacovigilance presentation,
- update on policy regarding insurance cover,
- update on regulatory changes:
  - approval procedure for audit-related engagements,
  - early warning procedure in cases of fraud.

#### **August 27, 2004**

- presentation of the interim consolidated financial statements to June 30, 2004,
- comments of the statutory auditors on the preparation of the interim financial statements,
- draft press release,
- update on non-audit fees and services.

#### **October 13, 2004**

- review of the interim accounts at August 31, 2004,
- review and approval of the proposed merger of Aventis into sanofi-aventis and related transactions, powers,
- review and approval of information documents as currently drafted, powers,
- powers for miscellaneous formalities associated with the merger.

#### **October 14, 2004**

- interim consolidated financial statements to June 30, 2004.

#### **December 15, 2004**

- evaluation of the Aventis balance sheet entry into the consolidated sanofi-aventis accounts,
- methodology of the financial statements for the year to December 31, 2004 and transition to IFRS.

### **■ Compensation, Appointments and Governance Committee**

At December 31, 2004, this Committee was composed of:

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

#### **The roles of the Compensation, Appointments and Governance Committee are:**

- issuing recommendations and proposals concerning the compensation, pension and welfare benefits of corporate officers, establishing rules for determining the variable portion of their compensation, and formulating general policy on the granting of stock options,
- reviewing the system for allocating attendance fees between Directors and, where appropriate, observers,
- assisting the Board in the selection of new Directors,
- advising on the future composition of management bodies,
- advising the Chairman and Chief Executive Officer on the selection of senior executives and their compensation.

The Compensation, Appointments and Governance Committee met three times in 2004. The main items on the agendas of these meetings were:

#### **May 24, 2004**

- reappointment and/or appointment of Directors,
- consideration of the composition of Board Committees,
- change in the overall amount of Directors' attendance fees.

#### **June 22, 2004**

- appointment of the Chairman and Chief Executive Officer and Senior Executive Vice President,
- composition of Board Committees,
- senior management structure for the new sanofi-aventis Group.

#### **December 6, 2004**

- proposed remuneration packages for the Chairman and Chief Executive Officer and Senior Executive Vice President, review of compensation of senior executives,
- principles for the allocation of attendance fees for 2004 and budget for 2005,
- Board Committees,
- consideration of a 2005 stock option plan.

## Directors' Code

Sanofi-aventis has drawn up a Directors' Code setting out the responsibilities of the Directors and the composition, duties and working procedures of the Board and the Committees.

### 1 - Board of Directors

- The Board of Directors determines the overall orientation of the company's operations and ensures that this is implemented.

In this capacity:

- the Board deliberates on the strategy of sanofi-aventis as proposed by the Chairman and Chief Executive Officer and transactions arising from that strategy, and more generally on any material transaction including major investments and divestments;
  - it appoints the senior executives responsible for running the business, and oversees their management;
  - it oversees the quality of information provided to shareholders.
- When attending and voting at Board meetings, a Director represents all shareholders and acts in the company's corporate interest.

- In preparing for all meetings of the Board and of Committees on which the Board has requested him to sit, a Director must devote adequate time to reviewing the documents provided to him. Directors must receive all the information necessary to fulfil their duties and may request disclosure to them of any document they see fit.
- Directors must inform the Board of any conflict of interest, including potential conflicts of interest, and may not be personally involved in any enterprise competing with the company without informing the Board and obtaining its approval.
- Any Director who holds insider information must, for as long as such information has not been made public, refrain from directly or indirectly entering into any transaction in the company's financial instruments.

### 2 - Committees

- The composition and responsibilities of the Committees are described above.
- Committee decisions are taken by simple majority. In the event of a tie, the Committee Chairman has the casting vote.

## Remuneration and stock-option programs

### ■ Attendance fees allocated to board members (other than the Chairman and Chief Executive Officer and the Senior Executive Vice President)

Attendance fees paid to board members for the financial year 2004 amounted to 823,250 euros <sup>(1)</sup>.

Attendance fees allocated to board members for the financial year 2004 and payable in 2005 amounted to 871,500 euros.

The fixed amount of sanofi-aventis fees is 15,000 euros per director (paid on the basis of time served in the event of a change during the period) plus a supplementary amount for each actual attendance at a meeting of:

- the Board (4,000 euros per director and per meeting);
- the committees (4,000 euros per meeting and 6,000 euros per meeting for committee chairmen).

Some of our Directors also hold options to purchase or subscribe for shares as they were formerly officers or executive officers of sanofi-aventis or its predecessor companies <sup>(2)</sup>.

### ■ Compensation of senior management

The compensation of our Chairman and Chief Executive Officer, our Senior Executive Vice President and of our other senior management members is based on an analysis of the practices of major global pharmaceutical companies and the opinion of the Compensation, Appointments and Governance committees.

In addition to base compensation, senior managers receive variable compensation, the amount of which is determined by the actual performance and growth of the business areas for which the senior manager is responsible. This variable compensation may exceed one-half of base compensation. Senior management may also be awarded stock options (for further information, see "stock options" below).

The total gross compensation before tax charges paid to the 21 members of sanofi-aventis senior management, including the Chairman and Chief Executive Officer and the Senior Executive Vice President in 2004 amounted to 18.74 million euros comprising base compensation of 10.11 million euros and variable compensation of 8.63 million euros.

*The table below sets forth the gross compensation before tax charges paid out in 2004 and 2003 to our Chairman and Chief Executive Officer and our Senior Executive Vice President.*

(in millions of euros)	Compensation paid in 2004			Compensation paid in 2003		
	Total	Base compensation	Variable compensation	Total	Base compensation	Variable compensation
Jean-François Dehecq	2.74	1.20	1.54	2.10	1.00	1.10
Gérard Le Fur	1.73	0.83	0.90	1.35	0.75	0.60

### ■ Stock Options

During 2004, no options to purchase or subscribe for shares were granted.

As of December 31, 2004 a total of 4,185,530 options <sup>(3)</sup> to subscribe or to purchase sanofi-aventis shares have been granted to the senior management of sanofi-aventis, including 740,000 stock options for the Chairman and Chief Executive Officer and 377,000 for the Senior Executive Vice President. During 2004, the senior management of sanofi-aventis exercised 317,900 options to purchase or to subscribe for shares including 32,000 sanofi-aventis shares at 21.46 euros per purchase option exercised by the Senior Executive Vice President.

As of December 31, 2004, 3,517,307 options held by senior management were outstanding including 680,000

stock options held by the Chairman and Chief Executive Officer and 345,000 held by the Senior Executive Vice President.

As of December 31, 2004, a total of 73,254,498 <sup>(4)</sup> options to subscribe or to purchase sanofi-aventis shares were outstanding, of which 39,905,179 were immediately exercisable.

The main characteristics of our stock option plans are described in the 20-F document for 2004.

(1) The remuneration paid to Directors in 2004 is detailed in the 20-F document for 2004.

(2) Information detailed in the 20-F document for 2004.

(3) Current plans including those closed during the year.

(4) Including 60,339,128 subscription options and 12,915,370 purchase options.

# ➤ A RELATIONSHIP BASED ON TRUST OUR SHAREHOLDERS

- ▶ **83 billion euros** market capitalization\*
- ▶ **2nd largest market capitalization** on the CAC40
- ▶ One of the **5 largest market capitalizations** in the pharmaceutical industry worldwide

\* At December 31, 2004.







**The new Group is up and running,**  
one year after Sanofi-Synthélabo launched  
its bid for Aventis

# Sanofi-aventis moved up to second place in the CAC 40 by market capitalization

- *Following the merger, sanofi-aventis moved up to second place in the CAC 40 by market capitalization, and its weighting in the CAC 40 is now 10.3%\**

## Outlook for 2005

When the Group's results for 2004 were published, Chairman and Chief Executive Officer Jean-François Dehecq stated: "Barring major adverse events, sanofi-aventis expects to see:

- 2005 sales growth, on a comparable basis, outperforming the world pharmaceutical market,

- at an exchange rate of 1 euro per 1.25 dollar, adjusted growth in earnings per share equivalent to that recorded in 2004."

*The sensitivity of this growth rate is estimated at 0.5% for a 1-cent change in the euro/dollar exchange rate.*

### ■ 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

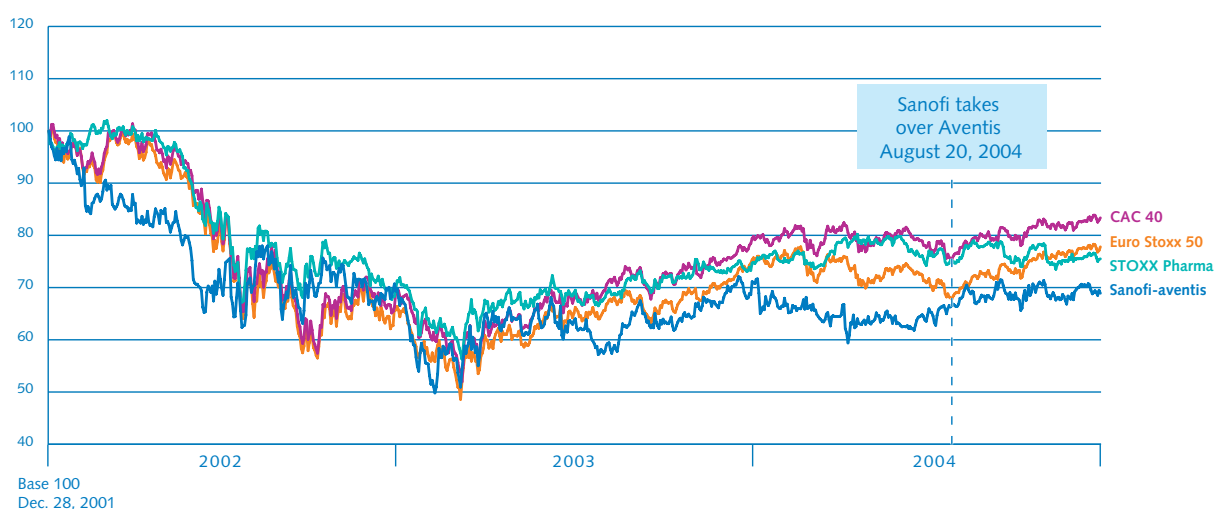
- Par value of share: **2 euros**
- Traded on
  - Eurolist Compartiment A – Paris (code SAN)
  - New York Stock Exchange (Ticker SNY)
- ISIN code **FR0000120578**
- Trading
  - continuous in Paris, eligible for the SRD deferred settlement service and for PEA saving schemes
  - continuous in New York.

\* At March 17, 2005.

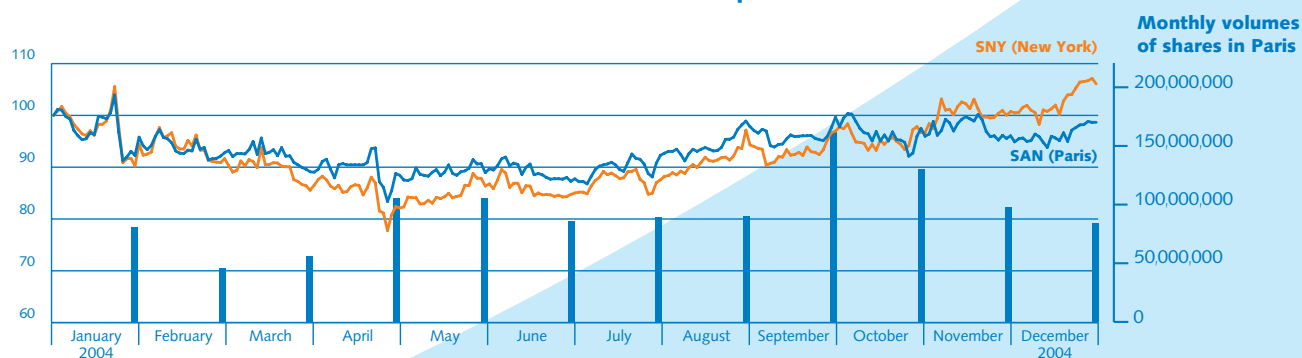
## Trend in share price

### ■ Sanofi-aventis on the Euronext Eurolist Compartment A in Paris

At December 31, 2004, the sanofi-aventis share price had progressed by 5.66% since the takeover of Aventis on August 20, 2004.



### ■ Sanofi-aventis in Paris on the Euronext Eurolist Compartment A and in New York on the NYSE

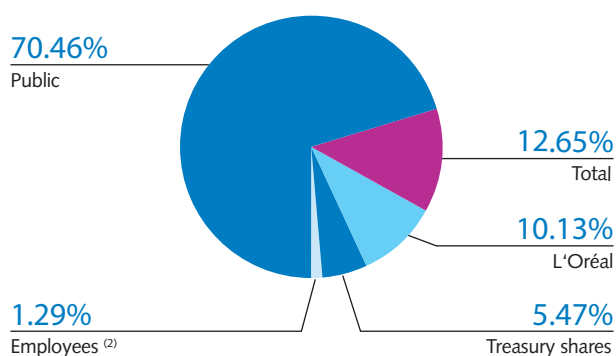


## Share ownership and evolution in 2004

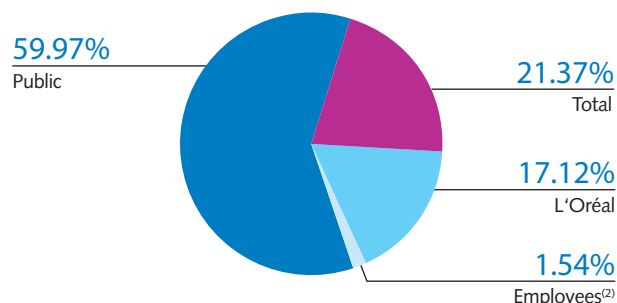
As of December 31, 2004, sanofi-aventis share capital amounted to 2,822,808,634 euros, divided into 1,411,404,317 shares with a par value of 2 euros.

### Sanofi-aventis Share Ownership as of December 31, 2004

#### ■ Shares



#### ■ Voting rights<sup>(1)</sup>



A shareholders' agreement between L'Oréal and Elf-Aquitaine (through which Total became a shareholder) signed on April 9, 1999 for an initial period of 6 years starting from December 2, 1998, ended on December 2, 2004.

(1) On the basis of the total number of voting rights as of December 31, 2004, after the acquisition by Sanofi-Synthelabo of Aventis and subsequent merger into sanofi-aventis.

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

### Shareholder information at a glance

	1999	2000	2001	2002	2003	2004
<b>Number of shares as of December 31*</b>	<b>731,143,218</b>	<b>731,441,746</b>	<b>732,005,084</b>	<b>732,367,507</b>	<b>732,848,072</b>	<b>1,411,404,317</b>
<b>Share price in euros</b>						
High	46.35 **	71.00	86.50	84.30	60.00	63.25
Low	34.72 **	34.70	52.60	49.78	41.50	49.42
Latest	41.34	71.00	83.80	58.25	59.70	58.80
<b>Market capitalization as of December 31 (in millions of euros)</b>	<b>30,225</b>	<b>51,932</b>	<b>61,342</b>	<b>42,660</b>	<b>43,751</b>	<b>82,990</b>
<b>Ranking in CAC 40 by market capitalization</b>	<b>15</b>	<b>8</b>	<b>4</b>	<b>3</b>	<b>6</b>	<b>2</b>

\* On the basis of shares issued.

\*\* From May 25, 1999.

# OUR SHAREHOLDERS

## Shareholder information

- *In 2004, sanofi-aventis was committed to ensuring that both individual and institutional shareholders, analysts and journalists were provided with a regular flow of transparent, comprehensive and readily accessible information on Group strategy and results.*



### ■ Group publications

The Letter to Shareholders is a vital link between the Group and its shareholders. As well as featuring information on stock markets and practical details for sanofi-aventis shareholders, it also includes regular updates on the Group's strategy, results and key therapeutic areas.

When preparing its detailed financial communication, sanofi-aventis goes well beyond its legal obligations to ensure that shareholders are fully informed of what is happening within their Group.

The annual report is a widely circulated document, available on request.

Regulatory filings—the Reference Document filed with the *Autorité des Marchés Financiers* and U.S. Form 20-F filed with the Securities and Exchange Commission—can also be obtained via the website or by calling the toll-free numbers indicated.

## ■ Information on-line

[www.sanofi-aventis.com/investors](http://www.sanofi-aventis.com/investors)

The sanofi-aventis corporate website provides the Group's stakeholders with real-time access to all available information (financial documents, Letters to Shareholders, press releases, live and recorded webcasts of financial events, etc.) needed to understand and monitor Group activities.

Individual shareholders can go direct to a specific page which contains information of particular interest to them, including helpful information, key dates of shareholder events and contact details.



## ■ Shareholder hot-line

Shareholders can obtain a current stock quote and the latest news from sanofi-aventis via a voicemail server<sup>(1)</sup>. An advisor is also available to answer any questions shareholders may have.

## ■ Regular information meetings

The Group's commitment to dialogue and information is demonstrated at the local level by shareholder information meetings, at which shareholders in cities around France have a chance to meet and put their questions to Group managers.

Sanofi-aventis also attends the Actionaria investor fair held every November, which offers an exceptional opportunity for informal contacts and exchanges of views with shareholders.

The Shareholders' General Meeting is also a keynote event in the year for shareholders keen to learn more about Group strategy and, by casting their vote, to play a part in the life of their Group. The 2004 Shareholders' General Meeting was, like its predecessor, relayed by live and recorded webcasts.

Meetings with international institutional investors provide opportunities for in-depth exploration of issues relating to the Group's operations and strategy.

## ■ Individual Shareholders Committee

The sanofi-aventis Individual Shareholders Committee is a consultative body which keeps sanofi-aventis management teams informed of the views of individual and minority shareholders and supports the Group by participating in strategic planning of communication projects, in producing documents for shareholders and posting information on the Individual Shareholder website and in preparing for Shareholders' General Meetings and local shareholder meetings.

(1) See contacts page 29.



## Financial communications calendar for 2005

- **Tuesday, March 1, 2005:**  
2004 Full Year earnings
- **Monday, March 21, 2005:**  
Analyst/Investor Meeting in New York
- **Thursday, April 14, 2005:**  
Analyst/Investor Meeting in Paris on the impact of IFRS norms
- **Friday, May 13, 2005:**  
2005 first-quarter sales and earnings
- **Tuesday, May 31, 2005:**  
Annual General Meeting of shareholders
- **Wednesday, July 20, 2005:**  
2005 second-quarter sales
- **Wednesday, August 31, 2005:**  
2005 first-half earnings  
Analyst/Investor Meeting in Paris
- **Tuesday, November 8, 2005:**  
2005 third-quarter sales and earnings

## ■ Contacts

	Individual Shareholders	Institutional Investors, Analysts	Journalists
<b>Tel.</b>	<b>France:</b> Toll-free +33 (0) 800 075 876 <b>Europe:</b> Toll-free +33 (0) 800 00 075 876 <b>U.S.:</b> Toll-free +1 (0) 888 516 3002 For individual shareholders holding shares registered with BNP Paribas Tel: +33 (0) 800 877 432	<b>Paris:</b> +33 (0) 1 53 77 45 45 <b>New York:</b> +1 (0) 212 551 40 18	+33 (0) 1 53 77 42 23
<b>Fax</b>	+33 (0) 1 53 77 91 57	+33 (0) 1 53 77 42 96	+33 (0) 1 53 77 42 65
<b>E-mail</b>	relations-actionnaires@sanofi-aventis.com	IR@sanofi-aventis.com	media-relations@sanofi-aventis.com
<b>Mail</b>	Sanofi-aventis Individual Shareholders Department 174, avenue de France 75013 Paris France	Sanofi-aventis Investor Relations Department 174, avenue de France 75013 Paris France	Sanofi-aventis Media Relations Department 174, avenue de France 75013 Paris France

# ➤ GROUP STRATEGY for more than 30 years



## ■ **AMBITIOUS RESEARCH** to ensure sustainable growth

Products developed through research are the key to medium and long-term growth. With the merger, sanofi-aventis demonstrated its capacity to select the best compounds and the best projects. Sanofi-aventis must now strengthen its R&D investments to accelerate product development, the condition for future growth.



## ■ **MEDICINES AND VACCINES – AN ORIGINAL STRATEGY**

Innovation regarding new public healthcare challenges and active efforts for basic medicines, generating solid results and savings for health systems

For sanofi-aventis, growth requires a solid basis for its product portfolio. This means strengthening the foundation, consisting of mature and local medicines, on which flagship products and novel medicines will build their growth.





# THE GROUP

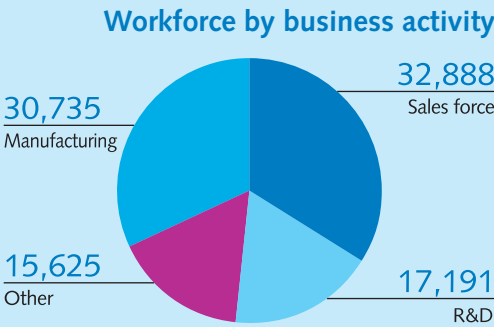


The sanofi-aventis Group is present in 80 Countries  
with its R&D, manufacturing and commercial  
business activities

is up and running



Our presence worldwide by business activity



# ➤ ENSURING STRONG, SUSTAINABLE AND PROFITABLE GROWTH

to continue providing therapeutic solutions  
to all patients worldwide



## ■ A RESOLUTELY GLOBAL PRESENCE

to facilitate access to health for all  
and to ensure the Group's growth

Because there are "no small markets", sanofi-aventis defends all its products throughout the world. To ensure their growth, the Group focuses on improving its manufacturing facilities and optimizing its marketing and sales resources.



## ■ RESOURCES MOBILIZED

to serve the greatest number

Sanofi-aventis is aware of the duties that accompany its position as a world leader, and makes every effort to act as a responsible corporate citizen. Ethics, quality, safety and social performance are the basis of the Group's commitment to society as a whole.



# Sanofi-aventis dedicates its research to finding solutions for future therapeutic challenges

## G rard Le Fur

Senior Executive Vice President,  
Executive Vice President, Science and Medical Affairs



### What are the major research issues facing sanofi-aventis?

Progress has been spectacular in cardiovascular disease, thrombosis and oncology, helping to increase life expectancy.

As populations age, however, other pathologies are emerging. They may not be new, but they are much more frequent than they used to be. This is true for Alzheimer's and Parkinson's diseases and multiple sclerosis. All these neurodegenerative diseases are indisputably the major issues we have to cope with.

Obesity and diabetes are also problems. Today, one American in three is obese and this epidemic—and it really is an epidemic—threatens many other countries.

Obesity is an important factor in cardiovascular risk and diabetes. In today's world, there are more people dying from obesity than from famine.

Research will also need to be on the alert for viral endemics, such as avian flu. This type of infection can develop into a modern pandemic like the Spanish flu in 1918. Finally, there is a need to develop new antibiotics with greater potency against infectious agents.

### What is so special about sanofi-aventis R&D?

Clearly, the most important sanofi-aventis characteristic is that we never privilege blockbusters to the detriment of other drugs. Every time we find a promising lead, we go right ahead, regardless of how large or small a market there may be for it.

"There are no small markets and no small products". This is not just a catch phrase. It is a system of values that holds both for sales strategies and for R&D.

The minute we are convinced that research can culminate in a successful treatment for patients, even if it is not going to be financially rewarding for us, we set to work with force and conviction.

As citizens of the world, we see ourselves as having a duty to carry out research that will both help poor countries and justify the price of innovative and effective products in countries that can afford to pay for them. We believe that this is our dual role: to earn money so that we can spend a great deal of it on R&D.

### How is sanofi-aventis programming its research to respond to the crucial issues of the future?

Above all, we are reaching out for new approaches, new targets and new pharmacological classes. For instance, as regards the central nervous system, we are searching for new psychotropic drugs to overcome depression, schizophrenia and anxiety, but we are also looking for medicines that could slow down the progress of neurodegenerative diseases. We are working on the idea of developing a neuroprotective drug that could prevent neurons from dying. In other words, we would be offering a treatment for the cause of a disease rather than its symptoms.

Over 17,000 research staff\*, a 4 billion euros budget, a portfolio of the most innovative drugs: are numbers important for sanofi-aventis?

Yes, of course, but other things are also important. Our international R&D approach is what enables us to make a qualitative rather than a quantitative difference. Whereas others may adopt a more dogmatic approach, centered on the notion that there is only one way of discovering a medication, we are more pragmatic. Our researchers are Italian, British, German, Hungarian, French, American, Spanish... So they are naturally diverse.

Although technology is the same for everyone, approaches to Research are deeply individual and embedded in a particular cultural methodology. This impressive cross-fertilization is a rich lode that we are very aware of and it makes an unquestionable contribution to the strength and pertinence of our Group.

\* Including: Vaccines, Industrial Development  
Medical/Regulatory staff of subsidiaries



# Sanofi-aventis is committed to building international development, responding to major therapeutic needs

## ■ Hanspeter Spek

Executive Vice President, Pharmaceutical Operations



### What are the major internationalization issues facing sanofi-aventis?

As we see it, the challenges of internationalization for our industry are concentrated in three key geographic areas. First of all Europe, the birthplace of sanofi-aventis. A Europe now made up of 25 different countries, each with as many similarities and differences as the next, especially when it comes to drug pricing regimes and health systems... And, of course, with all the consequences that can have in terms of marketing our products. Then there is the U.S., the pharmaceutical industry's biggest market. No pharmaceutical firm can call itself international unless it has achieved success and made its mark here.

