



Life can't wait.

Life can't wait.

Aventis 2003 Annual Report

2003 Annual Report



ADDENDUM

April 30, 2004

Recent Developments

Aventis Supervisory Board recommends substantially improved offer from Sanofi-Synthélabo in order to create Sanofi-Aventis

On April 25, 2004, Sanofi-Synthélabo submitted to the Aventis Management Board a substantially improved offer to acquire Aventis. After reviewing this new offer, which creates considerably more value for shareholders and provides for a balanced corporate governance structure, both the Management Board and the Supervisory Board of Aventis decided to recommend it to Aventis shareholders.

Aventis shareholders will be informed of all terms of the offer and the principles for the new combined company in the coming weeks.

Financial Highlights

	2003	2002	Total Variance
Net Sales (in € million)	16 791	17 591	-4.5%
Activity Variance ⁽¹⁾			5.9%
EBITA ⁽²⁾ Margin (in % of sales)	27.4	25.6	+1.8 p.p.
Net Income (in € million)	2 444	2 081	17.5%
Research and Development (in € million)	2 863	3 141	-9%
Capital Expenditures (in € million)	773	864	-11%

(1) Excluding currency translation effects
(2) Unaudited non-GAAP measure we define as operating income before goodwill amortization plus equity in earnings of affiliated companies




The above figures refer to the Aventis core business (prescription drugs, human vaccines, our 50% equity stake in the Merial animal health joint venture, and corporate activities).

This report is being provided for information purposes only. Aventis prepares a legally binding annual report in French known as the “Document de Référence” prior to its Annual General Meeting as well as an annual report in English on Form 20-F pursuant to the U.S. Securities Exchange Act of 1934.

Key Aventis Share Data

	2003	2002
Basic Earnings per Share (in €)	3.11	2.62
Basic Earnings per Share before Goodwill Amortization (in €)	3.72	3.31
Number of shares as of December 31	802 292 807	799 474 490
Per share information (in €)		
Dividend	0.82	0.70
Price-earnings ratio	16.85	19.77
Stockholders' equity (in € billion)	10.4	11.3
Year-end share price		
High	52.40	51.80
Low	54.55	85.95
	37.50	47.60
Market capitalization as of December 31 (in € billion)		
	42.04	41.41
Average daily trading volume (number of shares)		
Paris	3 512 837	2 920 038
New York	304 342	260 116
Frankfurt	52 640	64 766

Product Overview

Therapeutic Area	Key Developments	2003 Key Figures	
		Sales (in € million)	Activity Variance*
ONCOLOGY			
	<ul style="list-style-type: none"> Strong data presented at San Antonio Breast Cancer Symposium support U.S. and EU submissions for adjuvant breast cancer in 2004 Results of first direct comparison with paclitaxel show improved survival in women with metastatic breast cancer 	1 362	22.5%
	<ul style="list-style-type: none"> Follow-up and analysis continued on several major phase III trials in the adjuvant treatment of early-stage colorectal cancer and meta-static gastric cancer 	264	12.9%
METABOLISM/DIABETES			
	<ul style="list-style-type: none"> Becomes best-selling branded insulin analogue in