Then comes what we call the Intercontinental zone, in which we include Japan, the world's second largest pharmaceuticals market. This zone covers an immense variety of markets, from Latin America to Asia by way of Africa.

### How do you distinguish, or how do you intend to distinguish, between each of these geographic zones?

The fact that sanofi-aventis has its roots in Europe, that it is now Europe's number one pharmaceutical group, has a certain impact on our success in other countries around the world. In the light of European diversity and all that it entails, we can safely say that if sanofi-aventis can succeed in becoming number one in Europe, then we can succeed anywhere, and we have begun working towards that. Sanofi-aventis ranks fifth in the U.S.\* and has outperformed market growth for the past four years. The Group also has a strong presence in Latin America and Africa, and is one of the leading players in the health-care sector in Japan.

\* IMS 10 channels NSP, MAT December 2004, developed figures including 100% of sales of Plavix®, Avapro®/Avalide® and Copaxone®.

## What exactly is the sanofi-aventis method? In the U.S., for example...

When the group (just Sanofi at the time) moved into the U.S. market, our ambition was to succeed and we deployed the human and financial resources needed to achieve that success. Our sales team was oversized in comparison to our situation at the outset. But we knew there was great potential for growth in the future and were prepared for it.

We also made good use of every opportunity offered by the market, launching products that are still growth drivers today, from Plavix® in 1997 to Ketek® in 2003. We installed a management team made up of a perfect mix of U.S. and European talents. Today sanofi-aventis in the U.S. is a group with all the infrastructure needed to operate independently; industrial facilities, Research & Development, the second largest sales network in the market. The combination has proved itself a winner: if you don't believe me, just take a look at our results!

## You seem to consider European nationality as a decisive advantage for the future development of sanofi-aventis.

By its sheer diversity, Europe has to be the most difficult and most complex market around.

When you look at current trends in the U.S., you see a form of regionalization between different states beginning to emerge. That's a sign that the U.S. market is also becoming more complex in response to the country's economic constraints, pressure on prices, and so on. These are factors that we know and are used to dealing with; we have the experience and the knowhow to cope with them in all serenity.

The Intercontinental zone, which is made up of both developing and highly-developed countries, is vast not only in terms of distances but also, and most importantly, in terms of diversity of cultures. Once again, our experience in Europe is an advantage.

We are extremely fortunate in being a European pharmaceutical group with an international dimension. Fortunate in that we do not see the world from a single, standardized and monolithic viewpoint, but instead are able to adapt to the very different realities of our different markets.

## "No small markets and no small products": how can this approach still apply to the world's third largest pharmaceutical group and the number one in Europe?

This was always the firm belief of Sanofi-Synthélabo and now it has been adopted by the sanofi-aventis teams.

"No small markets and no small products": in essence, that means endeavoring to meet the needs expressed by patients, health professionals and the health authorities. To achieve this, we give each of our local managers the resources needed to keep our pledge, and we have laid down criteria that enable us to continue supporting our established reference medicines, a solid foundation on which to build growth for our flagship products.



# ➤ OUR RESEARCH AND DEVELOPMENT

- More than **17,000 research staff\*** around the world
- Rapid integration of R&D teams enabling a complete review of the compound portfolio and **selection of the most promising projects capable of meeting major public health challenges**
- **128 compounds in development** including
  - 48** projects in late-stage development (phases II and III)
  - 80** projects in phase I and preclinical development

\* Including: Vaccines, Industrial Development,  
Medical/Regulatory staff of subsidiaries

**7** major therapeutic areas



Cardiovascular ■ Thrombosis ■ Oncology





Our profession...

**Innovative, ambitious research**  
to ensure sustainable growth

▪ Central Nervous System ▪ Metabolic Disorders ▪ Internal Medicine ▪ Vaccines

# An extensive and well-balanced compound

	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Launched / LCM
<b>1 ■ CARDIOVASCULAR</b>						
	AVE 0657 AVE1231 AVE 3085 AVE 4454 AVE 4890	SL 65.0472 AVE 9488 HMR 1069	AVE0118 HMR 1766 AVE 7688	XRP0038 SSR 149744	dronedarone (SR 33589)	Aprovel® (irbesartan) Delix® (ramipril)
<b>2 ■ THROMBOSIS</b>						
	SSR 128428 SSR 128429 AVE 3247 AVE 6324	SSR 126517 AVE 5026 (octaparine)	SSR 182289	otamixaban (XRP 0673) SR 123781	Idraparinux (SR 34006)	Plavix® (clopidogrel) Lovenox® (enoxaparin)
<b>3 ■ CENTRAL NERVOUS SYSTEM</b>						
	SSR 101010 SSR 103800 SSR 125543 SSR 126374 SSR 180711 SSR 241586 SSR 411298 SSR 504734 AVE 1876 AVE 8112 AVE 8488	SSR 149415 AVE 1625 * AVE 9897 *	HP 184	SR 57667 SSR 591813 SL 65.0155 * eplivanserine (SR 46349) osanetant (SR 142801) M100907	zolpidem MR SR 58611 xaliproden * (SR 57746) teriflunomide® (HMR 1726) saredutant (SR 48968)	Stilnox® (zolpidem) Depakine® Chrono (sodium valproate) Rilutek®
<b>4 ■ ONCOLOGY</b>						
	SSR 97225 SSR 128129 SSR 244738 SSR 250411 AVE 1642 AVE 9633 CEP 11981	SSR 125329 CEP 7055 (Cephalon) AVE 0005 AVE 8062	uvidem (IDM) XRP 6258	SR 31747 meclinetant (SR 48692)	tirapazamine (SR 259075) XRP 9881 xaliproden * (SR 57746)	Eloxatin® (oxaliplatin) Fasturtec® (rasburicase) Taxotere® (docetaxel)
<b>5 ■ METABOLIC DISORDERS</b>						
	SSR 162369 AVE 0897 AVE 2865 AVE 5376 AVE 9423	AVE 0847 AVE 1625 * AVE 2268 AVE 5530 AVE 5688 AVE 8134	AVE0010	SR 147778	Acomplia™ (rimonabant) Exubera® (HMR 4006)	Amaryl® (glimepiride) Lantus® (HOE901) Apidra® (HMR1964)
<b>6 ■ INTERNAL MEDICINE</b>						
	SSR 126768 SSR 161421 AVE 0675 AVE 0950 AVE 1330 AVE 1701 AVE 4221 AVE 8680 AVE 8923	ferroquine (SSR 97193) SSR 150106 SSR 180575 SSR 240600 SSR 240612 AVE 5883 AVE 9897 * AVE 9940 XRP 2868	SL 65.0155 * pleconaril HOE 140	SR 140333	SR 121463 Alvesco® (XRP 1526/ AVE 2635) Flisint®	Xatral® (alfuzosin) Ketek® (telithromycin) Actonel® (risedronate) Allegra® (fexofenadine) Arava® (leflunomide)

# portfolio in seven therapeutic areas

	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Launched / LCM
<b>7 ■ VACCINES</b>	DTP-HepB-Hib <sup>(1)</sup> Meninge B Meninge A, C, Y, W infant Pneumo Flu pandemic Flu Cell Rabies Yellow Fever Melanoma Colorectal	Improved flu Dengue mild to severe	CMV HIV therapeutic	DTP-HepB-Polio-Hib <sup>(1)</sup> DTP-HepB-Polio-Hib <sup>(1)</sup> Menactra® toddler Flu intradermal	Pentacel™ HIV	Pediacel® Menactra®

## 128 compounds in development

	Preclinical	Phase I	Phase IIa	Phase IIb	Phase III	Total
CARDIOVASCULAR	5	3	3	2	1	14
THROMBOSIS	4	2	1	2	1	10
CENTRAL NERVOUS SYSTEM	11	3	1	6	5	26
ONCOLOGY	7	4	2	2	3	18
METABOLIC DISORDERS	5	6	1	1	2	15
INTERNAL MEDICINE	9	9	3	1	3	25
VACCINES	10	2	2	4	2	20
<b>TOTAL</b>	<b>51</b>	<b>29</b>	<b>13</b>	<b>18</b>	<b>17</b>	<b>128</b>

► 48 projects in phases II et III

► 80 projects in phase I and preclinical

\* Compounds in several therapeutic areas.

(1) D=Diphtheria, T=Tetanus, Hib=H influenzae b, HepB=Hepatitis B, P=Perfussis.

# ► Portfolio highlights in 2004

■ **128** compounds in development in 7 major therapeutic areas

**48** compounds in phases II and III

**80** compounds in preclinical development and phase I

**18** Life Cycle Management projects

## ■ 10 new compounds in preclinical development

Pharmaceutical activity in 2004 listed 10 new compounds entering the development phase of which six concern disorders of the central nervous system. Our portfolio for this therapeutic area includes:

- **SR 180711A**, a nicotinic alpha-7 receptor partial agonist, for the symptomatic treatment of **Alzheimer's disease and schizophrenia**;
- **SSR 126374P**, a CRF1 (corticotrophin releasing factor 1), receptor antagonist for the treatment of **depression and anxiety**;
- **SSR 101010**, a FAAH (fatty acid amide hydrolase) inhibitor, for the treatment of **anxiety and pain**;
- **SSR 103800A**, a glycine transporter 1 (Glyt1), inhibitor for the treatment of **schizophrenia**;
- **AVE 8112A**, a phosphodiesterase IV inhibitor, for the symptomatic treatment of **Alzheimer's disease**;
- **AVE 1876A**, a GABA-B (gamma-aminobutyric acid-B) receptor antagonist, for **depression and anxiety**;
- **AVE 8923A**, a tryptase inhibitor, for the treatment of **asthma**;
- **AVE 4454A**, a NHE-1 (sodium hydrogen exchanger type 1) inhibitor for the protection of **cardiac function**;
- **AVE 9423A and AVE 2865A**, two glycogen phosphorylase inhibitors, for the treatment of **type 2 diabetes**.

## ■ 5 compounds entered phase IIa

### ■ 13 phase IIb trials

for 12 compounds, including 2 trials in Japan.

### ■ 4 phase III programs

have been initiated for indications in breast cancer (XRP 9881, a new taxoid) multiple sclerosis (teriflunomide), major depressive disorders (saredutant) and hyponatremia (SR 121463).

## ■ New submissions expected in 2005

### Cardiovascular

- Aprovel® (irbesartan), new Combo dosage (300/25 mg), Europe
- Dronedarone, atrial fibrillation, Europe and U.S.

### Thrombosis

- Plavix® (clopidogrel), acute myocardial infarction, Europe and U.S.

### Central Nervous System

- Stinoxium™ (zolpidem MR), Mutual Recognition Procedure in Europe

### Oncology

- Taxotere® (docetaxel), gastric cancer, first line, Europe and U.S.
- Taxotere® (docetaxel), head and neck locally advanced neoadjuvant, Europe and U.S.
- Taxotere® (docetaxel), head and neck recurrent metastatic, Europe and U.S.

### Metabolic Disorders

- Acomplia™ (rimonabant), obesity, Europe and U.S.
- Acomplia™ (rimonabant), smoking cessation, Europe and U.S.

### Internal Medicine

- Allegra® (fexofenadine), orally disintegrating tablet, U.S.
- Allegra® (fexofenadine), pediatric liquid, U.S.

### Vaccines

- Pentacel™, pentavalent pediatric vaccine, U.S.

### ■ Many of these compounds are the first to be developed in their pharmacological class

The originality of these products underlines the innovative capacity of sanofi-aventis R&D. Above all, they bring the hope of real therapeutic progress for patients. These compounds include:

- **Rimonabant**, the first antagonist of cannabinoid CB1 receptors for the treatment of obesity, metabolic syndrome and smoking cessation.
- **Saredutant**, the first antagonist of the NK2 receptors, and SSR 149415, the first antagonist of the vasopressin V1b receptors, for the treatment of anxiety-depression syndromes.

- **Triapazamine**, the first anti-cancer agent active in hypoxic conditions (treatment of head and neck cancer) and SR 31747, the first ligand of the sigma sites in development for the treatment of prostate cancer.
- **Exubera®**, the first rapid-action inhaled insulin.
- **Idraparinux**, the first synthetic long-acting synthetic oligosaccharide for the treatment of thrombo-embolic events.

**"First in class"**: the first product to be developed for a specific biological target or for future therapeutic indications.

## New Drug Applications (NDA)

A New Drug Application (NDA) is a submission for approval of a novel compound for an initial indication. **Supplementary** applications are filed to obtain an extension of existing indications or complementary indications, or approval for new pharmaceutical forms of products already present on one of the three main markets (United States, Europe, Japan).

### ■ 34 NDAs, original and supplementary, were filed in the United States, Europe and Japan in 2004

- **4 NDAs** were filed in the United States and in Europe for Exubera® (inhaled insulin) in the treatment of diabetes and zolpidem MR for insomnia (in the United States, France and Switzerland; the mutual recognition process should be initiated in Europe in 2005).
- **1 NDA** was filed in France for Flisint® (fumagillin) for treatment of a very rare disease, microsporidiosis in severely immunocompromised patients. Sanofi-aventis maintains its commitment to developing new therapies in areas where unmet medical needs are still very

high, however small the population concerned. Flisint® has been granted orphan drug status in Europe.

- **2 NDAs submitted** in Japan, Plavix® in stroke and Allegra® for pediatric indications.
- **27 supplementary NDAs have been submitted**, of which 14 in the United States, 11 in Europe and 2 in Japan for flagship products such as Apidra®, Ketek®, Lantus®, Taxotere® and Eloxatin®.

*For further information on the above, see the "Medicines" section of this report.*

### ■ New NDAs were granted in 2004

In 2004, Apidra® (insulin glulisine) was approved for the treatment of diabetes in the United States and Europe and Ketek® was registered in the United States for the treatment of bacterial infections.

### ■ 21 supplementary NDAs were granted in 2004 and in January 2005

for major products such as Taxotere®, Eloxatin®, Allegra® and Lantus®, of which 8 in the United States, 11 in Europe and 2 in Japan.

# A productive and well-balanced portfolio with clear objectives

■ *Sanofi-aventis R&D gives priority to creativity, enterprise and innovation, with a single objective: patient health. With a global force of 17,191 research staff working to design new, effective and well-tolerated medicines, the Group now has one of the richest and most innovative portfolios of compounds in the whole of the pharmaceutical industry.*

## Project-based R&D organization

*The Discovery Research and International Development departments each have their own specific organizational approach, but both work towards the same goal: discovering and developing new compounds with the potential to become the groundbreaking drugs of the future and meet major public health needs.*

### ■ Discovery Research

Discovery Research is responsible for identifying the most promising research targets for therapeutic innovation, and capitalizes on its biological and chemical skills to discover and propose new candidate compounds for development.

Every year, Discovery Research puts forward 15 to 20 compounds potentially capable of providing solutions to unmet treatment needs or of improving existing treatments (enhanced efficacy, pharmaceutical forms offering greater patient comfort, etc.).

### ■ International Development

International Development takes the compounds proposed by Discovery Research and turns them into medicines. As soon as a compound enters development, a dedicated project team is set up with members drawn from a wide range of functions and including

researchers, clinicians, pharmacists, toxicologists and representatives from Regulatory Affairs and Marketing. The team's task is to pursue the development of the compound throughout its development and all the way to marketing. This matrix organization adopted by sanofi-aventis ensures effective monitoring and coordination of every aspect of development activity throughout the procedure and makes a major contribution to the success of each project.

## Targeted partnerships to support the development of innovative products

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

### ■ Discovery Research

Two types of partnership are employed to boost Discovery Research:

- **Technological partnerships** giving sanofi-aventis teams access to new technology and extending their research and skills areas. Examples:

**Cerep** (Rueil-Malmaison, France): screening new exclusive synthetic chemical libraries against promising new biological targets.

**GeneLogic** (Gaithersburg, Maryland, U.S.): two global licenses to use toxicogenomic technologies, enabling access to expression profiling databases.

**Amphora** (Durham, North Carolina, U.S.): an agreement was signed in 2004 on the screening of specialist chemical libraries using microfluid-based compound profiling.

**FunGenES** (a European public-private sector consortium, jointly financed by the EU): a collaborative initiative launched in 2004 for research on mouse embryonic stem cells in order to improve their characterization and use in screening.

- **Partnerships on innovative products, to maximize opportunities of exploring new leads in our therapeutic areas of excellence:**

**Millennium** (Cambridge, Massachusetts, U.S.): validating novel biological targets in the field of inflammation and taking high value-added compounds rapidly forward to the development phase.

**Astex** (Cambridge, U.K.): measuring the binding properties of proprietary compounds with P450 apoenzymes and selecting the best development candidates.

**Immunogen** (Cambridge, Massachusetts, U.S.): identifying and developing "naked" antibodies or immunoconjugates (monoclonal antibodies associated with an anti-cancer agent) in oncology.

**Coley** (Wellesley, Massachusetts, U.S.): global license and collaboration agreement on research into CpG oligonucleotides, which act as immunomodulators, for the treatment of certain respiratory disorders.

**Mitsubishi Pharmaceutical Corp.** (Tokyo, Japan): identifying and developing new protective agents for the treatment of neurodegenerative diseases.

- As part of the "Impact Malaria" program, three cooperative programs were continued in 2004. Ferroquine, co-developed with the *Université Scientifique et Technique de Lille (France)*, is currently in phase I of clinical development.

#### ■ International development:

Three R&D agreements

**Cephalon** (West Chester, Pennsylvania, U.S.): discovery and development of innovative small compounds able to inhibit tyrosine kinase pathways by blocking VEGF receptors and thus inhibiting angiogenesis. Angiogenesis, or the development of capillary blood vessels, is a crucial mechanism in tumor development.

CEP 7055, a VEGFR inhibitor, is currently in phase I.

**Regeneron Pharmaceuticals Inc.** (Tarrytown, New York, U.S.): joint development of a recombinant fusion protein, the VEGF Trap, that produces soluble decoy-receptors which bind to VEGF (Vascular Endothelial Growth Factor), stopping it from stimulating the natural VEGF receptor and thus preventing angiogenesis. Clinical phase I trials are ongoing.

**Immuno-Design Molecule** (IDM) (Paris, France): cooperation agreement on the development and marketing of immunological treatments for cancer. The purpose of the agreement is to develop autologous cell vaccines, using cellular therapy technology based on monocyte maturation using Interleukin-13. Therapeutic vaccine Uvidem, developed under the agreement, is currently in phase II trials for the treatment of melanoma in the U.S.

*For other products developed in the framework of other research agreements with various pharmaceutical companies, such as Alvesco® (Altana AG), Actonel® (Procter & Gamble Pharmaceutical) and Exubera® (Pfizer), details concerning the most recent progress made are to be found elsewhere in this report, in the chapter "Our main clinical studies on compounds" for Alvesco® and Exubera® and in the section on medicines for Actonel®.*

# ▶ OUR MAIN CLINICAL STUDIES ON COMPOUNDS in late-phase development in our seven main therapeutic areas

- *Today, the main priority for our R&D is to provide patients with effective, well-tolerated medicines as rapidly as possible. When it comes to diseases that are difficult to treat, such as Alzheimer's disease or depression, or to the fields of oncology and diabetes, we increase our chances of developing groundbreaking treatments that will provide a real patient benefit by pursuing a number of different pharmacological and scientific approaches: this explains why clinical trials may be carried out simultaneously on different compounds to treat the same disease and indication.*

## 1 ■ CARDIOVASCULAR

### **Dronedarone** Atrial fibrillation

#### **Phase III**

A potential new treatment for the most common cardiac rhythm disorder:

Atrial fibrillation affects up to 8% of the over-80s, around 1 million patients worldwide. Dronedarone is the potential successor to Cordarone® (amiodarone) the reference anti-arrhythmic marketed by sanofi-aventis since the late 1960s. The aim is to provide patients with a treatment that is at least as effective but with improved tolerability.

The first indication developed for dronedarone is to prevent recurrence of atrial fibrillation. The usual treatment for acute atrial fibrillation is delivery of an external electric shock to the heart, generally followed by medication 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 confirmed the efficacy and tolerability of dronedarone as an anti-arrhythmic, and in particular the absence of any pro-arrhythmic effect.

On the strength of these results, an NDA is being prepared for submission to the regulatory authorities.





## SSR 149744

Atrial fibrillation

### Phase IIb

Sanofi-aventis is continuing its efforts to pursue new treatments for cardiac arrhythmia, one of its fields of excellence. This new compound should prove highly effective on a once-daily dosage.

The compound entered phase IIb in December 2004.

## 2 ■ THROMBOSIS

### Idraparinux (SR 34006)

- Long-term treatment of thrombo-embolic events
- Prevention of thrombo-embolic events associated with atrial fibrillation

### Phase III

Idraparinux sodium is an injectable synthetic pentasaccharide that selectively inhibits coagulation factor Xa. Its potency and long duration of action, demonstrated in the course of clinical trials, suggest that a treatment regimen of one weekly injection may be possible.

Two phase III clinical trials, launched in 2003, are still under way: VAN GOGH and AMADEUS. The VAN GOGH program is studying the efficacy of idraparinux sodium in the long-term treatment and secondary prevention of thrombo-embolic events in patients presenting with deep venous thrombosis or pulmonary embolism. The AMADEUS program is studying the efficacy of idraparinux sodium in the prevention of thrombo-embolic events associated with atrial fibrillation.

### SR 123781

Prevention of major cardiovascular events in acute coronary syndrome

### Phase IIb

SR 123781 is an injectable synthetic oligosaccharide that inhibits coagulation factors Xa and IIa. This powerful anti-thrombotic has a shorter duration of action than idraparinux sodium and is currently being studied in a phase IIb clinical trial involving patients suffering from arterial thrombosis.

### Otamixaban (XRP 0673)

Acute coronary syndrome

### Phase IIb

Otamixaban is a selective direct inhibitor of coagulation factor Xa. This new generation of injectable non-saccharidic synthetic anticoagulants, fast-acting yet of short duration, offers a promising approach for the initial treatment of acute coronary syndrome.

### 3 ■ CENTRAL NERVOUS SYSTEM (CNS)

*Sanofi-aventis has one of the most extensive and promising portfolios in the field of Central Nervous System disorders. A number of strong candidates are currently being developed in the fields of Alzheimer's disease, schizophrenia, depression and anxiety. In this particularly complex therapeutic area, where there are many medical needs still unmet, these compounds hold out real hope of bringing forward new treatments.*



#### **SR 58611**

Treatment of depression

##### **Phase III**

SR 58611 is a beta3 adrenergic receptor agonist which stimulates neuronal activity in a specific area of the prefrontal cortex, and could give rise to a new class of anti-depressants. In a phase II trial of patients suffering from severe depression with melancholic features, SR 58611 has proved itself superior to fluoxetine, the reference treatment for depression, in terms of both efficacy and tolerability. The phase III program is ongoing.

#### **Saredutant (SR 48968)**

Treatment for depression

##### **Phase III**

A new pharmacological class with potential for innovation in the field of depression.

Saredutant is an NK2 receptor antagonist developed for the treatment of major depressive disorders.

The program of phase III clinical trials was launched at the end of 2004.

#### **Teriflunomide (HMR 1726)**

Treatment of multiple sclerosis

##### **Phase III**

Teriflunomide is a dihydroorotate dehydrogenase inhibitor. A phase II study completed in 2003 demonstrated the efficacy and tolerability of teriflunomide in patients with relapsing forms of multiple sclerosis.

An international phase II development program was launched in 2004.

## **Xaliproden (SR 57746)**

Treatment of Alzheimer's disease

### **Phase III**

Xaliproden is a non-peptide compound which activates synthesis of endogenous neurotrophins. Two phase III studies are currently under way in Alzheimer's disease and a phase II study in multiple sclerosis. Xaliproden is also the subject of a major phase II international development study in chemotherapy-induced peripheral neuropathy (cf. Oncology).

## **SL 65.0155**

Treatment for Alzheimer's disease

### **Phase IIb**

SL 65.0155 is a partial 5-HT<sub>4</sub> (central serotonin receptor) agonist with both promnesic and neuroprotective properties.

A phase IIb study in patients with Alzheimer's disease is under way: results are expected in 2005.

## **Osanetant (SR 142801)**

Treatment of schizophrenia

### **Phase IIb**

Sanofi-aventis developed an original study protocol, known as a Metatrial, to evaluate the therapeutic activity of four compounds with novel antipsychotic properties in patients with schizophrenia. Osanetant, an NK3 receptor antagonist, demonstrated an activity and efficacy profile close to that of haloperidol, the reference treatment for schizophrenia, combined with very good tolerability.

The phase IIb clinical trial is under way.

## **SSR 591813**

Smoking cessation

### **Phase IIb**

This partial nicotinic receptor agonist is being developed in smoking cessation.

A phase IIb clinical study program was launched in 2004: enrolment of patients in this study is now complete.

## **Eplivanserin (SR 46349) and M 100907**

Treatment of sleep disorders

### **Phase IIb**

Both these 5HT<sub>2A</sub> serotonergic receptors are being developed for the treatment of sleep disorders. They act on quality of sleep, increasing deep sleep.

- For eplivanserin, a phase II clinical trial in patients with chronic insomnia has been completed and a phase II study is under way in patients with fibromyalgia.
- For M 100907, a phase IIb development program was launched in 2004.



## SR 57667

Treatment of Alzheimer's and Parkinson's disease

### Phase IIb

Like xaliproden, SR 57667 is a non-peptide compound which activates synthesis of endogenous neurotrophins. One phase II study is under way in Alzheimer's disease and two phase II studies in Parkinson's disease.

## HP 184

Treatment of spinal cord injury

### Phase IIa

HP 184 is a potassium channel and sodium channel inhibitor. A phase II clinical trial completed in 2004 demonstrated an improvement in ASIA total motor score (a measure of sensory and motor function impairment developed by the American Spinal Injury Association, or ASIA), while confirming tolerability in patients with medullary lesions.

A second phase II study involving 240 patients was launched in 2004.



## 4 ■ ONCOLOGY

*Combating cancer is one of the greatest challenges in medicine today and sanofi-aventis has made this the focus of much of its R&D effort. The Group's oncology portfolio contains a wide range of novel agents with a variety of mechanisms for the treatment of cancer, including cytotoxic, anti-mitotic and bioreductive agents, angiogenesis inhibitors and receptor antagonists, as well as cancer vaccines and palliative therapies.*

## Tirapazamine (SR 259075)

Treatment of head and neck cancer in combination with radiotherapy and cisplatin

### Phase III

Head and neck tumors are generally hypoxic (with a low oxygen concentration). Tirapazamine is an anti-cancer agent activated under hypoxic conditions to promote the destruction of resistant tumor cells. This innovative mechanism of action has the potential to reduce the risk of relapse with this type of tumor.

Phase III clinical trials are currently under way to demonstrate the efficacy of tirapazamine in combination with cisplatin and radiotherapy in head and neck cancers. Exploratory phase I and II studies in other tumors associated with hypoxia are also under way.



### **XRP 9881**

Treatment of taxane-refractory metastatic breast cancer

#### **Phase III**

XRP 9881 is a new taxoid developed to overcome the problem of resistance to the existing taxoids, docetaxel and paclitaxel. XRP 9881 has proved active against metastatic breast cancers continuing to progress after taxane therapy. XRP 9881 has also demonstrated its ability to cross the blood-brain barrier, which suggests that it might be effective in the treatment of cerebral metastases. These new taxoids may also be more easily tolerated than those currently available.

### **Xaliproden**

Treatment of antimitotic-induced neuropathies

#### **Phase III**

Xaliproden, a neurotrophic compound, is also being developed for the treatment of chemotherapy-induced neuropathies.

### **Meclinetant (SR 48692)**

Treatment of small cell lung cancer

#### **Phase IIb**

Meclinetant is a specific neurotensin receptor antagonist that arrests the growth of neurotensin-dependent tumors (such as small cell lung cancer). Meclinetant is currently being studied as a maintenance therapy in patients with small cell lung cancer following chemotherapy using a combination of cisplatin and etoposide. New clinical trials are scheduled for 2005.

### **Genasense®**

Treatment of melanoma and chronic lymphocytic leukemia

In the wake of the FDA's rejection of the NDA for Genasense in advanced melanoma, and in the light of unconvincing results in chronic lymphocytic leukemia (CLL), sanofi-aventis decided in November 2004 to terminate its agreement with Genta concerning the development of Genasense®.



## 5 ■ METABOLIC DISORDERS



### **Acomplia™ (rimonabant), SR 141716**

Metabolic syndrome, obesity, smoking cessation

#### **Phase III**

Rimonabant is the first of a new class of drugs called "selective CB-1 receptor antagonists". We know now that CB-1 receptors, initially identified in the brain, are also to be found in several other peripheral human tissues, such as adipocytes (fatty tissues). These receptors are part of the endocannabinoid system, a natural physiological system that plays a crucial role in the regulation of body mass and weight, lipid metabolism, insulin resistance and sensitivity to positive modulators such as food or nicotine.

#### ■ **Obesity, metabolic syndrome and associated disorders**

The phase III clinical development program for rimonabant in obesity, metabolic syndrome and associated disorders, such as type 2 diabetes and dyslipidemia (the RIO program: Rimonabant In Obesity) is now drawing to an end. Initiated in 2001, this phase III program comprises four major studies of more than 6,000 patients combining excess weight with comorbidity factors and/or who are obese or even severely obese (BMI, body mass index >40). These four studies are:

- **RIO-Lipids**, involving untreated dyslipidemia cases, treated for a year with rimonabant or a placebo;
- **RIO-North America**, involving overweight patients with comorbidity factors, or obese patients (some severely obese) treated for a year with rimonabant or placebo—in this study, patients on the active product for the first year were re-randomized to rimonabant or placebo for a second year of treatment;
- **RIO-Europe**, involving overweight patients with comorbidity or obese patients (some severely obese) treated for two years continuously;
- **RIO-Diabetes**, involving patients with non-insulin-dependent diabetes (type 2 diabetes), overweight combined with comorbidity factors or obesity, for some severe obesity, treated with rimonabant for a year. Data from this study, completed in 2004, will complement the rimonabant profile for patients with type 2 diabetes. Results of the RIO-Diabetes study should be available during the first half of 2005.

### ■ Very consistent results after one year, confirmed at two years

At one year, preliminary results were extremely coherent in all the clinical studies and demonstrated:

- 1 – See box: “Metabolic disorders: a major health issue”;
- 2 – A significant waistline reduction, this being one of the markers of visceral fat (minus 6.1 to 7.1 cm in waistline circumference for patients treated with 20 mg rimonabant, versus 2.4 to 2.5 cm waistline measurement reduction for patients using placebo);
- 3 – Significant and marked loss of weight (minus 6.3 to 6.9 kg for the group on a daily dose of 20 mg rimonabant, versus 1.5 to 1.8 kg for the placebo group).

These results were confirmed at two years and in the RIO-North America study there was a continuing improvement of metabolic parameters during the second year of treatment compared to patients who were switched to the placebo group at the end of the first year. Side effects during these studies were moderate or transient.

### ■ Smoking cessation and maintenance of abstinence

Rimonabant is also developed in smoking cessation and long-term maintenance of abstinence, for which it is the subject of a vast Phase III program, STRATUS (STudies with Rimonabant and Tobacco USe), launched in 2002 and composed of three major studies outlined below. STRATUS enrollment was more than 5,500 patients.

Two short-term clinical trials, called STRATUS US (United States) and STRATUS EU (Europe), consisted in the administration of rimonabant during ten weeks. Efficacy of the product was measured in terms of abstinence stated by patients (verified by measuring the concentration of carbon monoxide in expired air and plasma levels of cotinine—the major metabolite of nicotine) in the last four weeks of treatment.

### Metabolic disorders: a major public health issue

Many obese or overweight patients seen in clinical practice are found to be at risk for a number of cardiovascular complaints. They are in fact suffering from “metabolic syndrome”, a condition combining fundamental metabolic dysfunction with insulin resistance. Patients with metabolic syndrome are particularly at risk of developing coronary diseases, or other disorders caused by the deposit of atheromatous plaque on arterial walls (e.g. cardiovascular episodes and peripheral vascular disorders) or type 2 diabetes.

The NCEP ATP III (National Cholesterol Education Program Adult Treatment Panel III) has identified **six criteria to define metabolic syndrome: abdominal obesity, atherogenic dyslipidemia, raised blood pressure, insulin resistance (with or without glucose intolerance), proinflammatory and prothrombotic states (proneness to thrombosis)**. NCEP ATP III recommends the following criteria to diagnose metabolic syndrome: waist circumference of over 88 cm for women and 102 cm for men; triglycerides higher or equal to 150 mg/dL; HDL cholesterol (High Density Lipoprotein, the “good” cholesterol), women <50 mg/dL, men <40 mg/dL; blood pressure more than 130/85 mmHg; fasting glucose >110 mg/dL. The diagnosis of metabolic syndrome is confirmed when at least three of the five criteria are positive. In the United States, for example, 47 million patients are affected.

In the RIO program, 40 to 80% of patients (depending on the studies) presented with metabolic syndrome before treatment began. After a year of treatment, rimonabant had statistically reduced sensitivity to insulin, increased HDL (the “good cholesterol”) and reduced triglycerides compared to placebo, with good tolerability.

A third study, called STRATUS WW (worldwide), evaluates maintenance of abstinence in the long-term. In this study, patients who were still abstinent after ten weeks of treatment with rimonabant were randomized into two groups taking rimonabant or a placebo, with follow-up for a year.

Results of STRATUS US and EUROPE are available and demonstrate that rimonabant significantly increases the probability of smoking cessation compared to placebo, whilst retaining a good tolerability profile. Furthermore, average weight loss for patients taking rimonabant was approximately 0.3 to 0.5 kg, as compared to a weight gain of slightly more than 1 kg for patients using placebo. Finally, in STRATUS-WWW, the 20 mg daily dose of rimonabant demonstrated statistically significant superiority over placebo regarding maintenance of abstinence for a year after smoking cessation, with good tolerability. Submissions for marketing approval will be filed simultaneously with U.S. and European authorities for all rimonabant indications (metabolic syndrome, obesity, smoking cessation) during the first half of 2005 with launch expected for 2006.



### **Apidra® (HMR 1964)**

Treatment for insulin-dependent diabetes

This rapid-acting insulin prevents the onset of postprandial hypoglycemia when administered before, during, or after a meal. Apidra® can also be used as an adjuvant to Lantus® basal insulin therapy. Apidra® has been approved in the United States and in Europe since 2004. It is presently under development in Japan for pediatric use.

### **Exubera (HMR4006)**

Treatment for insulin-dependent diabetes

### **Phase III**

Submission for approval has been filed in the United States and in Europe for this rapid-acting inhaled insulin, co-developed with Pfizer.



## 6 ■ INTERNAL MEDICINE

### Alvesco® (ciclesonide)

Treatment of asthma

#### FDA Approvable Letter in October 2004

In October 2004, the FDA agreed to consider Alvesco®'s metered-dose inhaler for approval. Sanofi-aventis and its partner ALTANA AG are preparing replies to FDA questions.

### XRP 1526 / AVE 2635 (ciclesonide/formoterol)

Treatment of asthma

#### Phase IIb

Sanofi-aventis is also developing a freeze-dried powder combining ciclesonide and formoterol for use in inhalers. The first patient for inclusion in the phase IIb clinical study, conducted by sanofi-aventis partner ALTANA AG, was enrolled in November 2004.

### SR 121463

Treatment of dilutional hyponatremia  
and cirrhotic ascites

#### Phase III

This vasopressin V2 receptor antagonist is a pure aquaretic compound. Following favorable results in the phase IIb clinical study to demonstrate efficacy in treating hyponatremia due to the syndrome of inappropriate anti-diuretic hormone secretion (SIADH), also called the Schwartz-Bartter syndrome, a phase III SIADH study

began in the second quarter of 2004. In addition, a vast phase IIb clinical development program was launched in March 2004 for the treatment of cirrhotic ascites.

### Fumagillin (SR 90144)

Antibiotic with antiparasitic properties

#### Submitted

A request for marketing approval was filed in France on December 13, 2004, for the treatment of intestinal microsporidiosis caused by *Enterocytozoon bienewisi* in severely immunocompromised HIV-positive patients. This is a rare invalidating condition and may in some cases be life-threatening. In 2001, the European Medicines Evaluation Agency (EMA) granted fumagillin orphan-drug status for this indication.

### Ferroquine (SSR 97193)

Treatment for malaria

#### Phase I

A novel 4-aminoquinoline analogue highly active against both chloroquine-sensitive and chloroquine-resistant *Plasmodium falciparum* strains. Malaria mainly affects the populations of developing countries, i.e. sub-Saharan Africa and, to a lesser degree, South-East Asia and Latin America. There are an estimated 300 million cases of infection per year worldwide, of which 1 to 3 million are lethal. The vast majority of victims are children. This compound entered into phase I in September 2004.

## 7 ■ VACCINES

**Sanofi-aventis is world leader with 20 products under development and 8 in late-stage clinical development**

*Our human vaccines R&D strategy is defined by the competitive position of our Group in new target areas, as well as a commitment to strategic assets that will further develop our leadership position in vaccines. While we remain focused on the development of new preventive vaccines, we are also active in new areas of research, in particular the development of innovative therapeutic vaccines for the management and/or the prevention of diseases such as HIV and cancer.*

### The main vaccines programs in advanced clinical development

Sanofi-aventis involvement in public health issues affecting the world's poorest populations is reflected by a large and varied portfolio of vaccines. Infectious diseases are the cause of more than 17 million deaths a year, children in the great majority, and sanofi pasteur plays a decisive role in the development of new means of prevention, adapted for use by the populations concerned.

#### **Menactra™**

Meningococcal disease

The first quadrivalent conjugate vaccine for the prevention of meningococcal disease (providing protection against the four most prevalent serogroups of *Neisseria meningitidis*) was submitted to the FDA in December 2003, for use with children aged eleven and upwards, and also for adults. The FDA licensed Menactra™ on January 14, 2005. A request for marketing approval will be submitted to European and Canadian pharmaceutical authorities early in 2005.

An application for extension of indication is being filed for children between 2 and 10 years of age. We are also studying new formulations of the conjugate vaccine for children.

#### **Adacel™**

Tetanus, diphtheria and pertussis

This trivalent vaccine protects adolescents and adults. Adacel™ is marketed in Canada and Germany and was submitted for approval to U.S. authorities in August 2004. A meeting of FDA Vaccines and Related Biological Products Advisory Committee (VRBPAC) is scheduled for the first quarter of 2005.

#### **Pentacel™**

Diphtheria, tetanus, poliomyelitis, pertussis and *Haemophilus influenzae* type b (Hib) meningitis

This vaccine, offering protection against five diseases, was developed for the American market and will be filed for registration in 2005.

Our portfolio of products in the early phases of development includes the following:

#### ■ Dengue

##### Hemorrhagic fever

Several approaches are being pursued to obtain an effective vaccine against the four virus serotypes, for the prevention of dengue and its more serious complications (hemorrhagic dengue). The disease is particularly widespread in Asia, Africa and Latin America. Phase I clinical trials now being conducted will therefore include inhabitants of the affected areas and travelers to those regions.

#### ■ HIV/AIDS

Through its long-standing research programs and agreements with leading government agencies and pharmaceutical companies, sanofi pasteur can be considered as a pioneer in HIV/AIDS vaccine research. Sanofi pasteur research in this area covers both prophylaxis and treatment.

#### ■ Pneumococcal infections

Several research programs are now investigating protection of elderly adults and children against pneumococcal infections.

#### ■ Influenza

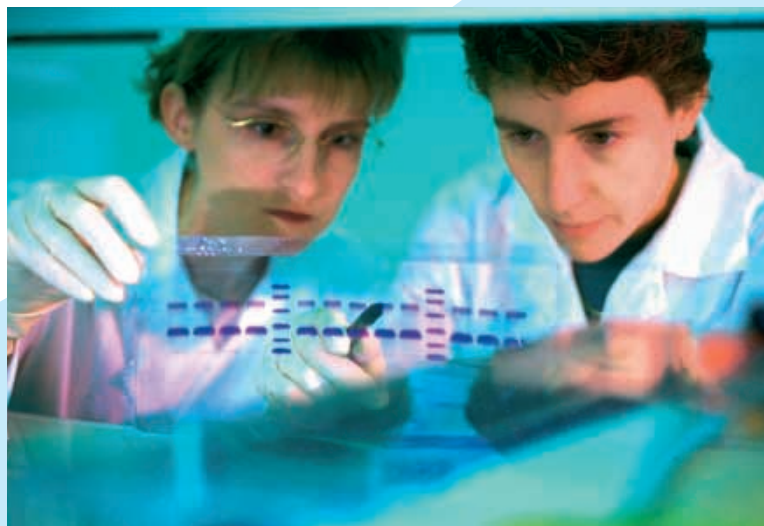
We are investigating innovative technologies including new injection modes (phase IIb), manufacturing processes and the prevention of pandemic influenza.

#### ■ Severe acute respiratory syndrome (SARS)

We have fulfilled our commitment to the NIH (National Institutes of Health) by delivering batches of vaccine for phase I clinical studies.

#### ■ Cancer

An ongoing development program is focusing on colorectal cancer and melanoma, seeking to activate the immune system so that it destroys cancer cells (therapeutic vaccine). Phase I clinical studies using proprietary ALVAC (Vivalis) technology in the treatment of patients with melanoma or colorectal cancer have provided evidence of a favorable innocuity profile.



# ▷ OUR PORTFOLIO OF MEDICINES

- ▶ Strong growth from our top **15 strategic products:**  
**+17.8%**
- ▶ **8 flagship products\***: Plavix<sup>®</sup>, Lovenox<sup>®</sup>, Aprovel<sup>®</sup>,  
Taxotere<sup>®</sup>, Eloxatin<sup>®</sup>, Ambien<sup>®</sup>, Allegra<sup>®</sup>, Actonel<sup>®</sup>  
plus **2 potential candidates**: Lantus<sup>®</sup> and Copaxone<sup>®</sup>
- ▶ **“No small products”**  
Strong capacity to support our basic products with pro forma  
net sales of **9,408 million euros**

\*Developed sales (see definition on Key figures page) + Actonel<sup>®</sup>.





## Medicines: a novel strategy

innovative to meet the new challenges of public health, active in support of base products, generating solid results and savings for health care systems

## CARDIOVASCULAR

# Aprovel®/Avapro®/Karvea®

irbesartan

2004 pro forma net sales

790 million euros

+16.7% \*

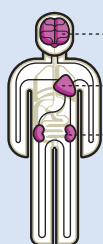
2004 developed sales

1,449 million euros

+20.6% \*

## Hypertension

### Possible complications



Stroke

Congestive heart failure  
Myocardial infarction

Renal insufficiency  
(dialysis or transplant)

- **Hypertension affects approximately 25% of the world's population**

Whilst this condition is generally asymptomatic, it is one of the main causes of severe kidney, heart, brain, blood vessel and eye complications.

- **A disorder leading to severe complications**

Hypertension is defined as blood pressure above the normal level of 140/90 mm Hg.

These figures are lower, however, when associated pathologies increase the risk of cerebral, cardiac or renal complications. This is the case with diabetes, which doubles risk levels. The WHO therefore recommends a complete risk profile evaluation for all hypertensive patients to provide them with the most appropriate treatment.

- **AIIRA is the most recent anti-hypertensive drug class, particularly recommended for type 2 diabetes**

The American Diabetes Association (ADA) recommends annual screening for early stages of renal impairment in diabetic patients and, if confirmed, treatment with an angiotensin II receptor antagonist (AIIRA), the most recent anti-hypertensive drug class. Diabetes now affects 190 million people worldwide, with 330 million forecast for 2025. The majority of cases are type 2 diabetes.

## TREATMENT FOR PRIMARY ARTERIAL HYPERTENSION

### A latest generation anti-hypertensive with a broad therapeutic potential

Aprovel® is a major drug with proven efficacy for the treatment of arterial hypertension, and good tolerability. A significant clinical development program will ensure its continued progress and success on the hypertension market.

### Main markets

At present, Aprovel® is available in more than 80 countries as monotherapy (Aprovel®/Avapro®/Karvea®) or in fixed-dose combination together with a diuretic, hydrochlorothiazide (CoAprovel®/Avalide®/Karvezide®). It is marketed in Europe, the United States and worldwide by sanofi-aventis, through agreements reached with Bristol-Myers Squibb and is in the process of registration in Japan.

### A leading angiotensin II receptor antagonist (AIIRA) for the treatment of hypertension, with documented renal protective effects

Aprovel® belongs to the class of AIIRAs, the new reference class in the treatment of hypertension. Highly potent and very well tolerated, AIIRAs impede the effects of angiotensin II through preferential blockade of angiotensin II (A-II), sub-type 1 receptors. Angiotensin II has a wide range of detrimental effects on the cardiovascular system, in particular vasoconstriction, changes in cardiac contraction, sodium retention and aldosterone secretion. Aprovel®, alone or in combination with a diuretic marketed as CoAprovel®/Avalide®, restores normal blood pressure in more than 80% of patients and offers very good tolerability.

\*Growth on a comparable basis.



Aprovel®/Avapro® was approved for a new indication in 2002: the treatment of diabetic nephropathy. The PRIME clinical program (IRMA2 and IDNT studies) has shown that it prevents the progression of renal impairment in hypertensive diabetic patients in both the early and late stages.

The importance of these results led the *American Diabetes Association* (ADA) to recommend the use of AIIRAs for first-line treatment of nephropathy in patients with type 2 diabetes.

At the request of the FDA, an Aprovel® application for extension to a pediatric indication was filed in the United States. A smaller tablet, a new improved version of Aprovel®, is already marketed in Europe.

#### 2004—Sustained performance and new clinical trials

Aprovel®/Avapro® continued to grow at a steady rate in Europe, where it shares the leading position, and throughout the world, with sales showing an increase of 20.6% on a comparable basis. Two clinical studies of Aprovel® efficacy were conducted in 2004:

**The COSIMA study**, presented in Europe in 2004, demonstrated the superior efficacy of CoAprovel® in lowering hypertension compared to another drug in the same class.

**The INCLUSIVE study** in the United States evaluated treatment using irbesartan in a fixed-dose combination with a diuretic on patients with uncontrolled hypertension, which is difficult to monitor.

**Results will be available in 2005.**

## Life Cycle Management

### ■ Dynamic management of the Aprovel® life cycle

**The IMPROVE clinical trial** was launched in 2004 to demonstrate the protective effects of irbesartan on target organs of high cardiovascular risk patients.

Two studies including 15,000 patients are under way to demonstrate the efficacy of irbesartan in protecting the cardiovascular system of patients whose risk of cardiovascular involvement is high.

**The I-PRESERVE study**, launched in 2002, evaluates the efficacy of irbesartan in treating and preventing the vascular complications of heart failure with preserved systolic function which are a frequent complication of hypertension. I-PRESERVE is the largest study ever carried out on this very frequent condition.

### ■ Results expected in 2006

**The ACTIVE study**, launched in 2003, evaluates the efficacy of irbesartan combined with clopidogrel in preventing stroke and other major cardiovascular complications in patients with atrial fibrillation.

### ■ Results are expected in 2007

#### Other indications

In the Middle East, Africa and Latin America, a trial including over 600 patients will compare the efficacy of CoAprovel®/Avalide® to that of another major treatment for hypertension (AMISH).

#### Launch of Avalide® 300/25 mg in the United States, in 2005

The launch of this new combination will reinforce irbesartan's efficacy profile. At a time when the use of anti-hypertensive combinations is on the increase, irbesartan 300 mg combined with a diuretic (hydrochlorothiazide 25 mg) will become a significant alternative option in the current management of hypertension.



## CARDIOVASCULAR

# Tritace®/Delix®/Altace®/Triatec®

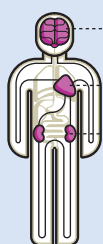
ramipril

2004 pro forma net sales

972 million euros

### Cardiovascular diseases

#### Possible complications



Stroke

Myocardial infarction

Renal insufficiency  
(dialysis or transplant)

- **Cardiovascular diseases are still the leading cause of death in industrialized countries**

In these countries, atherosclerosis—the result of thickening and hardening of the arterial wall—is far and away the most common form of cardiovascular disease.

In the United States for example, 900,000 people are hospitalized for myocardial infarction every year, and 600,000 succumb to coronary heart disease.

Moreover, an increasing proportion of the world's population is reaching an age when coronary heart disease is frequent. Although medical science is advancing, there are increasing numbers of people suffering from cardiovascular diseases.

Cardiovascular mortality (data not corrected for age) will therefore continue to rise, making effective and innovative products more essential than ever before.

### TREATMENT OF HYPERTENSION, CONGESTIVE HEART FAILURE AFTER MYOCARDIAL INFARCTION

Tritace®/Triatec®/Delix®/Altace® (ramipril) is an angiotensin converting enzyme (ACE) inhibitor for the management of hypertension, congestive heart failure after a myocardial infarction.

Due to the results of the HOPE<sup>(1)(2)</sup> study, it is the only ACE inhibitor so far approved for the prevention of stroke, myocardial infarction and cardiovascular-related death in high-risk patients and diabetics.

#### Main markets

The main markets for Tritace® are Canada, France and Italy, representing 50% of total sales. Although market exclusivity expired in Germany (January 2004), Delix® is still the market leader in its class and demand has remained steady since early 2004. Marketing rights in the United States were sold to King Pharmaceuticals in 1998.

Tritace® is the main ACE inhibitor on sanofi-aventis leader markets (except in the United States and Japan).



## Recent publications

According to a report published in the September 2004 issue of *Circulation*, Tritace® significantly reduces the number of fatal or non-fatal severe arrhythmic events. This sub-analysis of the HOPE study is the first to demonstrate that an ACE inhibitor can prevent arrhythmic events such as sudden death and cardiac arrest in patients at risk of atherosclerotic cardiovascular incidents.

A retrospective study published in July 2004 in the *Annals of Internal Medicine* set out to assess whether mortality rates in patients with a history of myocardial infarction were identical for all ACE inhibitors. The results showed that, compared to other ACE inhibitors included in the test, Tritace® was associated with the lowest mortality figures. This highlights the fact that the various ACE inhibitors present structural, kinetic and pharmacological differences which may give rise to significant variations in clinical results.

(1) Yusuf S, Sleight P, Pogue J, Bosch J, Davies R, Dagenais G. *NEJM* 2000; 342: 145-53.

(2) *Lancet* 2000; 355: 253.

(3) Yusuf S, Gerstein H, Hoogwerf B, Pogue J, Bosch J, Wolffenbuttel B.H.R., Zinman B. Ramipril and the development of diabetes. *JAMA*. 2001; 286: 1882.

(4) Gerstein H.C., Yusuf S, Holman R., Bosch J, Pogue J. Rationale, design and recruitment characteristics of a large, simple international trial for diabetes prevention the DREAM trial. *Diabetologia Clinical and experimental Diabetes and Metabolism* 2004.

## Life Cycle Management

### ■ Triapin

This is a fixed-dose combination of ramipril with a sustained release calcium channel inhibitor: felodipine. The two components of Triapin complement each other and act in synergy because of their different modes of action. Triapin is therefore able to lower blood pressure effectively because of its metabolic neutrality. Triapin is an excellent opportunity for entry on the calcium channel inhibitor market because its efficacy and tolerability are superior to those of calcium channel inhibitor monotherapy.

### ■ DREAM 15 mg

Glucose metabolism modifications, such as fasting glycemia and glucose tolerance, as well as the number of cases of diagnosed or non-diagnosed diabetes, are very much on the increase. During the phase which precedes established diabetes (the "prediabetic" phase), cardiovascular risks are augmented. The HOPE study demonstrated that administration of Tritace® 10 mg to non-diabetic patients at risk of cardiovascular events reduced the risk of developing diabetes by 34% (statistically significant). These results were the starting point of the **DREAM**<sup>(3)(4)</sup> study (Diabetes Reduction Assessment with Ramipril and Rosiglitazone Medication). The study compared the effect of ramipril 15 mg, rosiglitazone and a combination of ramipril 15 mg + rosiglitazone, with a placebo in the development of diabetes in at-risk patients. The **DREAM** study could position Tritace® on the market for the prevention of diabetes.

## THROMBOSIS

# Lovenox®/Clexane®

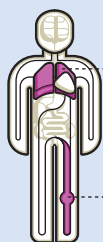
enoxaparin

2004 pro forma net sales

1,904 million euros

+22.4%\*

### Venous thrombosis



- **Main complication: pulmonary embolism**

Thrombosis occurs when a thrombus or blood clot is formed in a vein due to impaired circulation, which may be caused by certain diseases and by reduced mobility. Without treatment, the thrombus may become enlarged to the point where it occludes the vessel or it may move through the venous system until it reaches the lung and causes pulmonary embolism, still one of the main causes of death worldwide.

- **Third most frequent cardiovascular disease**

In Western countries, this disorder affects 2 to 3 people per 1,000. Every year, nearly 2 million Americans are affected, of whom 60,000 will suffer a pulmonary embolism with an estimated mortality rate of 8 to 10%. For the United States alone, the annual cost of venous thrombosis is 2.9 billion dollars.

- **Unstable angina and non-Q wave infarction**

Main complication: acute myocardial infarction. Unstable angina is an acute aggravation of angina pectoris. This occurs when the blood flow into the arteries supplying the heart is slowed down to the extent that blood and oxygen can no longer reach cardiac muscle cells. As a result, some cardiac cells may die, leading to infarction. Angina pectoris is the second most frequent cardiovascular disease worldwide.

PREVENTION OF 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)

In 2004, sanofi-aventis extended its campaign to raise awareness of deep venous thrombosis among U.S. patients, healthcare professionals and institutions, thereby boosting both market share and retail sales. Lovenox®/Clexane® is now the leading LMWH on every major European market, posting double-digit growth once again in 2004.

#### Main markets

Lovenox®/Clexane® is the leader on all the major markets (United States, France, Germany, Italy, Spain and the United Kingdom) and leader in terms of market share.

#### The most widely studied and prescribed Low Molecular Weight Heparin (LMWH)

Since it was launched in 1987, Lovenox®/Clexane® has been used to treat approximately 151 million patients in 96 countries and has the broadest spectrum of approved indications of any LMWH. A number of clinical studies have shown that the compound is not only safe and effective in significantly reducing the risk of venous thrombosis in a large variety of pathologies, but that it is also effective in preventing ischemic complications of stable angina and of non-ST-segment elevation myocardial infarction when administered in combination with aspirin.

\*Growth on a comparable basis.

\*\* IMS reference



The results of the SYNERGY study of 10,027 patients, presented on March 9, 2004 to the 2004 American College of Cardiology's Annual Scientific Session, demonstrated that Lovenox®/Clexane® is as effective as unfractionated heparin (UFH) for the management of high-risk patients undergoing coronary catheterization without acute coronary syndromes.

The SYNERGY study results led to the publication on July 7, 2004 of a meta-analysis of six major studies in the *Journal of the American Medical Association*. The review based on 21,946 randomized patients demonstrated the clear overall superiority of enoxaparin over UFH for the prevention of non-ST segment elevation myocardial infarction complications. The review also showed that major hemorrhage and transfusion at seven days was comparable in the two treatment groups compared to population at large.

On February 12, 2004, sanofi-aventis put forward a supplement to its *Citizen Petition (CP)*, which was initially submitted to the Food and Drug Administration (FDA) in February 2003. This supplement provides further information regarding the characterization of enoxaparin and responding to comment addressed to the FDA by third parties in reply to our first submission. This CP requested the FDA to withhold approval of any request for registration making reference to Lovenox® as the princeps product, unless (i) or until such time as enoxaparin has been fully characterized, the process used to manufacture the generic product is equivalent to the sanofi-aventis

process, or the generic product has been proved by clinical studies to be of comparable safety and efficacy and (ii) unless the generic product contains a 1.6 anhydro ring structure at the reducing ends of between 15% and 25% of its polysaccharide chains. This *Citizen Petition* is still awaiting a reply from the FDA.

In July 2004, the FDA approved a request for complementary registration for revision of the Summary of Product Characteristics and of the Chemistry/Pharmacy file underscoring the structural specificities in connection with the 1.6 anhydro cycle.

## Life Cycle Management

■ Two major clinical trials of enoxaparin are in progress

**EXTRACT:** Registration study on the reduction of ischemic complications in approximately 20,000 patients with Q-wave myocardial infarction (confirmed MI).

**EXCLAIM:** Study on the optimal length of treatment in approximately 4,000 patients at risk of thromboembolic complications due to temporarily restricted mobility as a result of various medical conditions.

## THROMBOSIS

# Plavix®

clopidogrel

2004 pro forma net sales

1,694 million euros

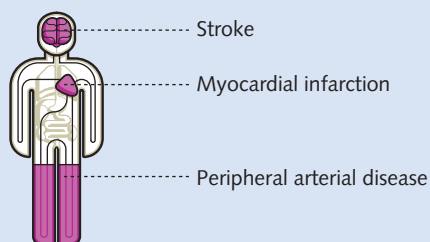
+ 28.9 % \*

2004 developed sales

4,108 million euros

+34.8% \*

### Atherothrombosis



- **Atherothrombosis: 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 through damage to the arterial wall, when fatty deposits—atheromatous plaque—build up. When plaque breaks up or ruptures, a clot is formed. It may expand locally or move into the blood stream, reducing flow or even completely obstructing a blood vessel; this is atherothrombosis.

The result is acute ischemia with tissue lesions, with severe or even lethal consequences: stroke, myocardial infarction or acute coronary syndrome.

- **The leading cause of death in developed countries**

These disorders cause **over a million deaths** every year in Europe and the United States, where over **17 million** people suffer from atherothrombosis-related conditions.

## PREVENTION OF ISCHEMIC EVENTS CAUSED BY ATHEROTHROMBOSIS

One of the world's 10 leading medicines, Plavix® is growing rapidly but still has very significant development potential.

### Extensive experience on efficacy and tolerability

To date, over **41 million patients throughout the world have been treated** with Plavix®, confirming the favorable benefit-to-risk ratio for long-term management of atherothrombosis.

Plavix® has consolidated its position as the foremost platelet antiaggregant agent for the secondary prevention of stroke.

### Main markets

Plavix® is marketed by sanofi-aventis in over 75 countries, through an alliance with Bristol-Myers Squibb. It is developed in partnership with Daiichi Pharmaceuticals in Japan, where it was filed for approval on February 24, 2004.

### The only platelet antiaggregant with extensive clinical exposure, indicated for all arterial locations

Plavix® is indicated for the prevention of atherothrombosis-related cardiovascular events in patients with a history of recent myocardial infarction, acute coronary syndrome, recent stroke or established peripheral arterial disease.

\*Growth on a comparable basis.

### Unparalleled clinical development for atherothrombosis

**The CAPRIE study on nearly 20,000 patients**, established the superior efficacy of Plavix® compared to acetylsalicylic acid, with at least equivalent tolerability.

**The CURE study involving over 12,000 patients** provided evidence that Plavix® in combination with aspirin reduced by 20% ( $p < 0.001$ ) the combined relative risk of myocardial infarction, stroke and cardiovascular death, also offering significant benefits in both the short and long term to patients suffering from acute coronary syndrome, with an acceptable increase of major bleeding (1%).

On the basis of these results, Plavix® obtained an extension of indication in 2002 for patients with acute coronary syndrome without increased ST segment.

### In 2004, very substantial growth for Plavix®

Standard treatment in combination with aspirin established for patients with non ST-segment elevation acute coronary syndromes (unstable angina or non-Q wave myocardial infarction).

An increase in treatment initiation, mostly in cardiology but also in all other indications, contributed to strong prescription increases. Moreover, duration of treatment is constantly on the increase.

**The CREDO study including over 2,000 patients** demonstrated the long-term efficacy of Plavix®, in combination with aspirin, in reducing the risk of future atherothrombotic events by 27% ( $p = 0.02$ ) for patients who had undergone coronary angioplasty. The difference in the risk of major bleeding was non significant at one year.

**The MATCH study including over 7,500 patients** demonstrated that acetylsalicylic acid does not contribute any added therapeutic value (benefit/risk) for secondary prevention in high-risk patients already taking Plavix® or other standard medication following stroke or transient ischemic attack.

## Life Cycle Management 2005-2008

**Unparalleled clinical experience on efficacy and tolerability—Over 100,000 patients in long-term studies** for different patient profiles with a high risk of ischemic events of atherothrombotic origin. By 2008, the results of these studies could increase the number of potential Plavix® users in several therapeutic areas.

### ■ Results in 2005

On March 9, 2005, during the 54th annual Scientific Sessions of the American College of Cardiology, the results of the COMMIT and CLARITY studies on more than 49,000 patients were presented, showed that Plavix®, in association with a standard treatment, improved coronary perfusion and reduced mortality in patients presenting with acute myocardial infarction.

### ■ Results expected in 2006

The CHARISMA study, launched in 2002, assesses Plavix® for the prevention of cardiovascular events in over 15,500 patients in a high-risk population for ischemic events of atherothrombotic origin, whether they merely carry the risk factors or have a previous history of atherothrombotic events (infarction, stroke).

CHARISMA is a phase III study which should enable the Group, if expectations are confirmed, to submit a request for approval in a new indication.

### ■ Results expected in 2007

- The ACTIVE study is evaluating the efficacy of Plavix® in the prevention of cardio-embolic complications in patients presenting with atrial fibrillation and a high risk of cardio-embolic events. Launched in 2003, the study includes 14,000 patients and is designed to support a submission for approval of this new indication.
- CASPAR, covering over 1,400 patients presenting with peripheral arterial disease who have recently had bypass surgery, should enable an assessment of Plavix® benefits for this category of patients.

## CENTRAL NERVOUS SYSTEM

# Stilnox®/Ambien®/Myslee®

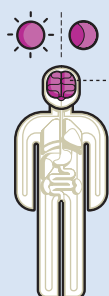
zolpidem

2004 pro forma net sales

1,423 million euros

+15.3%\*

### Insomnia



Sleep disorders,  
difficulties in sleeping,  
repeated nocturnal awakening

- **20% to 30% of the population affected**

Insomnia is a combination of unsatisfying sleep and its consequences during the day: irritability, short attention span and inability to concentrate. Nearly 150 million insomniacs have been identified on the seven leading markets.

If left untreated, insomnia can become chronic and may multiply by as much as eight-fold the risk of developing a state of depression, depending on the degree of severity.

- **An extremely high socio-economic cost**

Absenteeism, lower productivity levels, increased consumption of medication, a greater number of accidents—in particular car accidents, which are two to three times more frequent for insomniacs—and twice as many hospital stays. The high cost of insomnia is such that it justifies early treatment. In the U.S., direct and indirect costs have been evaluated at over 100 billion USD a year.

- **Many patients still untreated**

The percentage of the insomniac population suffering from untreated sleep disorder is large: 73% in the United States, 65% in France, 64% in Japan, according to the 2003 Harris Medical International study.

## TREATMENT OF INSOMNIA

The world's leading hypnotic<sup>(1)</sup>  
More than 12 billion treatment  
nights<sup>(2)</sup> since launch

Already a longstanding market leader in Europe and the United States, Myslee® also became no. 1 in Japan in November 2003.

A new formulation, which offers even better sleep continuity, was filed for approval in the United States in June 2004, in France and Switzerland in November 2004, and will be filed shortly in other European countries and later in Australasia and Latin America.

### Main markets

Available in nearly 100 countries, Stilnox®/Ambien®/Myslee® is the world's leading hypnotic with more than 64% of the market in terms of sales.

It is marketed by sanofi-aventis, except in Japan, where marketing is handled through a joint-venture with Fujisawa (Astellas).

### The only medication with proven efficacy when used "as needed"

Chemically different from benzodiazepines, Stilnox® is distinguished by its selective binding to brain receptors mediating hypnotic activity. As a result, it rapidly induces sleep that is qualitatively close to natural sleep.

Its effects last six to seven hours. It is well-tolerated and allows the patient to awaken refreshed. In addition, the risk of dependency, the main drawback of hypnotics, is kept to a minimum when the recommended doses and treatment times are followed.

(1) In sales figures and treatment days IMS 12/04 (including defensive generics + co-marketing).

(2) Sanofi-aventis internal data/IMS 1988-2004.

\*Growth on a comparable basis.





■ **Stilnox® has been better studied than any other hypnotic in the world**

Its efficacy and tolerability have been established, based on data collected for 140 clinical studies in over 80,000 patients from all continents.

Stilnox® is the only product to have demonstrated its efficacy when used "as needed", to suit individual requirements, through a series of eight clinical studies involving 6,000 patients. Patients suffering occasional insomnia can thus avoid taking it on a regular basis.

**2004 Global leader: in Europe, the United States and also Japan**

Stilnox® remains market leader in Europe, despite the arrival of generic products in a number of markets. Ambien® enjoys the status of undisputed market leader in the United States, by both value and treatment nights, accounting for a prescriptions market share of more than 47% (*IMS NPA Plus MAT 12/2004*). With almost 2.3 million prescriptions monthly, Ambien® is sanofi-aventis' leading prescription product (*IMS NPA Plus 12/2004*).

Three years after its launch, Myslee® has established itself as market leader in terms of sales in Japan, with a market share which exceeds 25% at the end of 2004 (*IMS November 2004*).

**Life Cycle Management**

■ **2005: A new optimized formulation**  
**A modified-release formulation to improve sleep continuity**

Sanofi-aventis has developed a modified-release formulation for zolpidem, "zolpidem MR" (modified release). Thanks to its optimized pharmacokinetic profile, it is able to retain zolpidem's distinctive benefits (rapidly induced sleep and awakening refreshed) whilst improving sleep continuity (by reducing premature awakening and sleep disruption) which is one of the main complaints of patients (70% of patients, *US, HMI 2003*).

The two Phase III clinical studies, one in adults and the other in elderly patients, have clearly established zolpidem MR's sleep continuity properties. These studies are supported by two clinical pharmacology studies that show the excellent tolerance of this new formulation and the absence of residual effects upon waking, in both adults and the elderly.

This clinical trial program was the basis for zolpidem MR registration in the United States in mid-2004, under the brand name Ambien® CR (controlled release).

## CENTRAL NERVOUS SYSTEM

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

sodium valproate

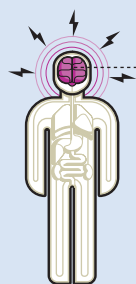
2004 pro forma net sales

303 million euros

+10.2%\*

## TREATMENT FOR EPILEPSY AND BIPOLAR DISORDERS\*\*

### Epilepsy



Sudden surges of brain cell activity,  
manifested through repeated crises

- **Affecting 1% of the world's population**

Epilepsy is a frequent chronic neurological disorder involving repeated spontaneous seizures with unpredictable onset, resulting from abnormally high electrical activity in the brain's neurons. It affects approximately 1% of the world's population. Children under the age of 10 and adults over 65 are the most commonly affected.

- **A better understanding of the disorder**

The origin, characteristics and effects of the seizures, the uncertainty as to whether specific symptoms can be associated with the illness and the varying responses to treatment all make epilepsy difficult to grasp.

The physical, psychological and social repercussions of epilepsy on sufferers and their families are considerable. Thanks to progress in genetics, brain electrophysiology and new functional cerebral imaging techniques, however, a better understanding of the disease is emerging.

- **A chance to live a normal life**

Much of the distress brought about by the disorder can be avoided with early diagnosis and appropriate care. With adequate management, the vast majority of patients can lead normal lives.

It is therefore essential that access to diagnosis, treatment and medical advice be made easier.

### A broad-spectrum anti-epileptic, a reference treatment throughout the world

Depakine® is an effective treatment for all types of epileptic seizures and syndromes. It is generally well-tolerated and, unlike other anti-epileptic medicines, does not cause paradoxical aggravation of seizures, and it has been successfully prescribed for over 35 years.

The efficacy and broad-spectrum of Depakine® position it as a reference treatment, despite the advent of new anti-epileptics.

#### Main markets

In most European countries, Depakine® has consolidated its position as the market leader in terms of days of treatment. It is marketed in over 100 countries, including the United States, where Abbott holds the relevant license.

\* Growth on a comparable basis.

\*\* The bipolar disorders indication has been obtained for some countries.



### **A new pharmaceutical formulation with longer-lasting effect**

Depakine® is available in a large variety of formulations (syrups, soluble drinks, injections, tablets), in order to cover a wide range of patient needs. The Chrono® form, for instance—extended-release tablets to be taken once or twice a day—improves compliance and overall patient management. Depakine® Chrono® is marketed in most countries.

In 2003, Depakine® Chronosphere®, a new sustained-release chronosphere form, was launched in France under the name Micropakine®. This new innovative form is easier to use, particularly for children and the elderly. In 2004, the new stick pack Chronosphere® form was launched in Austria.

Approval for this form is currently being sought in Europe, with product launches planned in most European countries in 2005 and 2006.

### **A new indication in Europe for the treatment of bipolar disorders**

Sodium valproate also has a role to play in treating the bipolar disorders that affect approximately 2% of the population and are characterized by alternate manic and depressive episodes.

Filings for approval were made in most European countries in 2003.

This indication, which constitutes an important growth driver, has already been granted in Finland, Poland, Norway, France, Slovakia, Sweden, Belgium, Luxembourg, United Kingdom, Czech Republic, Lithuania, Estonia, Latvia, Austria, Denmark, Portugal, Turkey, Hungary, Italy and Switzerland.



## CENTRAL NERVOUS SYSTEM

# Copaxone®\*\*

*glatiramer acetate*

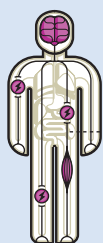
2004 pro forma net sales

742 million euros

+27.3%\*

REDUCTION IN THE FREQUENCY  
OF RELAPSES IN AMBULATORY PATIENTS WITH  
RELAPSING-REMITTING MULTIPLE SCLEROSIS  
CHARACTERIZED BY AT LEAST TWO RELAPSES  
IN THE LAST TWO YEARS.

### Multiple sclerosis



Interruption of neuronal connections

- **Multiple sclerosis (MS) is a chronic inflammatory disease that affects the white matter regions of the central nervous system. Over 2.5 million people currently suffer from the disease**

MS is characterized by progressive destruction of the myelin sheath that surrounds and protects the nerves, leading to the appearance of demyelinated plaques on certain neurons and subsequent degeneration. Onset of the disease generally occurs in early adulthood, on average around the age of 30, and is much more prevalent in women (sex ratio: 1.7:1). It is an auto-immune disease whose exact causes are still poorly understood. Characterized in clinical terms by episodes of focal disturbance, MS evolves insidiously, either as a series of relapses punctuated by an almost complete recovery (relapsing-remitting MS or RRMS), or in the primary progressive form of the disease (PPMS, progressive from onset), or as secondary progressive MS (SPMS).

- **Clinical expression of the disease varies widely from one patient to another**

The main symptoms are visual, motor and sensory. MS typically evolves over a period of several decades, with a mortality rate that differs little from that of the general population but accompanied by the gradual development of disability varying from one patient to another but which may culminate in total loss of autonomy.

\* Growth on a comparable basis.

\*\* IMS classification: oncology/immunology.

### In 2004

- Over 80,000 patients around the world treated with Copaxone®.
- Continued penetration of the European market.
- In 2004, marketing partners sanofi-aventis and Teva Pharmaceutical Industries Ltd launched the Copaxone® prefilled syringe, a new presentation that offers easier administration of treatment.

### Main markets

Copaxone® is licensed by Teva to sanofi-aventis and commercialized through an alliance with Teva.

In Europe and Australia, Copaxone® is marketed by sanofi-aventis and Teva Pharmaceutical Industries Ltd. In the U.S. and Canada, Copaxone® is promoted by Teva and will be marketed by sanofi-aventis until March 2008. At this date, Teva will take over marketing and will report sales of Copaxone® in the U.S. and Canada.

### Treatment for relapsing-remitting multiple sclerosis providing prolonged efficacy and good tolerability

After the launch of three beta interferon drugs in succession for the treatment of MS, Copaxone® (glatiramer acetate), a new immunomodulator indicated for reducing the frequency of exacerbations in patients with relapsing-remitting multiple sclerosis (RRMS). It is characterized by a dual mode of action that is both anti-inflammatory and neuroprotective. In clinical terms, after a 2-year period of treatment, Copaxone® was more effective against relapses than placebo.

### Life Cycle Management

A major phase III clinical study, PreCISE, was launched in Europe in September 2004 to demonstrate the benefits of Copaxone® in early-stage relapsing-remitting MS when the medicine is prescribed after the first relapse. If this objective is achieved, an application for extension of indication for Copaxone® will be filed.



## ONCOLOGY

# Taxotere®

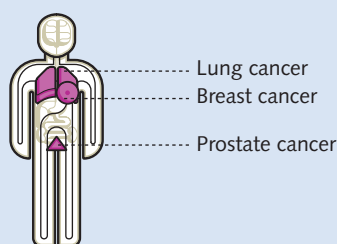
docetaxel

2004 pro forma net sales

1,436 million euros

+11.3%\*

### Solid tumors



- **Breast cancer, non-small cell lung cancer (NSCLC), prostate cancer, cancers of the head and neck and gastric cancer are the cause of high morbidity and mortality.**

In the United States and in Europe, cancer-related mortality comes second after cardiovascular disease. In both men and women, lung cancer is the first cancer-related cause of death.

Breast cancer in women and prostate cancer in men are the second leading causes of cancer-related mortality.

According to the EUCAN 1998 European statistics, there were 210,631 cases of breast cancer, with 73,592 deaths; for lung cancer the figures were 196,863 cases leading to 183,653 deaths in Europe.

## TAXOTERE® FOR SOLID TUMORS

The reference chemotherapy agent  
for several types of cancer

### Main markets

Taxotere® is one of the mainstays of our oncology franchise, and has marketing approval in more than 86 countries. Taxotere®'s main markets are respectively the United States, France and Germany.

### The most prescribed taxane in the United States

Taxotere® is a chemotherapy agent for which the main indications at present are breast cancer, non-small cell lung cancer and prostate cancer. Some of the major development possibilities for Taxotere® are cancers of the head and neck and gastric cancer.

### ■ Chemotherapy is the reference treatment of all these cancers in the metastatic phases

Taxotere® significantly prolongs the life of patients suffering from these various kinds of cancer and contributes to better quality of life. As a result, Taxotere® has eight marketing approvals, the first of which was granted in 1995 as a single agent for the treatment of metastatic breast cancer. Further approvals for metastatic breast cancer were later given for combination therapy with anthracycline in 2000, capecitabine in 2003 and trastuzumab in 2004 (HER2/Neu positive patients).

### ■ In metastatic breast cancer

Taxotere® improves response rates and significantly increases patient survival. Since August 2004 in the United States and December 2004 in Europe, Taxotere® is also approved in less advanced breast cancer after surgery (adjuvant treatment). The efficacy of Taxotere® in breast cancer adjuvant therapy has been demonstrated in two major phase III studies TAX 316 (BCIRG001) and PACS01,

\*Growth on a comparable basis.

in which the five-year survival rate was as high as 91% for patients who had benefited from the sequential regimen with Taxotere®.

According to Doctor Edith Perez of the Mayo Clinic, this data would amount to saving the lives of some 300,000 women every year worldwide.

#### ■ In non-small cell lung cancer (NSCLC)

Taxotere® obtained marketing approval in 2000 in monotherapy after failure of prior chemotherapy, and in combination with cisplatin as first-line treatment in November 2002 in the United States and January 2003 in Europe. With Taxotere® as first-line treatment, two-year survival rates are higher than the reference treatment and quality of life is improved.

#### In 2004, Taxotere® continued to make outstanding progress and brought new hope to cancer patients

In two plenary session presentations at the conference of the American Society for Clinical Oncology, Taxotere® was demonstrated as providing unprecedented survival benefit for men with hormone refractory prostate cancer. The trials, which have since been published in the *New England Journal of Medicine*, demonstrated a 30% increase in the two-year survival rate after treatment with Taxotere® compared to the reference treatment. In addition, in May 2004 the FDA approved treatment with Taxotere® in combination with prednisone for men with hormone refractory prostate cancer. European approval was granted in November 2004.

### Life Cycle Management

#### ■ Taxotere® is being evaluated for treatment of other tumors, in particular gastric and head and neck cancers.

Intermediate results in a phase III Taxotere® trial for gastric cancer have demonstrated significant gain as regards response rates and time to progression, and there is a promising trend as regards overall survival.

In head and neck cancers, final results of a phase III trial of Taxotere® in combination with standard therapy, delivered prior to radiotherapy, were presented at ASCO 2004. These results showed that Taxotere® provides significant gain as regards response rates and improvement of overall survival, without increase of toxicity compared to standard treatment. According to Professor Jan Vermorken, principal investigator for this trial, the so-called "neoadjuvant" therapeutic strategy used in the trial is likely to bring fundamental changes in the management of this disease for which prognosis is very guarded.



## ONCOLOGY

# Eloxatine®/Eloxatin®

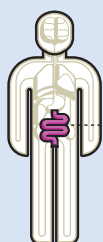
oxaliplatin

2004 pro forma net sales

1,220 million euros

+56.8%\*

### Colorectal cancer



Cancer of the colon  
and the rectum

- **One million people affected each year**

Colorectal cancer is the third most common type of cancer worldwide, with a million new cases diagnosed every year and nearly 500,000 fatalities a year. It is particularly prevalent in the Western world. Between 5 and 10% of colorectal cancers are hereditary in origin, but behavioral factors such as diet, excess calorie intake and sedentary lifestyle are the main causes.

- **Treatment includes chemotherapy**

In non-metastatic stages, surgery is the curative treatment of choice. The risk of recurrence, however, frequently warrants the use of adjuvant chemotherapy.

In metastatic forms, chemotherapy has demonstrated its efficacy in stopping or slowing tumor growth and extending patient lifespan.

## REFERENCE TREATMENT FOR COLORECTAL CANCER

### A new reference in the treatment of colorectal cancer

**Eloxatin® is a cornerstone of chemotherapy for metastatic colorectal cancer in combination with new, targeted therapies.**

While continuing to maintain sustained growth in Europe, where it is now the leader for this indication, Eloxatin® rapidly made its mark in the U.S. following its launch in 2002: it is now prescribed as the first-line treatment for 44%<sup>(1)</sup> of new patients.

#### Main markets

Eloxatin® makes a major contribution to the treatment of metastatic colorectal cancer.

Eloxatin® is licensed from Debiopharm and is registered in 70 countries. It is marketed by sanofi-aventis in Europe, the United States and the rest of the world excluding Japan, Argentina, India, Pakistan and Uruguay.

#### A new-generation platinum salt of unrivalled efficacy in colorectal cancer

Eloxatin® is a new-generation platinum salt that has brought major progress in the treatment of metastatic colorectal cancer:

- achieving median survival times of 20 months or more when used as first-line treatment;
- making surgery possible for a significant proportion of patients with isolated hepatic metastases by rapidly and significantly reducing metastasis size. Eloxatin® holds out the hope of an extended lifespan and possible recovery for these patients.

Pursuing the aim of constantly improving therapeutic strategies and extending survival times for patients suffering from metastatic colorectal cancers, a number of clinical trials have been launched into combinations of biological agents with Eloxatin®-based chemotherapy.

\*Growth on a comparable basis.





The pivotal role of Eloxatin®-based chemotherapy has been confirmed: the E3200 randomized phase III study carried out by U.S. cooperative research group ECOG showed a 26% reduction in the risk of death for patients receiving chemotherapy based on Eloxatin® in combination with a biological agent targeting tumor vascularization. Results from other trials in progress are due for publication in 2005 and 2006.

#### **2004: Registration in Europe and the U.S. for the adjuvant (post-surgical) treatment of colon cancer**

Eloxatin® has been further developed as an adjuvant treatment for colon cancer, the aim being to prevent recurrence in patients for whom surgery alone may not be sufficient to achieve recovery (stages II and III).

The MOSAIC study, involving over 2,200 patients having undergone surgery for stage II or stage III colon cancer in over 20 countries, showed that Eloxatin® as an adjuvant treatment reduces the risk of recurrence at 3 years by 23% compared to the standard treatment (5FU/leucovorine). By eradicating residual tumor cells, post-surgical adjuvant chemotherapy helps to increase cure rates. These positive results were published in June 2004 in the *New England Journal of Medicine*<sup>(2)</sup> and provided the basis for registration of Eloxatin® for the adjuvant treatment of stage III colon cancer in Europe on September 12, 2004 and in the U.S. on November 4, 2004. Eloxatin® is now the adjuvant treatment of reference for stage III colon cancer. New studies initiated by cooperative research groups or pharmaceutical companies now include an Eloxatin®-based control arm.

At end 2004, 45% of patients undergoing surgery for stage II colon cancer in the U.S. are given adjuvant treatment based on Eloxatin®.

### Promising life cycle management

#### **Treatment of other cancers**

Investigations are under way into the potential benefits of Eloxatin® in the treatment of other cancers, in particular **digestive tract tumors** including pancreatic and gastric cancer, but also lung cancer (non-small cell lung cancer).

Eloxatin® is registered in South Korea for the treatment of gastric cancer.

#### **■ Development of a new liquid formulation**

For greater ease of handling and enhanced safety, a new aqueous solution formulation of Eloxatin® has been developed, requiring no reconstitution prior to dilution and administration.

Registration of the new formulation in the U.S. was obtained on January 31, 2005, and the product is due for launch in the U.S. and Europe in the course of 2005.

(1) Source: Intrinsiq Research—Rolling 3-month totals—December 2004.  
(2) André et al. *NEJM* 2004, 350; 2343-2351.

## ONCOLOGY

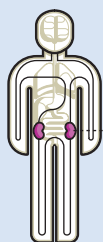
# Fasturtec®/Elitek™

*rasburicase*

2004 pro forma net sales  
**31.6 million euros**  
**+12.8 % \***

### Tumoral lysis syndrome

Possible complication



Renal insufficiency  
due to chemotherapy

- **Need to prevent and control side effects of chemotherapy**

Now that modern chemotherapy cures an ever increasing number of leukemias and lymphomas, more particularly those affecting children, the medical profession is focusing on the need to prevent and control side effects of chemotherapy. Paradoxically, it is the efficacy of treatment that may lead to severe or even life-threatening side effects. In certain cancers, the very rapid destruction of the tumor by chemotherapy gives rise to a massive release of cellular waste and residual materials that may overwhelm the kidneys' capacity to eliminate. One of these waste materials, uric acid, plays a particularly important role because it is not easily soluble, so that it may precipitate in the form of crystals in the kidneys and obstruct them, causing a vital risk.

- **Tumor lysis syndrome** frequent results in acute renal failure which may require dialysis and leads to significant morbidity. At the very least, it delays chemotherapy and may therefore reduce its efficacy.

## TREATMENT AND PREVENTION OF TUMOR LYSIS SYNDROME

Two major publications, B. Coiffier et al<sup>(1)</sup> and M. Cairo & M. Bishop<sup>(2)</sup>, consolidate the role of Fasturtec®/Elitek™ for treatment and prevention of tumor lysis syndrome.

### Main markets

Fasturtec® (1.5 mg form) was granted marketing approval in Europe in February 2001 and was first launched in certain European countries in May of that year. In April 2002, the 7.5 mg form was registered in Europe and marketing coverage of Europe was completed when the medicine was made available to the medical profession in France and Italy in October 2002. In the United States, the FDA approved the drug for pediatric indications in July 2002 and it was marketed in the month following approval under the brand name Elitek™.

### Fasturtec® is an authentic therapeutic breakthrough which prevents or treats an extremely severe side effect of chemotherapy used to treat some blood cancers: tumor lysis syndrome

Fasturtec®/Elitek™ is a recombinant enzyme produced by genetic engineering. Within less than four hours, it converts uric acid into highly soluble allantoin, which is then easily eliminated in the urine, thereby preventing tumor lysis syndrome.

By administration prior to or in combination with chemotherapy, Fasturtec® allows clinicians to almost completely prevent the occurrence of side effects and so effectively administer anti-cancer treatment without delay or dose reduction.

(1) B. Coiffier et al\*, Efficacy and Safety of Rasburicase for the Prevention and Treatment of Hyperuricemia, Journal of Clinical Oncology, Vol 21, N°23, 2003.

(2) M. Cairo & M. Bishop, Tumor Lysis Syndrome: new therapeutic strategies and classification, British Journal of Haematology, 127, 3-11, 2004.

\*Growth on a comparable basis.



**Fasturtec®/Elitek™** is the first biotechnology product entirely discovered and developed by sanofi-aventis and manufactured in its state of the art facility in Labège. Given that the market potential is fortunately limited, due to the rarity of the pathology, sanofi-aventis has undertaken to also develop orphan drugs addressing major vital risks which do not have a satisfactory therapeutic response.

**2004: Fasturtec® is a unique medication, the first choice for the prevention and treatment of tumor lysis syndrome**

Administered concomitantly with chemotherapy, Fasturtec® eliminates uric acid as fast as it is released by tumor cells. Its action is very rapid (4 hours after onset of treatment) and particularly prolonged (nearly 17 hours). Its efficacy and speed of action recommend Fasturtec® for the prevention of renal complications.

Pre-approval studies of Fasturtec® demonstrated the need for at-risk patients to be treated with a sufficient dose (0.2 mg/kg) and for a sufficient period of time (5 to 7 days). Registration of the 7.5 mg form in Europe provides healthcare professionals with a full product range, simplifying administration of the drug and facilitating good treatment conditions.

## Life Cycle Management

### ■ Registration of the 7.5 mg form in the United States and Canada

In order to complement the product range, the 7.5 mg form has recently been filed for approval in the United States and Canada, and launch is expected in the second half of 2005.

■ **Continuation of clinical development in Japan** where it is expected that registration procedures for the prevention and treatment of tumor lysis syndrome in adults and children will be filed in 2006.



## METABOLIC DISORDERS

# Lantus®

*insulin glargine*

2004 pro forma net sales

843 million euros

+79.7%\*

## TREATMENT OF TYPE 1 AND TYPE 2 DIABETES

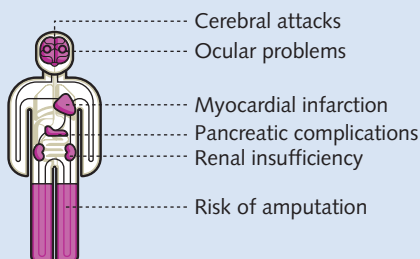
The first long-acting basal insulin  
analog providing 24-hour coverage

### Main markets

Lantus® was launched in Germany in 2000 and in the U.S. in 2001, and is now marketed in over 70 countries.

## Diabetes

### Possible complications



### • A chronic disease

Diabetes is a chronic disease in which the body fails to produce or properly use insulin, a hormone needed to convert glucose into energy. In diabetics, this conversion process is impaired or even fails to function, leading to a high blood glucose level, known as hyperglycemia.

In type 1 diabetes, the body fails to produce or secrete any insulin at all because the pancreatic beta cells that produce insulin have been destroyed by the body's own immune system. Type 2 diabetics suffer from a progressive form of the disease. The pancreas continues to produce insulin, but not in sufficient quantities to keep blood glucose levels under control. In addition, insulin production by the pancreas tends to diminish over time.

### • Controlling diabetes to minimize risks

Although diabetes cannot be cured, it can be treated or controlled very effectively. The parameters to be monitored closely in diabetes are:

- blood glucose (glycemia) level, which should be held as close as possible to normal;
- glycosylated hemoglobin or HbA1C (A1C) levels, which give an estimate of average blood glucose levels over the past two to three months. Non-diabetics naturally maintain an HbA1C level of between 4 and 6%, while diabetics attempt to keep their HbA1C level below 7%.

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

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

### • Soaring epidemiology

Millions of people around the world suffer from diabetes and its complications. This disease affects 200 million people today and WHO statistics predict that over 300 million people will be affected by 2025.

\*Growth on a comparable basis.

**Lantus® (insulin glargine [rDNA origin] injection) is the first and only basal (long-acting) insulin analog to provide 24-hour glycemia control through a once-daily injection.**

Lantus® is indicated for once-daily administration by a single subcutaneous injection in patients with type 2 diabetes requiring basal (long-lasting) insulin to control their hyperglycemia, and in adults and children (aged 6 and over) suffering from type 1 diabetes.

Lantus® may be administered at any time of the day (but at the same time every day), in both type 1 and type 2 diabetics (U.S./Europe).

**Meeting the challenge of insulin supply**

Millions of people around the world depend on insulin to manage their diabetes. Sanofi-aventis, world leader in the development and production of innovative treatments for diabetes, has built up its insulin production capacities to record levels. Our state of the art facilities in Frankfurt are capable of meeting the insulin needs of over two million diabetics around the world.

**Outstanding facts**

- As of end October 2004 (MAT Q3 2004), Lantus® is the most frequently prescribed brand of insulin in the world with a market share of 13.7%, outstripping all its main rivals.
- Two new studies involving Lantus® were presented to the medical community in 2004:

**The LAPTOP study** (Lantus® + Amaryl® + metformin vs. premixed\* insulin in Patients with Type-2 diabetes mellitus after failing Oral treatment Pathways) showed the benefits of Lantus® in combination with oral antidiabetics as compared to two premixed insulins. In this study, more patients achieved optimal glycemia control (A1C < 7%) with no episodes of nocturnal hypoglycemia (low blood glucose levels during the night) in the Lantus® group than in the premixed insulin group.

**The LANMET study** demonstrated the glycemia control provided by a combination of Lantus® + metformin with remote monitoring of glucose levels, enabling patients to find their individual optimum Lantus® dosage.

- Finally, **the ATLANTUS study** showed the benefits of self-directed titration of doses by the patient.
- **OptiClick™: a new reusable pen**  
OptiClick™, a new reusable pen for the injection of Lantus® by type 1 and type 2 diabetics, received approval in the U.S. and Europe (August 2004) and in Japan (August 31, 2004).

**Apidra™ receives approval in Europe and the U.S.**

Apidra™, a rapid-acting human insulin that complements the Lantus® range, was approved in the U.S. (April) and in Europe (September).



## METABOLIC DISORDERS

# Amaryl®/Amarel®/Solosa®

glimepiride

2004 pro forma net sales

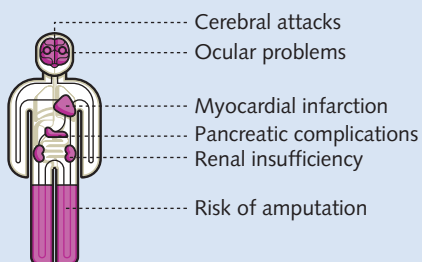
684 million euros

+18.8%\*

## Non insulin-dependent diabetes mellitus (NIDDM) or type 2 diabetes

See also the box on diabetes on page 78

### Possible complications



A chronic progressive disease influenced by genetic and environmental factors, type 2 diabetes affects both rich countries and the developing world alike. It is most prevalent in the U.S., India, the Caribbean and the Gulf states. There is a strong correlation between diabetes and the rise in obesity.

## TREATMENT OF TYPE 2 DIABETES

Amaryl® is now a reference first-line oral treatment for type 2 diabetes and is growing strongly in both the U.S. and Japan, two markets where it has become the leader in its drugs class, the hypoglycemic sulfonylureas.

### Main markets

(1, 2, 3 and 4 mg, maximum dose 8 mg) was launched in 1995 in Europe and in 1996 in the U.S. and is now marketed by sanofi-aventis in 100 countries. The main markets for Amaryl® are the U.S., Japan, Germany, France, South Korea and Algeria. Amaryl® is the fastest-growing sulfonylurea on the U.S. market and the leader in its class in Japan. Amaryl® has also established itself as the leading oral diabetic treatment, all classes considered, in Germany, South Korea, Poland and Scandinavia. Amaryl® is the only sulfonylurea to have demonstrated 24-hour efficacy against both fasting and postprandial hyperglycemia in a once-daily dose, by stimulating the physiological mechanism of biphasic insulin release. This advantage positions Amaryl® as a first-line treatment for patients with type 2 diabetes.

\*Growth on a comparable basis.

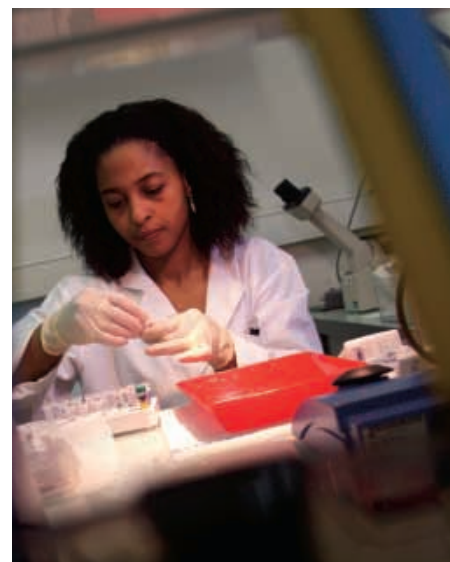
### A unique profile for worldwide success

Amaryl® now has a track record of over 100 million patient years. It is a new-generation, once-daily sulfonylurea which, used either as a monotherapy or in combination with metformin or insulin, provides fast and effective 24-hour control of both basal and postprandial hyperglycemia in NIDDM patients. Its dual mechanism of action, both pancreatic and extra-pancreatic, acts on the two physiopathological factors involved in this disorder, insulin deficiency and insulin resistance, to restore the physiological action of endogenous insulin.

The 2004 congresses of the American Diabetes Association (ADA) in Orlando and of the European Association for the Study of Diabetes (EASD) in Munich confirmed Amaryl® as the treatment of reference both as first-line therapy or in combination with other oral diabetes drugs or insulin, and with Lantus® in particular.

Studies already published or in the process of publication establish Amaryl® as the treatment of choice in combination with insulin, and Lantus® in particular, enabling patients unable to achieve sufficient blood sugar control with oral diabetes drugs alone to begin treatment with Lantus®, while continuing to take Amaryl® for more effective control of their glycosylated hemoglobin (HbA1C) level. A monitoring study carried out in 2004 illustrated the considerable value of the efficacy and tolerability of Amaryl® in special situations. Amaryl® was shown to be remarkably effective in correcting hyperglycemia in NIDDM patients observing Ramadan, i.e. fasting during the day and feasting at night, with no increased risk of hypoglycemia.

This information on efficacy and tolerability is of great importance to patients who may find themselves in such special circumstances.



### Life Cycle Management 2005-2008

■ The patent on Amaryl® expires at end October 2005 in the U.S. (if the FDA approves the filing for pediatric indication, which will give a 6-month extension), and at end December 2005 in most European markets. Amaryl® will continue to be protected by patent in Japan until December 2005.

■ Sanofi-aventis is pursuing two complementary solutions in order to protect its investment in Amaryl®. In the first instance, the Group is partnering other companies in exploring different options for developing a fixed-dose combination with metformin, with the aim of launching in certain target markets between 2005 and 2008. At the same time, the Group is also working closely with Winthrop to provide generic versions of Amaryl® for certain markets.

## INTERNAL MEDICINE

# Allegra®/Telfast®

fexofenadine

2004 pro forma net sales

1,502 million euros

## RESPIRATORY DISORDERS

TREATMENT OF THE SYMPTOMS ASSOCIATED WITH SEASONAL ALLERGIC RHINITIS (SAR) AND CHRONIC IDIOPATHIC URTICARIA (CIU) OR HIVES

### Main markets

Allegra® is marketed in over 55 countries, including the U.S. (number 1, with a market share of 38.9%), Japan (number 2, 17.7% market share) and Australia (number 1, 42.6% market share).

### New-generation antihistamine

Allegra®/Telfast® is an effective, long-lasting and non-sedating prescription antihistamine that can be taken once or twice daily (depending on dosage and indication) for the treatment of seasonal allergy (hay fever) and hives (chronic idiopathic urticaria). It provides patients with potent relief from the symptoms of allergy without inducing drowsiness.

Sanofi-aventis also markets Allegra-D 12 Hour®, a formulation combined with an extended-release decongestant for effective and non-sedating relief of seasonal allergy symptoms including nasal congestion. Allegra-D 24 Hour®, a combined antihistamine and decongestant in a single once-daily dose, received FDA approval in October.

The three main markets for Allegra-D 12 Hour® are the U.S. (number 1, with a market share of 49%), Brazil (number 4, 12.5% market share) and Mexico (number 8, 2.4% market share).

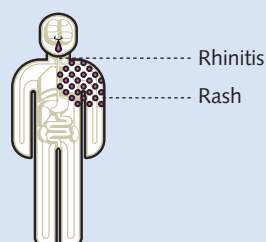
### Recent advances

A submission for approval was filed in the U.S. in December 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 and two new pediatric forms are also under development: a 30 mg orodispersible tablet and a 6 mg/ml oral suspension.

All three will be filed for approval in the U.S. in 2005.

## Allergy



### • 1 child in 15 around the world affected

Allergy is an excessive reaction or hypersensitivity of the immune system to certain specific substances (allergens) such as pollen, mold, house dust mites, animal fur/dander and insect bites/stings.

When an allergic person is exposed to a specific allergen, the immune system produces antibodies known as IgE (immunoglobulin E) antibodies; IgE is a protein that acts as a signal to the immune system. Each IgE antibody is always specific to a particular allergen.

### • Symptoms associated with allergies

Sneezing, blocked or runny nose, cough, itchy or watery eyes, itchy nose or throat, post-nasal drip, itching skin or rash.



## INTERNAL MEDICINE

# Nasacort®

*triamcinolone acetonide*

2004 pro forma net sales

287 million euros

+10.8% \*

## RESPIRATORY DISORDERS

TREATMENT OF THE SYMPTOMS ASSOCIATED WITH SEASONAL AND PERENNIAL ALLERGIC RHINITIS IN ADULTS AND CHILDREN 6 YEARS OF AGE AND OLDER

### Main markets

Nasacort® AQ Spray is available in 44 countries around the world, including the U.S. (number 3, with a market share of 14.4%), France (number 2, 19.3% market share) and Canada (number 3, 9.8% market share).

### Nasal spray containing an unscented aqueous suspension

Nasacort® (triamcinolone acetonide) AQ Spray is a nasal spray containing an unscented aqueous solution and delivering metered doses of a microcrystalline suspension of triamcinolone acetonide. It is indicated in the treatment of the nasal symptoms of seasonal and perennial rhinitis in adults and children aged 6 and over.

In April 2004, FDA approval was granted for Nasacort® HFA Nasal Aerosol, the first intranasal corticoid dry-aerosol formulation approved in the U.S. that contains hydrofluoroalkane (HFA) rather than chlorofluorocarbons (CFC).

### Recent advances

Nasacort® HFA Nasal Aerosol will offer physicians and patients a new option for those seeking dry-aerosol formulation for the management of nasal allergy symptoms. It replaces the Nasacort® Nasal Inhaler which was taken off the market in July 2003 to comply with Environmental Protection Agency (EPA) and FDA regulations on protection of the ozone layer that required all nasal inhalers containing CFCs to be withdrawn from the U.S. market.



\*Growth on a comparable basis.



## INTERNAL MEDECINE

# Ketek®

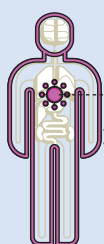
*telithromycin*

2004 pro forma net sales

189 million euros

+66.5%\*

### Respiratory infections



High and low respiratory infections

Contamination

- **A frequent cause of morbidity and mortality**

The World Health Organization considers that respiratory tract infections cause more than 4 million deaths a year. In the United States, 14 million cases of exacerbation of chronic bronchitis are reported yearly and smokers are particularly affected. Pneumonia, with 2 or 3 million cases a year in the United States, gives rise to 500,000 hospital admissions annually and can have very serious consequences as regards morbidity and mortality in elderly patients.

- **Combating bacterial resistance**

In recent years, there has been a progressive and rapid increase in resistance acquired by the principal germs causing respiratory infection, particularly pneumococcus and *haemophilus*. Probabilistic antibiotherapy must take this growing development of antibiotic resistance into consideration.

## ANTI-INFECTIVES

TREATMENT OF MILD TO MODERATE ACUTE COMMUNITY-ACQUIRED PNEUMONIA, ACUTE EXACERBATION OF CHRONIC BRONCHITIS, ACUTE BACTERIAL SINUSITIS AND TONSILLITIS/PHARYNGITIS CAUSED BY GROUP A BETA-HEMOLYTIC STREPTOCOCCI

Ketek® met with great success on its August 2004 launch in the United States, with sales totaling 51 million euros and a higher prescription rate on launch than that of many market leaders when they were launched.

### Main markets

Ketek® was launched in Germany in 2001 and in 2002 in other major European markets.

In Japan, Ketek® is marketed by two partners, Fujisawa Pharmaceuticals Co. and Sankyo Co.

### A new class of antibiotics: ketolides

Ketek® is the first drug in a new class of antibiotics, ketolides, developed for the treatment of upper and lower respiratory tract infections in adults, and to respond to present needs regarding bacterial epidemiology: in France for example, one out of two pneumococci is resistant to the two main classes of antibiotics, beta-lactamines and macrolides.

\*Growth on a comparable basis.



**More than 13 million patients have already been treated with Ketek® worldwide**

Ketek®'s anti-bacterial activity spectrum targets the main germs causing respiratory infection, with in particular potent activity against resistant pneumococci, so that successful treatment for most indications can be achieved in as little as five days. Because of a "3-keto" function included in the compound—which is how this new class acquired the name ketolides—Ketek® has a lesser selection potential for resistant pathogens and thereby meets the needs of present day epidemiology.

**2004: New developments**

Two major clinical trial programs, enrolling several thousand patients, were initiated in 2004 to demonstrate the clinical and microbiological benefits of Ketek® for the treatment of respiratory infections:

- The PERSPECTIVE study, to evaluate bacterial eradication in a large cohort of patients (more than 5,000), presenting with an exacerbation of chronic bronchitis.
- The KEYS study, to evaluate the benefit of Ketek® in terms of "Health Outcomes", such as number of hospitalizations or of return visits for 4,000 patients suffering from pneumonia or exacerbation of chronic bronchitis.

**Life Cycle Management**

**■ A pediatric formulation for Ketek® to treat respiratory tract infection in children**

Sanofi-aventis has developed a pediatric formulation for Ketek®, to treat respiratory tract infection in children. A large-scale phase III clinical development program is to be organized in 2005 for the following indications: acute otitis media, pneumonia and tonsillitis/pharyngitis caused by group A beta-hemolytic streptococci. If results are favorable, the ease of use of this new antibiotic (short term treatment with a once-daily dose), together with its excellent efficacy against respiratory germs, will make it a first-choice drug for pediatric purposes, since children are particularly exposed to the risk of carrying resistant germs.



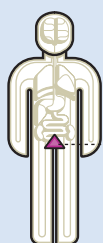
# Xatral®/Uroxatral®/Benestan®/Dalfaz® alfuzosin

2004 pro forma net sales

281 million euros

+27.7%\*

## Benign prostatic Hyperplasia



Benign tumor of the prostate,  
accompanied by urinary disorders

- **55 million men affected**

Benign prostatic hyperplasia is the most frequent benign tumor affecting men. It causes considerable discomfort because it is accompanied by an urgent and frequent need to urinate, particularly during the night. About one man in two is affected by these urinary symptoms after the age of 70, which represents a potential of more than 55 million men in 2004 and 59 million in 2009.

- **The disorder is under-diagnosed and under-treated**

A recent survey (MSAM-7) in seven countries (United States, France, Italy, United Kingdom, Spain, Germany and the Netherlands) involving 14,000 men over 50, revealed that only 19% of men with moderate symptoms were being treated and 43% of those with severe symptoms.

An increasing concern for quality of life should lead to a 50% increase in the number of patients being treated by the end of the decade. In addition, men over 50 suffering from benign prostatic hyperplasia are also four times more at risk of developing sexual dysfunction, an area in which there is growing demand for treatment.

- **Complications**

If left untreated, benign prostatic hyperplasia may worsen and in the long term lead to acute urinary retention for which emergency surgery is frequently required.

## UROLOGY

### TREATMENT OF BENIGN PROSTATIC HYPERPLASIA AND OF ACUTE URINARY RETENTION

#### Main markets

Registered in 95 countries in its most optimized once daily version, Xatral® OD is marketed by sanofi-aventis worldwide, except in Australia and Japan.

#### A unique position, the most dynamic drug in its category

- **A uroselective alpha 1-blocker which does not affect sexual function**

Xatral® is the first alpha 1-blocker on the market for the treatment of benign prostatic hyperplasia (BPH) symptoms with a selective effect on the urinary system.

It is immediately active after administration of the first dose. Xatral® provides rapid and lasting relief of urinary symptoms improves quality of life and is well tolerated, in particular as regards the impact on the cardiovascular system.

Quality of life and sexuality in particular, is a dimension that must be considered when selecting treatment for benign prostatic hyperplasia. Unlike certain other medications, Xatral® does not impair patient sexual function. The sexual side effects are similar to those observed with a placebo.

- **The first alpha-blocker to obtain an indication as adjuvant treatment during episodes of acute urinary retention**

In addition to evaluation of symptomatic treatment of BPH, major clinical development work is proceeding on the main complication of the disorder, i.e. acute urinary retention (AUR), as regards both management of the acute phase and prevention.

\*Growth on a comparable basis.



Results of the ALFAUR study have shown in particular that Xatral® OD doubles the probability of a return to spontaneous miction after an episode of acute urinary retention with insertion of a urethral catheter. It has also been demonstrated that Xatral® OD reduces the risk of recurrence within six months of an initial episode of AUR. Results of the ALFAUR study have been included in the summary of the product's characteristics in many countries, including Canada and the main European markets. The submission is under evaluation in many other countries, in particular Spain, the Netherlands and Switzerland.

#### **U.S. launch: a major growth opportunity**

With a potential of approximately one billion dollars, the U.S. market in 2004 represents more than 38% of global sales of benign prostatic hyperplasia medication, growing by 22%.

Launched from November 2003 to February 2004, the marketing of Uroxatral® in the United States is an excellent growth opportunity for the product.

## **Life Cycle Management**

### **■ Management and prevention of acute urinary retention**

The results of two international studies, ALFAUR US for the management of acute urinary retention and ALTESS for primary prevention of acute urinary retention, will be available in 2005/2006.

### **■ Management of benign prostatic hyperplasia in Japan**

Clinical development of the OD (once daily) version for benign prostatic hyperplasia was initiated in Japan in 2003. Phase I for Japanese patients is completed. A phase II study is ongoing.

### **■ Management of abacterial prostatitis**

Abacterial prostatitis is one of the most frequent disorders that urologists encounter on a daily basis (about 8% of patients). Etiology is uncertain, but symptomatology is similar to benign prostatic hyperplasia, with increased pain.

Some preliminary studies have shown that alfuzosin has a favorable effect on the disorder and a full-scale development procedure has been started in Europe and in the United States to obtain a new indication.

## INTERNAL MEDECINE

# Actonel®

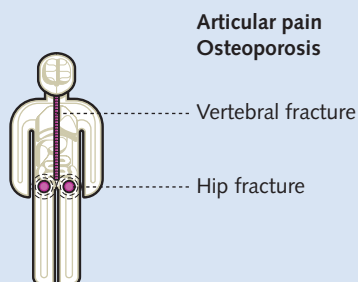
*risedronate sodium*

2004 pro forma net sales

305 million euros

+59.7%\*

## Osteoporosis



- **One woman in three and one man in seven will suffer from an osteoporosis-related fracture in their lifetime and one woman in five will suffer a second such fracture within twelve months of the first.**

200 million women over the age of 50 suffer from post-menopausal osteoporosis. Only 53% of them are diagnosed and treated. The clinical consequences of lack of treatment may lead to an increased mortality rate.

Osteoporosis is a progressive disease characterized by low bone mineral density (BMD) and decreased bone mass, weakening the skeleton and increasing the risk of fracture. Osteoporosis exists when bone mass is resorbed faster than it is replaced.

- **A disease of ageing**

Osteoporosis is a disease of ageing, generally triggered by post-menopausal hormone changes. Other factors, however, can contribute to an increased risk of developing osteoporosis, including slight body frame, ethnic origin (Caucasoid or Asian), a diet low in calcium, nulliparity. The disease may also be triggered by hormone changes induced by glucocorticoid treatments, and is thus a recognized side effect of prolonged glucocorticoid therapy.

## RHEUMATOLOGY

TREATMENT AND PREVENTION  
OF POST-MENOPAUSAL OSTEOPOROSIS  
TREATMENT OF PAGET'S DISEASE

In 2004, Actonel® enjoyed both strong sales growth and a significant increase in the number of treatment days (source IMS: +40%).

### Main markets

Since its initial launch in 2000, Actonel has received approval in 92 countries.

Actonel® is licensed by Procter & Gamble Pharmaceuticals to sanofi-aventis and co-distributed by Procter & Gamble Pharmaceuticals and sanofi-aventis in Europe, the United States and Canada via the *Alliance for Better Bone Health*. In Japan, Actonel® is marketed by sanofi-aventis under license to Ajinomoto.



\*Growth on a comparable basis.





**In 2004, an extension to the range, combining Actonel® 35 mg and calcium tablets.**

The *Alliance for Better Bone Health* obtained marketing approval for a number of European countries to release an extension to the range, combining Actonel® 35 mg and calcium tablets in the same box. This innovative combination will simplify treatment for osteoporosis sufferers, which should improve treatment compliance and thereby increase the efficacy of the therapy still further. The first launch of the new combination was in February 2005 in Germany.

**The only biphosphonate providing rapid and prolonged protection against vertebral and non-vertebral fractures.**

Actonel® is a third-generation biphosphonate which prevents bone loss by inhibiting bone resorption.

Actonel® 35 mg weekly and Actonel® 5 mg daily tablets are indicated in the treatment of post-menopausal osteoporosis and Actonel® 5 mg daily tablets are also indicated in the prevention of glucocorticoid-induced osteoporosis in patients either initiating or continuing systemic glucocorticoid treatment (daily dosage  $\geq 7.5$  mg of prednisone or equivalent) for chronic diseases.

Actonel® 35 mg is also indicated in the treatment of Paget's disease, a rare bone disease. It is the only osteoporosis therapy to have demonstrated a rapid effect on reducing the risk of fracture in the first year of treatment. According to the findings of a long-term clinical study presented at ENDO 2003, Actonel® maintains a low incidence of new vertebral fractures in patients suffering from Paget's disease over a treatment period in excess of seven years.

**The Alliance for Better Bone Health**

is widely recognized by the scientific community for the quality of its research aimed at providing a better understanding of the pathology of osteoporosis.

The Alliance published new data in 2004 demonstrating the efficacy of Actonel® in maintaining bone quality, a key factor in the reduction of fracture risk that is the ultimate objective of any osteoporosis treatment.

## A portfolio based on sound products

■ *Alongside its flagship medicines, sanofi-aventis made a strategic decision some years ago to continue to support its mature products with appropriate promotional investment, keeping faith with one of the Group's fundamental principles: that there is no such thing as a small product, since each contributes to meeting a medical need and provides a certain economic advantage.*

Physicians need in their therapeutic armamentarium tried and tested drugs of excellent quality, of which they have long and objective experience. There is also strong demand from health care systems for medicines of this kind, which are essential in keeping costs down. With its extensive portfolio of medicines, sanofi-aventis is ideally placed to address the concerns of patients, health care professionals and payers alike.

### Prescription medicines

Sanofi-aventis mature products cover numerous therapeutic areas, including:

#### ■ Antibiotics

Sanofi-aventis has been involved in antibiotics research from the outset and offers a vast range of solutions for health professionals to choose from. The range of classic antibiotics includes products as varied as Claforan®, Tarivid®, Pyostacine®, Rulid®, Targocid® and Tavanic®. Sanofi-aventis is also engaged in the fight against tuberculosis, a major public health problem in certain emerging countries, with Rifadine®, Rifater® and Rifinah®.

#### ■ Cardiovascular

The Group's portfolio includes brands which are references in their class, such as Lasilix®, the loop diuretic of choice, Cordarone®, the world's top-selling anti-arrhythmic or Tildiem® (calcium antagonist), Celecol® and Sectar® (beta blockers) and Torental® (peripheral vasodilator).

#### ■ Antidiabetics

These include classic products which round out the Group's offering in this therapeutic area: the Insuman® human insulin range, the top-seller in its class in Germany (Europe's biggest market for insulin) or Daonil®, still a sulfonylurea of reference for diabetologists.

#### ■ Central Nervous System

Sanofi-aventis also offers a full range of classic products with Solian®, indicated for schizophrenia and Rilutek® for patients suffering from amyotrophic lateral sclerosis (ALS).

#### ■ Pain relief

The portfolio of analgesics for the management of pain is ideally structured, with every level of pain relief represented: flagship prescription products include Profenid®/Orudis® (ketoprofen) and, among the anti-spasmodics, No-Spa® which is much in demand in Russia and in Poland.



### Sales of main mature medicines

Sales of classic medicines show certain specific regional characteristics: they are more strongly represented in the Group's domestic markets, France (62% of the portfolio) and Germany (40% of the portfolio). They are also to be found in emerging markets (56% of the portfolio), however, where such mature products are better suited to local economic constraints and patient needs.

The mature products portfolio serves as a solid base for the Group's global sales and underpins the growth of strategic products. The aim is to leverage renewed growth for this portfolio through innovative approaches to promotion and resource allocation, to ensure continued profitability.

### ■ Consumer health products (OTC)

Sanofi-aventis is a key player in the OTC (over the counter) market, ranking eighth in the world by sales\*. OTC products are those which can be sold directly by the pharmacist, without prescription, whether or not they are reimbursed.

Widely recognized and appreciated by physicians, pharmacists and patients alike, they play a vital role in the day to day management of family health. They offer the whole family effective relief for a range of common disorders for which self-medication is becoming an increasingly popular choice. In so doing, they make an active contribution to better management of health care spending.

The Group's five main OTC markets are France, Italy, Brazil, Mexico and Russia.

The OTC portfolio covers mainly the following therapeutic areas: gastro-enterology (Maalox®, Enterogermina®), analgesics (Doliprane®, Aspegic®...), respiratory disorders (Rhinathiol®), circulatory disorders, vitamins and dietary minerals, dermatology.



**Winthrop** a brand dedicated to generics

The world market for generics currently represents 25% of unit consumption and 12% of total spending on medicines (IMS 2003), and is growing two and a half times faster than the world market. By 2010, it is estimated that 50% of unit consumption of medicines will be represented by generics.

As a means of strengthening its involvement in controlling health care costs and in providing access to medicines for developing countries, sanofi-aventis has opted to gather all its generic products into a single dedicated business under the name of Winthrop, thereby guaranteeing the highest standards of quality, not only in terms of product efficacy and safety but also of strict manufacturing quality control.

Sanofi-aventis is already operating in generics in seven countries, with different market shares: UK, France, Portugal, Colombia, Germany, Czech Republic and a newly-launched business in South America. Winthrop is planning to extend its operations rapidly to some fifteen or more countries by end 2006.

As of January 2005, all Group generics activity worldwide comes under the Winthrop Pharmaceuticals® brand name.

\*Source: Nicholas Hall reports based on DB6 2004-MSP.

*Sanofi pasteur is the vaccines division of the sanofi-aventis group, and is the largest company worldwide focusing exclusively on vaccines. 500 million people a year are protected around the world, equivalent to 1.4 million individuals a day. Offering the broadest range of products in the industry, its vaccines provide protection against 20 diseases, both bacterial (e.g. cholera, pertussis and tuberculosis) and viral (influenza, rabies, rubella, yellow fever or mumps).*

## Sanofi pasteur: a company entirely committed to vaccines

### ■ In 2004

Sanofi pasteur sales totaled 1.624 million euros, a growth rate of 7.5% over 2003.

### ■ Worldwide presence

**Sanofi pasteur is present in over 150 countries, in position to meet the needs of 80% of the world's population:**

- North America (Canada and the U.S.),
- Western Europe, in 19 countries, through Sanofi Pasteur MSD, in a joint venture with the pharmaceutical company Merck & Co.,
- Developing countries,
- Emerging countries.

**Sanofi pasteur has over 8,500 employees worldwide.**

### **Sanofi pasteur is in a leading position in most countries.**

In the United States and Canada, which together represent more than 50% of the global vaccine market, sanofi pasteur is one of the two premier vaccine manufacturers. The North American continent represented 50% of sanofi pasteur vaccine sales in 2004.

In Europe, vaccines are supplied by Sanofi Pasteur MSD, a 50/50 joint-venture between sanofi pasteur and Merck & Co. Inc. which sells vaccines in 19 countries. With a market share of 36%, Sanofi Pasteur MSD is one of the leaders on the European market, in particular in France, the United Kingdom and Germany. In 2004, Sanofi Pasteur MSD equity-accounted sales totaled 651 million euros, representing 30% of sanofi pasteur's overall activity.

Sanofi pasteur leads the field in Latin America, is expanding in Asia, particularly in China and Japan, and continues to be a major vaccine supplier to humanitarian agencies such as UNICEF. The remaining sales are made in emerging countries.

## The widest range of vaccines in the world, protecting against 20 diseases

### ■ Influenza

World leader with a market share of 37% and 1 billion doses of influenza vaccines distributed to date since launch.

### ■ Meningitis

Three vaccines are on offer: the first immunizes against *Haemophilus influenzae type b* meningitis, the second against type A and C meningitis, the strains prevalent in Africa, and the third protects against groups A, C, Y, W-135 meningococcal infections.

In January 2005, sanofi pasteur was granted a license to market Menactra™, a quadrivalent conjugate vaccine.

### ■ Polio myelitis

Inactivated injectable vaccine and oral polio vaccine (OPV). Sanofi pasteur is the world's leading manufacturer of injectable polio vaccines and a major corporate partner of the Global Polio Eradication Initiative spearheaded by the WHO and UNICEF.

### ■ Pediatric combinations

Boosters against several diseases: vaccines for children and adults to meet the requirements and immunization schedules of individual countries.

### ■ Traveler/endemic area vaccines

Vaccines against tuberculosis, typhoid fever, rabies, yellow fever, Japanese encephalitis, hepatitis A and cholera.

## Access to immunization in developing countries: sanofi pasteur's strong corporate commitment

Infectious diseases are one of the primary causes of infant mortality in developing countries. In some parts of the world, almost 70% of children fail to receive their full complement of childhood vaccinations, thereby increasing considerably their risk of dying from a vaccine-preventable disease. To address this major public health issue, sanofi pasteur has for a number of years been actively engaged in partnerships with international organizations to ensure that the people of developing countries benefit from maximum immunization coverage.

### ■ The challenges

Dengue, leishmaniasis, malaria, tuberculosis, AIDS, tetanus, pertussis (whooping cough), hepatitis B, invasive Hib infection, measles, etc. These infectious diseases are a major cause of morbidity and mortality in developing countries.

### ■ Partnerships with international organizations for local implementation of sanofi pasteur immunization actions in these countries.

• **WHO partnership for the eradication of poliomyelitis:** After smallpox, poliomyelitis should be the next infectious disease to be eradicated by immunization. The disease is still active in Africa and Asia where it causes great suffering for thousands of children.

The WHO launched a global program for the total eradication of polio in which sanofi pasteur is a major partner together with Rotary International Club, the American Centers for Disease Control (CDC) and UNICEF. The WHO hopes to achieve certification of global eradication of poliomyelitis by 2005-2006.

### • Partnership with the Global Alliance for Vaccines and Immunization (GAVI):

The Global Alliance for Vaccines and Immunization aims to facilitate access to and use of existing vaccines, and to accelerate the introduction and development of new vaccines to achieve the goal of immunization for at least 80% of the world's population by 2005. To reach this objective, a Global Fund for vaccines was created to collect funds and finance immunization programs (vaccination and infrastructure).

### • EPIVAC—partnership with the Association for Preventive Medicine ("Association pour l'Aide à la Médecine Préventive – AMP")

EPIVAC is the first training program on the organization and management of public systems for disease prevention through immunization in developing countries. This program is implemented by AMP, and was developed in partnership with the governments of recipient countries, the Universities of Abidjan Cocody and Paris IX Dauphine and in cooperation with the WHO, UNICEF, the Global Vaccine Fund and other partners in Africa.

# ▷ OUR INTERNATIONAL PRESENCE

- ▶ **Above-market growth** in all regions\*  
**+6.2%\*** in Europe  
**+13.3%\*** in the United States  
**+8.6%\*** in other countries
- ▶ A historic base in Europe, a very strong presence in the United States as well as **solid and growing presence throughout the world**
- ▶ **A considerable growth potential** in Asia, Latin America and Africa

\* IMS MIDAS GERS all available channels, December 2004.

Europe ■ United States



Asia ■ Australia / New Zealand



Our commitment...

## A resolutely global presence

to facilitate access to healthcare for all  
and ensure growth for the Group

■ Latin America ■ Africa / Middle East ■ Central / Eastern Europe

## EUROPE

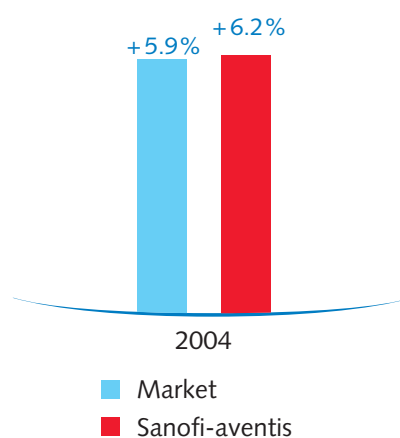
2004 pro forma net sales:  
**11,122 million euros**

Across the whole of Europe, 2004 saw a further tightening of government policies aimed at containing health costs. These new measures continue to exert pressure on the price of medicines and encourage the prescription of generic versions of medicines that are no longer patent-protected.

Sanofi-aventis, the pharmaceutical industry leader in Europe\*, has confirmed its ability to outperform market growth. The Group is leading the top five players in the pharmaceutical industry in terms of growth rate and is first in terms of growth in absolute value. Certain European affiliates, such as Portugal, Greece and Hungary, have even achieved growth rates above 15%\*.

**In Europe**, where controls on healthcare costs are being strengthened, sanofi-aventis has one of the highest growth rates in the pharmaceutical industry and underlines its aim to become the leader of the European pharmaceutical industry.

\* IMS MIDAS, GERS for France, IMS NPA for Spain, Europe: 22 countries and 34 channels, MAT December 2004.



*Sales growth in Europe\**

Europe is the core of the Group's historic presence:

- Almost all of the Group's chemical manufacturing plants are located in Europe (France, Germany, Italy and Hungary);
- Europe is home to 19 of the 27 sanofi-aventis research and development sites.

The Group's vaccines business also has a strong presence in Europe, where in most countries it is conducted through Sanofi Pasteur MSD, a joint-venture with Merck & Co.

## FRANCE

**Ranking: N°1\***

2004 was marked by the introduction of a series of health service reforms that will only impact the pharmaceutical industry as of 2005.

In the year 2004, measures introduced in the previous year to cut drug spending had the biggest impact on the distribution chain and supplementary insurance providers, due to the lowering of reimbursement rates on certain medications. Additionally, the earlier than planned publication of the list of generic drugs authorized for substitution accelerated the penetration of generics. Stilnox®, which lost its patent protection in June 2004, was affected by this measure.

Lastly, pharmaceutical companies were once again heavily taxed, with increases in the tax on promotional activities and the corporate tax on pharmaceutical sales, which now becomes a permanent fixture.

Despite this difficult context, sales figures for sanofi-aventis continued to increase. The cardiovascular range performed well thanks to Plavix®, Aprovel®/CoAprovel® (co-marketed with BMS), Lovenox® and Triatec®. Lantus®, which was launched in 2003, has confirmed its potential as a major product. Strong growth of the Group's cancer treatments, particularly Taxotere® and Eloxatine®, was driven by extended indications. In internal medicine, Inipomp® and Xatral® continued their progression. Actonel®, which is co-marketed with Procter & Gamble (sales not consolidated into Group figures), registered growth in excess of 50%\*.

Today, with a market share of over 16%\*, sanofi-aventis is the leader on the French market.

\* GERS retail and hospital sales, MAT December 2004.





## GERMANY

Ranking: N°1\*

The German market, already constrained by the reference price system introduced in the late 1980s, tightened even further. The health authorities introduced numerous measures to continue limitations on spending in 2004. A mandatory 16% price discount was imposed on all medications, with the exception of hospital medicines, reference-price medicines and privately-prescribed medicines. This discount was reduced to 6%, as of January 2005. Additionally, patented medicines removed from the reference-price system in 1996 were reinstated if they failed to prove superior therapeutic action as defined by the Joint Federal Committee.

**The new Frankfurt manufacturing facility for the active ingredient in Lantus® came into service in 2004.**

Production capacity at the plant will be able to meet market demand as of 2005. In addition, the new Opticlik® assembly line has started producing the quantities needed for the 2005 market launch in the United States.

Sanofi-aventis is the leading pharmaceutical manufacturer in Germany in terms of sales\* with a 6.9% market share. The Group's presence is further strengthened by its Frankfurt and Cologne industrial sites, producing active ingredients for products such as Lantus®, Apidra® and Tritace®, as well as its Frankfurt research center and two clinical research units, one in Frankfurt and the other in Berlin.

Plavix® and Clexane®, the German affiliate's two leading products, both registered strong growth. Eloxatin®, Taxotere® and Lantus® also performed extremely well, while Aprovel® continued to grow. Sales of Delix®, however, were hit hard by the release of generic versions of ramipril in January 2004.

\* IMS retail and hospital, MAT December 2004, after the reallocation of parallel imports.

## ITALY

Ranking: N°2\*

Overall performance of the affiliate exceeded that of the market. All products contributed to this growth, both leading medicines and strategic local products such as Targosid®, Avanic® and Muscoril®.

Triatec®, Aprovel® and Clexane® registered good growth rates. These medicines now constitute a leading franchise in the field of cardiovascular/thrombosis. Rapid growth in oncology was driven primarily by Eloxatine® and Taxotere®.

Sanofi-aventis is ranked second\* on the national market. This position is supported by a strong manufacturing presence, with six facilities, and by an R&D center.

Copaxone®, Stilnox®, Lantus®, Depakine® and Xatral® all contributed to this growth.

In addition, sanofi-aventis is second on the consumer health (OTC) market with a 7.8% market share\*\*. This solid business franchise is led by Enterogermina®, the leading product on the Italian OTC market, which is particularly well-positioned in the gastro-intestinal and circulatory segments.

\* IMS retail and hospital, MAT December 2004.

\*\* AC Nielsen December 2004.

## UNITED KINGDOM

Ranking: N°4\*

The Pharmaceutical Price Regulation Scheme (PPRS) was renegotiated in 2004 and the pharmaceutical industry reached a five-year agreement with the British government that cuts the prices of brand-name medicines by 7% as from January 1, 2005.

Sanofi-aventis UK received the Pharmaceutical Marketing Effectiveness Award (PMEA) for Marketing Campaign of the Year for Lantus® and the PMEA Brand Revitalization Award for Taxotere®. The UK subsidiary was also highly commended in the PMEA Company of the Year category.

Overall growth for the subsidiary was adversely affected by the patent expiry of Tritace®. Excluding the effect of Tritace®, however, net sales grew, with a significant contribution made by the major products Plavix®, Clexane®, Aprovel® and Lantus®.

Sanofi-aventis also has a strong manufacturing presence in the United Kingdom with four facilities, manufacturing principally Taxotere®, Plavix® and Aprovel® as well as a research and development site in Alnwick.

**Sanofi-aventis UK pursued its 62 million euro investment plan** for the construction of ultramodern manufacturing facilities in Fawdon, near Newcastle. A further 3 million euros were invested in the Alnwick research and development center.

\* IMS retail and hospital, MAT December 2004, after the reallocation of parallel imports.



## SPAIN

Ranking: N°2\*

Sanofi-aventis was the fastest-growing of the top five companies on the Spanish market in 2004, with a growth 10 points above that of the market\*. Plavix®, Lovenox®, Aprovel®, Actonel®, Taxotere® and Eloxatine® all contributed significantly to growth.

**Sanofi-aventis has three manufacturing sites and two research and development sites in Spain.** R&D spending in Spain passed the 10 million euros mark for the first time in 2004.

\* IMS NPA retail and IMS hospital, MAT December 2004.



## TURKEY

**Ranking: N°2\***

2004 was marked by the introduction of a reference price system based on the lowest price listed in five European countries. The measure had a significant impact on the price of medicines in Turkey.

Despite a challenging economic environment, Sanofi-aventis continued to register above-market growth, particularly due to Ketek®, Aprovel®, Taxotere®, Tritace®, Muscoril® and Eloxatine®. Plavix®, however, was affected by restrictions placed its prescription.

\* IMS retail MAT December 2004.

## GREECE

**Ranking: N°2\***

The regulatory environment was unchanged in 2004. Sanofi-aventis significantly outperformed the local market\*. The main contributors to growth were Actonel®, Plavix®, Eloxatine®, Aprovel®, Lovenox® and Lantus® (launched in February 2004). Within the space of three months, Lantus® became the leading product on the insulin market.

\* IMS retail, MAT December 2004.

## BELGIUM

**Ranking: N°3\***

Belgium has also been affected by the debate on controlling healthcare costs. Medicines which had been reimbursed for many years were subject to price cuts. Sanofi-aventis, however, registered above-market growth. The drivers for growth on the retail market were Plavix®, Aprovel®, Clexane®, Copaxone® and the launch of Lantus®, alongside Eloxatine® on the hospital segment. In the OTC range, two products in the portfolio were leaders in their class: Omnivit® and Rhinathiol®.

\* IMS retail MAT December 2004.

## PORTUGAL

**Ranking: N°1\***

Sanofi-aventis is the leading pharmaceutical company in the country, providing a solid product portfolio, with five medicines featuring among the top 30 on the market (Aprovel®, Plavix®, Tritace®, Nimed® and Actonel®) in addition to a strong presence in the generic market. Portugal is also home to a production unit in Loures, near Lisbon, which mainly manufactures products for the local market.

\* IMS retail and hospital, MAT December 2004.

## HUNGARY

**Ranking: N°1\***

Sanofi-aventis was able to maintain a very high rate of growth, in great part due to Tritace®, Plavix®, Clexane® and Actonel®. The OTC portfolio also registered strong growth on its main brands.

**Sanofi-aventis also has a strong industrial presence in Hungary**, which was reinforced by investments made in 2004 for the construction of a pharmaceutical manufacturing facility in Veresheghaz and the opening of a pilot chemical production facility.

\* IMS retail and hospital, MAT December 2004.

## THE NETHERLANDS

Ranking: N°5\*

The Dutch subsidiary continued to register vigorous growth, much higher than the market, with the highest growth rate among the top eight pharmaceutical companies\*. Lantus®, Eloxatine®, Taxotere®, Aprovel® and Amaryl® were the main growth drivers.

\* IMS retail and hospital, MAT December 2004, after the reallocation of parallel imports.

## SWITZERLAND

Ranking: N°5\*

In 2004, market growth in Switzerland was half that of 2003.

Despite this slowdown, the Swiss affiliate was able to maintain double-digit growth. Aprovel®, Plavix®, Taxotere® and Eloxatine® and Stilnox® were major contributors to growth.

The subsidiary launched a new generic activity in response to the shift in market trends triggered by the latest government measures.

\* IMS retail, MAT December 2004.

## POLAND

Ranking: N°5\*

Despite an almost stagnant market, the Polish subsidiary registered an excellent performance, its growth driven by Clexane®, Amaryl®, Depakine® and No-Spa®. The active promotion of key brands such as Plavix®, Lantus® and Arava® was launched despite the fact that they are not reimbursed.

\* IMS retail and hospital, MAT December 2004.

## SCANDINAVIA

All four Scandinavian subsidiaries performed very well in 2004:

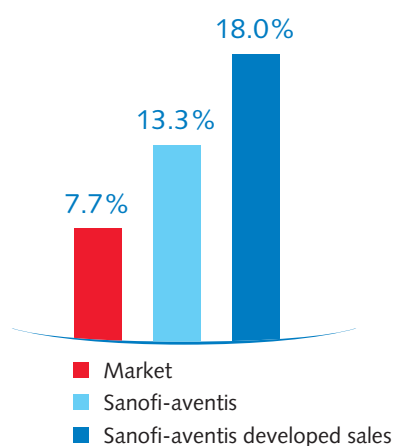
- In **Sweden**, Group sales outperformed the market\*, despite an upturn in parallel imports of some of the affiliate's most important products.
- In **Finland**, the pharmaceutical market grew by nearly 8% in 2004\*. Sanofi-aventis sales grew much faster than the market, thanks to strong performances from Plavix®, Taxotere®, Eloxatine®, Copaxone®, Actonel® and Lantus®, which continued its market penetration following its launch in 2003.
- In **Denmark** and **Norway**, despite the patent expiry of Tritace® and measures to accelerate the transition to generics, sanofi-aventis nevertheless increased sales mainly thanks to Plavix®, Amaryl®, Eloxatine® and Taxotere®.

\* IMS retail and hospital, MAT December 2004.

# NORTH AMERICA

## UNITED STATES

- 2004 pro forma net sales:  
8,772 million euros
- Ranking: N°5\*\*



2004 Sales Growth in the United States\*\*

Sanofi-aventis is a major player on the pharmaceutical market in the **United States**. With eight flagship products, the Group consolidated its excellent positioning in major therapeutic areas: **cardiovascular, thrombosis, cancer, diabetes, central nervous system, internal medicine, metabolic disorders and vaccines**. For the past four years, sanofi-aventis has posted the strongest growth of any of the top five major pharmaceutical manufacturers in the country\*\*.

\* Pro forma net sales, growth on a comparable basis

\*\* IMS 10 channels NSP, MAT December 2004, developed sales include 100% of Plavix®, Avapro®/Avalide®, Actonel® and Copaxone® sales.

\*\*\* IMS hospital, MAT December 2004.

The Group's products are marketed through various channels in the United States:

- the sanofi-aventis subsidiary;
- alliances:
  - with Bristol-Myers Squibb for Plavix® and Avapro®,
  - with Teva Pharmaceuticals for Copaxone® and
  - with Procter & Gamble Pharmaceuticals for Actonel® (sales of which are not consolidated by sanofi-aventis);
- licensing agreements (in particular on Cordarone® and Depakine®).

Sanofi-aventis in the United States outperforms the market as a whole and the top ten pharmaceutical manufacturers, with the exception of Amgen.

The main contributors to growth in 2004 were:

- Plavix®, still the Group's best-selling product in the United States with 34%\*\* sales growth;
- Ambien®, up by 21% and keeping its number one position on the hypnotics market\*\*;
- Lovenox®, which again outperformed the market with 20%\*\* growth in sales;

With almost 8,000 medical sales representatives, the second-largest U.S. sales force, sanofi-aventis is strengthening its positioning for future product launches.

- Despite a faster than expected downturn in the allergy medication market, Allegra® performed well thanks to a successful direct-to-consumer campaign—sales were down only 6%\*\*;
- Growth for Taxotere® remained stable, in line with the cytotoxics market as a whole. Its position was strengthened by recent FDA approval for use in the treatment of early-stage breast cancer;
- Eloxatine® recorded growth of 68%\*\*\*, obtaining the first FDA approval for a new adjuvant chemotherapy treatment in over 10 years;

- Sales of Ketek®, the latest brand to be launched by the Group, were in line with forecast. Most physicians see it as first-line treatment for mild to moderate pathologies.

The Group's activities in the United States also include vaccines, which reported sales growth. This strong performance was driven by a successful Fluzone® campaign due to a strong pre-booking season and Chiron's unexpected withdrawal.

Sanofi-aventis and the Department of Health and Human Services signed three agreements in 2004 on vaccination against pandemic influenza. Another reason for the Group's strong performance was the success of strategies designed to defend market share in whooping cough and *Haemophilus influenzae* type b infections.

Sanofi-aventis operates industrial facilities in Kansas City, St. Louis and Puerto Rico. Research and development centers are located in New Jersey, Arizona and Pennsylvania.

\* Pro forma net sales, growth on a comparable basis.

\*\* IMS 10 channels NSP, MAT December 2004, developed sales include 100% of Plavix®, Avapro®/Avalide®, Actonel® and Copaxone® sales.

\*\*\* IMS hospital, MAT December 2004.



## CANADA

Ranking: N°5\*

The Canadian subsidiary registered an annual growth rate of 16%\*, significantly higher than the market. Five of the subsidiary's strategic products are number one in their markets: Altace®, Avapro®, Lovenox®, Plavix® and Taxotere®.

Actonel® posted growth of over 35% in 2004 and is now number two on its market\*\*.

The Avapro® and Plavix® ranges are distributed by Bristol-Myers Squibb in Canada, while Actonel® is co-marketed with Procter & Gamble.

The subsidiary's industrial facilities—a manufacturing plant and a distribution center—are located in Quebec. Sanofi-aventis also operates two clinical research units in Canada and a research center dedicated to vaccines.

The performance of the Group's vaccines business grew was largely due to strong sales of Adacel®.

\* IMS retail and hospital, MAT December 2004, developed sales include 100% of Plavix®, Avapro®/Avalide®, Actonel® and Copaxone® sales.

\*\* IMS, Retail & Hospital dollars audit.



# ASIA

## JAPAN

Ranking: N°13\*

The price cut scheduled for application every two years was implemented in April 2004, impacting overall market growth. The market progressed by 1.5%\* for the year.

Sanofi-aventis posted an above-market 5.4%\* growth rate of developed sales in 2004, made possible by the performance of strategic drugs such as Amaryl®, Taxotere®, Actonel® and Lantus®, the latter of which was launched at the end of 2003.

Co-marketed products also achieved excellent results during the year:

- Myslee® (zolpidem), in partnership with Fujisawa, is number one on the hypnotics market;
- Ancaron® (amiodarone), in partnership with Taisho, took a 10%\* share of the market, proving its potential on the anti-arrhythmics market.

Prior to the merger, Sanofi-Synthelabo had already begun laying the foundations for a direct operational presence in Japan. The marketing teams were reinforced in order to promote medicines already on the market and to prepare for the launch of new products coming onto the Japanese market. In April, sales forces started promoting Ancaron®; this activity was fully integrated into the sanofi-aventis sales organization which now comprises 1,500 sales representatives.

Taxotere® was approved for the treatment of esophageal cancer in 2004. Applications for an extension of indications for Allegra® and Actonel® were submitted to the Japanese Ministry of Health, Labor and Social Protection, along with an application for marketing approval for Plavix®. Opticlick® was approved as a medical device for use with Lantus® and will be put on the market in 2005.

\* IMS retail and hospital, MAT December 2004, developed sales include 100% of Kerlong®, Milrila®, Ganaton® Fujisawa, Meilax®, Miradol®, Barnetil® Schering, Barnetil® Dainippon® sales.

## SOUTH KOREA

Ranking: N°3\*

Sanofi-aventis operates not only through its subsidiary, but also through a joint-venture with Handok. Combined with Handok-Aventis, the Group is number one on the South Korea market\*.

The Korean market grew by 14% in 2004\*\*.

Sanofi-aventis consolidated sales rose by 24.4%\*\*; the second strongest growth performance among the top five pharmaceutical companies in South Korea.

2004 once again saw continued strong growth of flagship products such as Plavix® and Aprovel®, as well as the successful take-off of sales for Actonel®.

Vaccine sales climbed during the course of the year, driven by an effective flu vaccination campaign as well as the introduction of a polio vaccine on the public market.

\* IMS retail, MAT December 2004.

\*\* IMS retail, MAT December 2004, developed sales include 100% of Handok-Aventis sales.

## TAIWAN

Ranking: N°2\*

Despite the introduction of a hospital global budget in 2004, sanofi-aventis reported the strongest rate of growth among Taiwan's top ten pharmaceutical manufacturers\*. Increased sales for Plavix®, Aprovel®, Taxotere® and Amaryl® were the main driving force for growth.

\* IMS retail and hospital, MAT December 2004.



## INDIA

Ranking: N°7\*

Sanofi-aventis has been present in India since 1956 and includes a company listed on the Mumbai stock exchange. Sanofi-aventis is the second largest foreign pharmaceutical company on the Indian market.

Despite the forthcoming recognition of pharmaceutical patents, the market remains highly regulated and the pressure on drug prices is intense.

In this context, growth of the affiliate was centered on strategic products and the continued progress of Rabipur®. The launch of Plavix® at the end of 2003 and of Lantus® and Actonel® in 2004 reinforced the affiliate's market base.

The Group operates two pharmaceutical plants and a chemical plant in India at two industrial sites, Goa and Ankleshwar.

\* IMS retail, MAT December 2004.

## CHINA

Ranking: N°11\*

2004 was another year of strong growth for sanofi-aventis in China, especially for strategic products.

This performance was achieved despite the fact that 12 products were not eligible for reimbursement. At the close of 2004, China's national health authorities finally agreed to include the 12 products on the list of reimbursed medicines, creating significant potential for growth for the Group's Chinese affiliate in 2005 and 2006. In this context, sanofi-aventis reported strong growth on all its brands and in particular for Plavix®, Aprovel®, Eloxatine® and Taxotere®.

Sales of vaccines increased during the course of the year due to brisk sales of flu and rabies vaccines.

The Group has industrial sites in China, located mainly in Hangzhou and Beijing.

The Group invested heavily in the local sales force, hiring over 200 people in 2004, to keep on sustaining its growth in China. The sales force was also reorganized into regional structures to make promotion throughout the country more efficient.

\* IMS hospital, 16 cities/regions, MAT September 2004.

## SOUTHEAST ASIA

In Southeast Asia, **Hong Kong** and **Singapore** registered significant growth compared with 2003, a year hard hit by the effects of SARS (Severe Acute Respiratory Syndrome).

**Thailand** continued to report strong growth, largely thanks to Plavix®.

The Group's main plants in Southeast Asia are located in Vietnam, Indonesia, Bangladesh and Singapore.

## AUSTRALIA/ NEW ZEALAND

Ranking: N°3\*

2004 was a year of above-market growth in **Australia**, due to the development of Actonel®, Eloxatine®, Taxotere® and Plavix®. Negotiations with local health authorities on reimbursement terms for Lantus® are in progress.

Ranking: N°7\*

In **New Zealand**, where greater restrictions were placed on health spending with hospital expenses now subject to control, sanofi-aventis reported growth in line with the market\*, with good performances in particular from Eloxatine®, Taxotere®, Plavix® and Clexane®.

Sanofi-aventis also has a clinical research unit and a vaccines business operating in Australia and New Zealand.

\* IMS retail and hospital, MAT December 2004.

## LATIN AMERICA

### MEXICO

Ranking: N°3\*

The Mexican pharmaceutical market, the largest in Latin America, remained dynamic in 2004, with growth due to price increases. Sanofi-aventis has a strong local presence, with a market share of 7.1%\*, and the largest portfolio of drugs in the industry. Plavix®, Actonel®, Lovenox®, Taxotere®, Aprovel® and Lantus® were the main growth drivers in this market.

Sanofi-aventis is also present on the OTC market with products such as Histiacyl®, Novalgine® and cough suppressants.

Overall sales of vaccines grew, mainly thanks to the flu vaccination campaign in 2004.

The Group's development in Mexico is based on its two manufacturing facilities and the opening of a clinical research unit.

\* IMS retail, MAT December 2004.



## BRAZIL

Ranking: N°1\*

Despite a challenging economic environment, noteworthy for the prevalence of generic drugs and copies, difficult access to medicines and strict price controls—Brazil is the world's eleventh largest market for pharmaceutical products, reporting 16%\* growth in 2004.

Sanofi-aventis sales growth was mainly powered by Plavix®, Lovenox®, Aprovel® and Lantus®.

Although Brazil is a major contributor to the vaccines business, sales dropped slightly for the 2004 financial year because of supply problems with measles, mumps and rubella vaccines (MMR) and rabies vaccines.

\* IMS retail, MAT December 2004.



## OTHER LATIN AMERICAN COUNTRIES

The region enjoyed a vigorous economy recovery in 2004 and the Group benefited from these conditions to optimize its resources (reorganization in **Argentina**) and seize opportunities for growth (reinforcing its sales force in Venezuela). The two main growth drivers were **Venezuela**, where the market was primarily bolstered by price effects and by calls for tender fuelled by a buoyant oil market, and **Colombia**, in the wake of the restructuring of business activities carried out in 2003.

All fifteen strategic products achieved very high levels of growth.

Sales of vaccines in Argentina performed well, mainly due to flu vaccination campaigns and to the combined measles, mumps and rubella (MMR) vaccine.

\* IMS, MAT December 2004 (Venezuela retail, Argentina retail, Uruguay retail, Puerto Rico retail and hospital, Colombia retail, Chile retail, Peru retail, Ecuador retail).

## AFRICA/ MIDDLE EAST

### AFRICA

In a challenging economic context, growth was driven mainly by dynamic markets in **Algeria** and **Tunisia**, which helped offset slowdowns in **sub-Saharan Africa**.

In these markets, sanofi-aventis is predominant, with its leadership position based on a market share above 13%.\* In **South Africa**, where sanofi-aventis is the fourth leading pharmaceutical company\*\* with a 6.9% market share\*\*, the Group is committed to the fight against tuberculosis through a partnership with the South African authorities. The support provided by sanofi-aventis for this project, "TB Free", is both financial, in the form of nine patient treatment monitoring centers, and industrial, with its manufacturing facility in Waltloo.

The vaccines business remained stable overall throughout the 2004 financial year. Strong growth in polio vaccines and pediatric combinations were offset by the decreasing sales of the meningitis vaccine.

\* IMS, MAT December 2004 (Morocco, South Africa, Tunisia, West Africa: Ivory Coast, Cameroon, Gabon, Senegal, Congo, Guinea, Benin, Togo, Mali, Burkina Faso).

\*\* IMS Retail MAT December 2004.

The Impact malaria program, aimed at providing the world's poorest with effective means to combat malaria, is progressing as planned.



### MIDDLE EAST

Ranking: N°4\*

Sales in the Middle East remained stable, despite lower exchange rates and political instability. Sanofi-aventis improved its competitive position in most Middle Eastern countries with a market share of 5.3%.

The Group's main industrial operations in the region are located in Egypt (Cairo) and Pakistan (Wah and Karachi).

\* IMS, MAT December 2004 (Lebanon, Egypt, Saudi Arabia, United Arab Emirates, Jordan and Kuwait).

## CENTRAL AND EASTERN EUROPE

### RUSSIA

Ranking: N°2\*

With a market share of 6.1%\*, sanofi-aventis reported strong growth in 2004 thanks to satisfactory performances from flagship products. In the vaccines business, sales of flu vaccines increased considerably.

Research activities in Russia were reinforced in 2004 with the opening of a new clinical research unit.

\* RMBC retail and hospital MAT September 2004.



### EASTERN EUROPE

- Despite economic and political instability in the **Adriatic** zone, Plavix® and Depakine® in Serbia, and Tritace® in Bosnia, continued their growth. New reference price systems based on Western European models were introduced in Croatia and Serbia. The Albanian and Macedonian markets were developed through agreements reached with local distributors.
- In **Romania**, sanofi-aventis is market leader in the cardiology, thrombosis and oncology ranges, and a key player in the areas of diabetes, neurology, rheumatology and antibiotics, and ranks third on the Romanian market, with a 6.1%\* market share.
- The countries of the **Commonwealth of Independent States (CIS)** constitute a new zone, managed from Kazakhstan, where the economy is registering rapid growth: good results were achieved on the traditional product portfolio and the launch of Plavix® proved successful.
- Market conditions in **Bulgaria** were challenging in 2004. In this context, sanofi-aventis products performed well, in particular Taxotere®, Eloxatine®, Cordarone® and Depakine®.
- Sanofi-aventis registered good results in the **Ukraine**, reporting excellent figures for Plavix® and Clexane®.

\* Ex-Market Cegedim retail and hospital, MAT December 2004.

# OUR RESPONSIBILITIES

- ▶ **96,439 employees** around the world
- ▶ A **Social Charter** published in every country
- ▶ Ethics and expert committees to **ensure compliance with codes of best practice**
- ▶ Global programs to provide **access to medicines for the world's poorest**





Our commitment...

MOBILIZING RESOURCES  
to serve the greatest number



# Our responsibility as a pharmaceutical group

- *The mission of sanofi-aventis is to discover, develop and make available to physicians and their patients treatments that are innovative, effective and well-tolerated. Because this mission affects society as a whole, the Group is committed to acting as an ethical and socially responsible company. Sanofi-aventis sees the scope of its commitment as extending from clinical trials and pharmacovigilance to wider issues of ensuring access to medicines for the poorest countries and of combating rare yet serious diseases.*



## Ensuring Good Practice in Clinical trials

Clinical trials, which evaluate the therapeutic efficacy of medicines in humans, are carried out in accordance with Good Clinical Practice and medical ethics and in close cooperation with the health authorities.

These practices include constant monitoring to ensure the highest possible levels of patient safety

## Animal testing

Tests on animals, which are required by law before clinical trials can be authorized, are designed to gather as much information as possible on a medicine's therapeutic and toxic effects before beginning tests in humans. Sanofi-aventis applies a policy of strict controls and minimal recourse to animal testing, by using and developing alternative methods.

Studies involving the use of animals are only undertaken when no other alternative exists, and with the aim of advancing knowledge that will contribute to health and safety for both humans and animals.

An Ethics Committee systematically scrutinizes all protocols and procedures before any experiments are performed.

## Bioethics

Scientific progress over the last few decades has led to major therapeutic advances. The implications of some recent discoveries in genetics and molecular biology, however, are such that society as a whole is called upon to take a stance on the issues arising from medical research and the resources it uses.

Sanofi-aventis carries out research on human and animal stem cells in accordance with national legislation, for the purpose of furthering our scientific knowledge and discovering new medicines in fields involving cell degeneration or proliferation.

## Targeting all diseases

The Group considers that it has a moral obligation to address not only widespread diseases but also rare diseases with serious effects that are currently untreated or poorly treated, regardless of the fact that the sales potential of medicines for such "orphan" diseases is low.

Targeted research effort has already culminated in the launch of:

- Rilutek® (riluzole) in 1997, the only treatment available to slow the development of amyotrophic lateral sclerosis (ALS) and extend the survival of patients suffering from this neurodegenerative disease.
- Fasturtec® (rasburicase) in 2001, for the management of plasma uric acid levels due to tumor lysis in pediatric patients with malignant hemopathies.

Sanofi-aventis continued to develop a number of other compounds in 2004, and New Drug Applications were filed for two of these:

- Colimysine® (colimycin) in aerosol form for the treatment of mucoviscidosis, on November 16, 2004. Although its patent has expired, the compound was developed in response to a public health need at the request of patients' associations.
- Flisint® (fumagillin), to combat intestinal diarrhea of parasitic origin in immune-deficient patients, on December 13, 2004.

In parallel to its own in-house research, the Group is also a member of two European research programs, Erditi and OrphanXchange, which promote the development of new avenues of research and close cooperation between all those engaged in combating rare diseases.

## Drug quality and safety

The pharmaceutical industry operates to the most demanding standards as regards drug quality and safety. Sanofi-aventis quality teams are an integral part of every sector of activity and all our subsidiaries worldwide. The Quality Network is equipped with communication tools that provide instant access to all information gathered by the Group.

Regular Quality audits are carried out as part of Group in-house inspections of facilities and departments, and for the certification of suppliers and subcontractors.



## Pharmacovigilance

All medicines are closely monitored throughout their life cycle to identify the effects they have on patients. This process, known as pharmacovigilance, is designed to evaluate and monitor the risks associated with taking a given medicine, such as unwanted side effects, and to suggest measures to mitigate these risks and to promote and ensure proper use of the medicine concerned.

The Group has pharmacovigilance units operating in every country, collecting, analyzing, documenting and circulating information provided by patients, investigators in charge of clinical trials and healthcare professionals. These units also interface with local health authorities.

A central pharmacovigilance structure collates information from all over the world to build up a unique safety profile for each product. This profile is regularly updated and provides vital information for healthcare professionals and patients. Early warning systems have been developed to pick up the first signs that a medicine's safety profile might be in question and to notify all those concerned simultaneously.



## Access to medicines

Poverty, lack of infrastructure and medical skills, conditions of public service and cultural behavior patterns can all pose obstacles to progress in healthcare around the world. As a socially responsible global player in the field of health, sanofi-aventis devotes considerable resources to helping the populations of developing countries gain access to the medicines needed to treat the major diseases from which they suffer.

Our commitment is expressed in a number of concrete campaigns including:

■ **Impact malaria:** this program is wholly internal to sanofi-aventis, from discovery research to deployment on the ground, to combat one of most prevalent diseases affecting developing countries by providing an active product, a combination of artemisinin and amodiaquin, sold on a "no profit, no loss" basis.

### The ravages of malaria

- 500 million new cases of infection annually around the world
- 1 to 3 million deaths annually = 5,000 dying every day

■ **Sleeping sickness:** sanofi-aventis provides drug donations and funding for two World Health Organization (WHO) programs—one to monitor and control the disease, the second for research into new treatments.

### Sleeping sickness: a widespread disease

- 60 million people at risk
- 500,000 people infected



■ **Stepping up the fight against tuberculosis:** A partnership with the Nelson Mandela Foundation in South Africa to create skills centers and train assistants in treatment adherence. We are also reviewing our industrial policy to include the production of another tuberculosis treatment.

■ **Leishmaniasis:** We have resumed production of our medicines for the treatment of this disease, in order to reduce costs substantially and thus enable more patients to be treated on a "no profit, no loss" basis. This policy regarding access to medicines could be extended to other therapeutic areas in the future.

# Risk management in the interest of all our stakeholders

- *Sanofi-aventis operates a rigorous and demanding Health, Safety and Environment (HSE) policy to protect the health and safety of employees, to develop and implement the safest possible industrial processes and to minimize the environmental impact of our business activities.*

## The basis of our policy

### ■ Anticipating risks

Two multidisciplinary scientific committees function independently of operational structures, whose tasks are to identify and assess the risks inherent in product development.

- The COVALIS committee evaluates and establishes occupational exposure levels for chemical substances handled in the Group;
- The TRIBIO committee evaluates and defines risk prevention rules for biological agents used by the Group.

We have also put in place major risk prevention methods covering all situations, processes and projects. These methods are applied by all of our establishments at all levels, and are set out clearly in the guidelines issued to all employees with HSE responsibilities.

### ■ Strengthening Group standards

The Group has chosen to apply standards that are more demanding and broader in scope than current regulations. We are committed to the continuous strengthening of our standards and their implementation on all of our sites throughout the world.

### ■ Ongoing improvement in HSE performance

Culture and motivation are driving forces for HSE and as such need constant attention; to maintain both at optimal levels we give particular importance to:

- learning from feedback;
- understanding events, their causes and consequences, through the systematic analysis of accident reports and of causal trees; and
- the prevention plans which result from the knowledge we acquire—this includes sharing information on the difficulties encountered in executing prevention plans and the lessons learned.

### ■ Support from the HSE Network

We have created an HSE support network to exchange information, provide training and communicate. Our Central HSE Department provides support to:

- Operational staff
- Facility managers
- HSE coordinators
- Company physicians
- Project teams
- HSE experts.



## Risk management

### ■ Meeting HSE Challenges

The Central HSE Department is part of the Corporate Affairs Division and is responsible for developing measures to prevent occupational and environmental risks within the Group. Part of its work involves setting HSE targets and issuing guidelines on the implementation of HSE policy.

The Corporate HSE Department draws up policy implementation standards, defines HSE reporting practices and trend charts and consolidates results. It also runs the network of HSE coordinators set up to exchange information and organize training and communication. In addition, it provides support and expertise to all Group facilities, schedules and carries out HSE audits and represents the Group in its dealings with regulatory bodies and industry organizations on HSE-related issues.

The department is staffed by 37 operational staff and experts in the fields of occupational safety, industrial toxicology, industrial hygiene, occupational medicine, fire safety, environmental technologies, life sciences and industrial risks.

The department coordinates a network of partners both internal (operational divisions and project teams) and external (manufactures, suppliers and service providers) and is in constant contact with facility managers, HSE coordinators and company physicians who are backed up on the larger sites by teams of Group employees.

## Recognizing dangers and identifying risks

■ **Identifying chemical and biological risks** requires constant up-dating of the information available on the substances handled in facilities. The Group has two bodies, the COVALIS and TRIBIO committees, dedicated to identifying and assessing these risks.

■ **Occupational and environmental risks** are assessed in normal and sub-normal working conditions. Particular attention is paid to the risks of road accidents, to which all of our sales representatives are exposed. All workstations are assessed for risks related to the immediate surroundings and the risk of occupational exposure to the substances in use.

■ **Risk reduction, once the risk** has been identified, consists of:

- formulating and developing means of prevention;
- making the required investments;
- providing individual and collective protection equipment;
- providing training to make HSE practices an integral part of work procedures.



■ **Throughout the world** the following approach is systematically applied at each of our sites:

- an HSE progress action plan is devised, implemented and monitored annually at every one of the Group's industrial and research sites;
- initial and ongoing workstation training to guarantee the integration of HSE practices into work procedures;
- investments in HSE that specifically target risk prevention and employee safety, as well as promoting environmental protection by minimizing consumption of natural resources, developing clean manufacturing, reducing and recycling waste.

■ **Monitoring performance and providing feedback**, by means of several different methods:

- a set of indicators is used to consolidate safety and environmental data for all Group facilities throughout the world. These indicators form the basis for the HSE steering trends chart used by all facilities, and are also used—along with the comparative analysis of the current situation and established objectives—to put in place corrective measures;
- HSE data are verified by auditors in compliance with French legislation on the New Economic Regulations (Nouvelles Régulations Économiques—NRE). Auditors also review the collection, verification and consolidation of the data by the Corporate HSE Department;
- audit programs are carried out every year by the HSE Department for all Group facilities, with the aim of verifying that HSE management and the HSE programs, practices and actions in place at each facility comply fully with Group standards and government regulations;
- major events and accidents in facilities are compiled and analyzed at Group level. This feedback is essential; it enables us to learn from events, accidents and any failures in compliance that occur at our sites.

The knowledge thus acquired is used to regularly revise our internal standards.

#### ■ **Involving subcontractors and suppliers**

The Group makes HSE concerns a factor in its relations with subcontractors and suppliers, communicating its commitment and inviting them to participate in our health, safety and environmental protection policies.

## Employee health

#### ■ **Promoting rigorous industrial hygiene practices**

The aim of industrial hygiene is to continually decrease exposure to occupational risks of a physical, chemical or biological nature in all activities.

The Group's objective is to prevent exposure to risk at source, by giving higher priority to collective rather than personal protection.

#### ■ **Focusing on employee health**

**The role of our Occupational Health Departments** is to prevent occupational risks by:

- contributing to lowering the number of new cases of an illness through risk awareness and risk assessment;
- preventing the aggravation of existing disease by detecting its effects on health and acting early on the occupational factors that contribute to the emergence of diseases; and
- mitigating occupational injuries that are the result of illnesses or accidents.

**The toxicovigilance network** studies the causal relations between the occurrence of an undesirable event and occupational exposure of Group employees to a substance. Our Occupational Health Departments are part of the Group's toxicovigilance network. The aim of toxicovigilance is to avoid the occurrence of similar events with employees handling the same substance; this involves identifying new hazards and establishing the appropriate means of prevention and protection.



## The safest possible industrial processes

### ■ Building risk control into product design

The Group assesses industrial and environmental risks and controls these risks by working on products and processes in the early stages of product development and during production.

**Incorporating employee health and environmental protection issues** into the early stages of research is essential. The teams in charge of developing new compounds take HSE criteria into account. This can lead to the exclusion of certain raw materials and dangerous solvents or to the use of smaller quantities of solvents so as to reduce air emissions and waste from mass production.

**Laboratories specialized in process safety** carry out studies on behalf of the Group into powder explosiveness, thermal stability of products, the safety of chemical reactions, potential environmental impacts on water, air and soil and into product and material incompatibilities. The data obtained from the studies are used to optimize product design and determine the nature and scale of the plant safety and environmental protection measures required.

**The “Hazard Vetting” system** is used to systematically reassess risks, before the implementation of any modification in a procedure, a product, equipment, or batch size. This vetting process uses the data compiled and analyzed by the process safety laboratories. Systematic reassessment of risks enables us to evaluate the consequences of any modification.

### ■ Preventing major accidents

Chemical facilities in the Group that fall under the Seveso II Directive have established a methodology for the prevention of major accidents. This involves identifying and assessing sources of danger and determining those factors (operations, instruments or equipment) *“Important to Safety or the Environment”* in order to control industrial risks by strengthening risk prevention and protection measures.

### ■ Hazardous substance management

We are currently taking action to harmonize our hazardous substances transport procedures.

The main actions under way concern stricter verification procedures and staff training, in particular training for transportation safety advisors who are specifically trained to supervise this type of operation.

## Environmental impact

A commitment to clean design and manufacturing, minimizing use of natural resources and reducing the environmental impact of our activities lies at the heart of the Group's industrial policy.

### ■ Promoting the environmental component of HSE

The implementation of the environmental component of our HSE management system exemplifies our commitment to protecting the environment. Fourteen indicators are used to monitor progress made in environmental areas throughout the Group's industrial and research facilities.

### ■ Certification

Working towards ISO 14001 certification has inspired teams at all Group facilities and fuelled progress in limiting the environmental impact of their activities.

### ■ Monitoring sites

We have put in place a systematic, multi-year program of preliminary studies, preventive monitoring and extensive soil and sub-soil studies, **and the necessary remediation action is being taken.**

# Combining strong economic performance with good employee relations

- *The merger between Sanofi-Synthélabo and Aventis was the keynote event of the year 2004, setting new priorities and raising the stakes for the Group's human resources policy. Now more than ever, sanofi-aventis is called upon to combine strong economic performance with effective employee relations.*

The challenge now facing the men and women of sanofi-aventis in the wake of the takeover is to pool all our talents, skills and know-how, working together towards a shared objective.

Thanks to a process of rapid integration, the new teams were formed during the last quarter of 2004 in readiness to become operational in the first quarter of 2005. At the same time, intensive dialog was engaged with employee representatives to provide a clear understanding of the challenges and impacts of integration.

## Working together towards a shared objective

Once the Management Committee members were appointed, a review of potential candidates was held in order to form the new teams. With equal emphasis on speed and the need to create homogeneous teams, the process was applied all along the management chain, bringing together the skills of the two groups.

As this process was under way, a "Mobility Network" was set up to facilitate mobility for employees wishing to change posts within the new organization: identifying vacancies and applications, following up interviews, résumé management and file termination. A network of correspondents was nominated in each country and each business sector to ensure a smooth flow of information on opportunities.



## 96,439 employees in 80 countries

(at December 31, 2004)

The merger virtually tripled the Group's total headcount, with Europe (including Turkey) accounting for over half (56.6%) of the total. France (28.7%) has the highest headcount, followed by the U.S. (16.4%) and Germany (10.5%). The Group employs 2,752 people in Japan, 2.9% of total headcount. Gender parity between the new Group's employees is maintained in every single professional category.

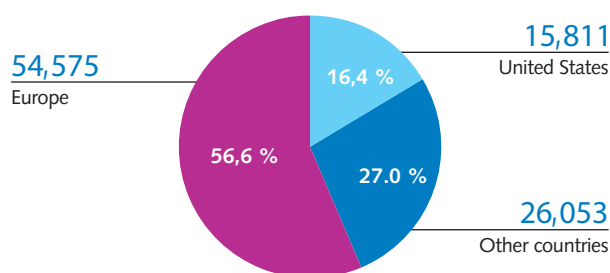
### Gender parity

Men	52,579
Women	43,860

Recruitment was cut back as from summer 2004, in preparation for the forthcoming merger. The Group recruited a total of 9,536 people in 2004: 6,670 on permanent contract and 2,866 on short-term contracts. Recruitment was particularly high in the United States (35.3% of recruitment on permanent contract). With a total of 1,756 new employees on permanent contract, Europe accounted for 26.3% of recruitment.

- 96.9% of Group employees are on permanent contract.
- Vaccines: 8.1% of total headcount.

Changes in headcount between the end of 2004 and the end of 2003 (excluding Behring) show a reduction of 3,295, including the 671 fall in headcount following the divestment of the Notre-Dame de Bondeville facility (Arixtra®/Fraxiparine®) as required by the competition authorities in the context of the Aventis acquisition.



Employees by geographic area

### Almost 50 forums worldwide

Sanofi-aventis has stepped up its presence in schools and universities in order to promote its business activities in Europe and around the world. Action plans are in place on the ground (case studies, site visits, interview simulations, etc.). In France, the Group won an award for the best stand at the Pharmaceutical Industry Forum, for the quality of its stand design, welcome and pertinence of information and advice to students.

## Sharing our values

The values enshrined in Sanofi-Synthélabo helped to lay the foundations for the new Group's approach to employee relations. Over the course of 2004, the Social Charter published by Sanofi-Synthélabo in 2003 was put into practice in most countries. Since the announcement of the merger, this charter has been extended to cover the whole of the new Group.

### Management guidelines

In order to give concrete, everyday expression to its values, the Group issued a set of "Management Guidelines", showing how the values should impact upon management behavior. These give examples of the standards of behavior expected of managers, to illustrate the six Group values of Audacity, Respect, Creativity, Courage, Solidarity and Performance.

## Encouraging dialog

The Group has always been committed to dialog with all its employees around the world, in accordance with local practices and legislation.

With the merger, sanofi-aventis has continued and extended the employee dialog already established in Europe by each of the two groups. As of June 21, 2004, a temporary information and concertation body (*Instance Temporaire d'Information et de Concertation*—ITIC) was set up to bring together the members of the Sanofi-Synthélabo and Aventis European Works Councils. ITIC met five times during the second half of 2004. A Special Negotiating Group is also now in place to negotiate the terms of constitution of the new sanofi-aventis European Works Council.

On February 24, 2005, an agreement was signed concerning the implementation of a new sanofi-aventis European Works Council.

One of the discussion topics addressed with the European Works Committees was the underlying principles of European employment policy which sets out the framework for Group undertakings in this area.

In France, the management of the new Group and unions representing staff at national level set up a negotiating body in October 2004. An intense series of joint meetings in the first quarter of 2005 covered a wide range of subjects and reached a number of agreements on issues, negotiations and timetables, such as:

- the scope of the Group Works Council in France;
- the structure of staff representation in France (introduction of Economic and Social Units for Corporate Center functions, Commercial Operations France, Science and Medical Affairs and Production/Distribution-Chemicals);
- an early retirement scheme;
- support measures for office-based employees changing workplace in the Paris region.

### A framework agreement on early retirement ("Cessation Anticipée d'Activité"—CAA)

In France, four out of the five unions representing employees signed a framework agreement at the end of 2004, establishing a single early retirement scheme for the Group. Sanofi-aventis intends the scheme to facilitate introduction of the new organization without resorting to involuntary redundancies. The scheme, which is entirely voluntary, provides employees taking early retirement with a substitute income until they reach full pensionable age. The scheme is funded entirely by sanofi-aventis, with no call on public funds.

## Training for career development

Career development is the product of real partnership between the individual employee and the employer; training is a guarantee of development, for employee and employer alike.

With this in mind, sanofi-aventis offers its staff not only the technical training specific to each business sector but also a range of cross-functional programs designed to reinforce Group culture and break down barriers between functions and business areas.

Over the year, a total of 3,161,431 training hours were provided to 68,876 employees, equivalent to 71.4% of the global workforce.

## A competitive salary/benefits package

The remuneration policy applied by sanofi-aventis contributes to the Group's performance and worldwide development. The aim is for every employee in every subsidiary to receive above the median salary for the pharmaceutical industry. This policy takes into account individual and collective performance. Added to this, in different countries, is a variable collective component linked to Group performance. In France, profit-sharing and incentive schemes have been in force for a number of years. Sanofi-aventis also pays particular attention to employee benefits and welfare, and the Group has taken care to maintain its policy of providing a high level of benefits and welfare coverage for all its employees worldwide. Under the terms of the "Protection 2000" scheme, tangible progress has been made in a number of countries and geographical areas, including the Middle East with the introduction of death benefits and Singapore with the extension of health insurance cover to the families of employees.

Sanofi-aventis also plans to press on with the expansion of employee share ownership schemes worldwide.

### **In France, introduction of an employee pension savings plan ("Plan d'Épargne Retraite Collectif" – PERCO)**

Sanofi-aventis has always emphasized its support for compulsory contributory pension schemes. The Group decided in March 2004 to introduce a supplement to the statutory schemes in order to partially compensate for the decline in yields, in the form of its own employee pension savings plan whereby employee contributions, which are voluntary and optional, are topped up by the company. These savings can be withdrawn on reaching retirement as a supplement to the statutory pension, thereby ensuring future pensioners an income on a par with that received by employees currently taking retirement. There are plans for the scheme to be extended throughout the new Group as of 2005, subject to collective bargaining agreements.

## Contributing to a dynamic local economy

By providing support for local business start-ups or development, Group subsidiary Sopran\* helped to create 444 jobs in 2004 in areas where sites face restructuring.

The sanofi-aventis spin-off policy also makes a powerful contribution to job creation. The Spin-off Mission, the personal brainchild of a sanofi-aventis employee, provides tailored support throughout the different stages of the project, calling as needed on internal and external expertise. In 2004, the two Groups helped 24 projects off the ground in France.

## Continued commitment to employment opportunities for the disabled

Sanofi-aventis has been committed for many years to providing opportunities for disabled people to remain in or enter employment, and ran a number of awareness campaigns in 2004, including the screening of a film entitled *"What If It Were Us?"* and the issue of an information leaflet, *"Using skills. Integrating difference"*. Sites made special efforts to take on more trainees, on alternating job-study schemes but also on temporary assignments and short-term contracts. As a result, 34 disabled people were taken on at 9 sites; for most of those concerned, this was their first work experience.

\*Société pour la Promotion d'Activités Nouvelles  
(Society for the Promotion of new Business Activities)

# INFORMING, COMMUNICATING, SHOWING SOLIDARITY

## Our corporate responsibility

*Communicating with all the Group's stakeholders, internal and external, while respecting the diversity of languages and cultures... is the essential challenge facing sanofi-aventis Corporate Communications. The Group's values are also given concrete expression through a policy of humanitarian sponsorship initiatives focused on health and solidarity.*

### Building the image of sanofi-aventis throughout the world

Coordinated by a dynamic Corporate Communications Department, the task of building the Group's image lies in the hands of a network of over 300 communication managers at country or site level.

This decentralized structure is highly effective in disseminating the Group's messages in real time and in over 20 languages, ensuring that they reach official bodies, key opinion leaders, healthcare professionals, the financial community and the media, not forgetting patient support groups and the general public at large.

### Corporate website and affiliate websites remodeled less than three months after the merger.

The new corporate website provides all key information about the Group: worldwide growth, strategy, financial performance plus the full range of financial reports, details of research areas and progress to date, information about its therapeutic targets and medicines, the organization of manufacturing, sponsorship policy, sustainable development, etc. The site is updated daily and, at key moments, financial information is released via live webcast.

An Intranet, modeled around the Group and its activities, provides staff with customized access to Group information and news.

### Two new internal magazines, Tonic and In'Tonic.

The twin pillars of internal communication are Tonic, which reports on major events and public health issues, and In'Tonic which focuses on the everyday life of the Group. Both feature new editorial content designed to provide insightful information about the Group to all its employees. Over 100,000 copies are circulated to all affiliates.



### Informing the medical community and playing a preventive role by raising public awareness of disease-related risks

The Group regularly reports the results of clinical trials carried out on compounds identified by its research and development, and of post-marketing studies of existing medicines. This information is directed at the national and international medical community and also the media, both general and specialized. Sanofi-aventis also keeps the general public informed through public health awareness and prevention campaigns, which are frequently organized in partnership with key players in the field of healthcare, and with doctors' and patients' associations.



## Sponsorship: A long-term commitment to fairer access to healthcare and a world more inclined to solidarity

Sanofi-aventis is committed to humanitarian causes, primarily in areas at the interface between health, solidarity and children in need, in aid of the world's poorest populations: its campaigns address issues as varied as prevention, education, hygiene, access to healthcare, the fight against poverty and exclusion, etc. Founded on skills-sharing and voluntary engagement, these campaigns provide more than just financial support; Group employees are encouraged to become involved in practical action on the ground, with one shared aim: to rekindle hope where it is most needed.

### ■ The generosity of the human heart knows no frontiers

Headed by Professor Francine Leca, the *Mécénat Chirurgie Cardiaque* association helps children from developing countries who suffer from severe heart malformations to come to France for surgery. The Group's financial support is backed up by the active involvement of its network of medical reps in finding host families for the children, and the generosity of sanofi-aventis employees who offer back-up, support and a home to these young patients until they are able to return to their families.

### ■ France: supporting Neurodon

Sanofi-aventis has partnered France's *Fédération de recherche sur le cerveau* (Federation for Brain Research) and its annual Neurodon fundraising campaign from the very first; initially through financial sponsorship, but also through the mobilization of its teams of medical reps and the voluntary support of employees, both active and retired, in raising general awareness, partly in order to appeal to the public's generosity but also to promote a

wider knowledge of these neurodegenerative diseases that are affecting more and more families.

### ■ Asia: helping the most vulnerable

In 1993, Sister Elisabeth built her first dispensary for the poor of Vietnam's Ho Chi Minh City. 11 years later, she has now opened 5 dispensaries from north to south of the country, an orphanage for the blind, a school for street-children, dedicated to fighting child prostitution, and sculpture and sewing workshops to help the very poorest earn a living. Sanofi-aventis has supported her exemplary work from the outset.

### ■ Africa: a helping hand for villagers on the path to development

After working alongside development aid agency EAST (*Eau Agriculture et Santé en milieu Tropical*) in Vietnam, Burkina Faso, Benin and Senegal, the Group is now supporting the NGO's work in Togo. EAST development programs focus on providing clean water supplies and improving sanitation, mainly through the digging of latrines. The NGO also establishes micro-credit systems, sets up medical dispensaries for mothers and children and promotes health education in schools.



Support for a school healthcare education program (EAST, Senegal)



### ■ Latin America: fighting leishmaniasis in Brazil's Pernambuco state

This comprehensive program of screening, treatment and family follow-up was instituted by the Aggeu Magalhães Research Center run by the Oswaldo Cruz Foundation, thanks to the support of sanofi-aventis. The program targets both leishmaniasis and other endemic diseases, such as tuberculosis or dengue, rife in this region of Pernambuco state in Brazil. The screening and treatment center set up as part of the program means that close monitoring can be provided to 4,000 families who previously had to travel over 300 kilometers to the nearest screening facilities.



Prevention and screening for leishmaniasis (Aggeu, Magalhães Center, Brazil)

### ■ Central and Eastern Europe: a bridge between East and West

Sanofi-aventis is actively involved with the *Pont Neuf Association* which enables young doctors from 8 European countries (Croatia, Hungary, Poland, the Czech Republic, Romania, Russia, Slovakia and Ukraine) to train in French hospitals. The initiative promotes the sharing of knowledge as well as strengthening scientific and human ties between the different countries.

Sanofi-aventis is a partner of long standing to many other key players in the world of solidarity, including Reporters Without Borders, *Médecins du Monde*, *Handicap International*, *Enfants Réfugiés du Monde*... The Group's commitment to solidarity is also expressed through the dedication and involvement of affiliates and employees around the world, reflected in over a hundred projects undertaken in 2004.

### The Group also responds to humanitarian crises.

In the wake of the havoc wreaked by the tsunamis of December 26 in South East Asia, the Group and its affiliates in India, Indonesia, Sri Lanka and Thailand moved swiftly to make tons of medicines available to the stricken populations.

To give sanofi-aventis employees an opportunity to make their contribution to the task of long-term reconstruction, a World Solidarity Day was organized at over 300 Group sites around the world, raising the sum of 870,000 euros to fund twinning and sponsorship projects.



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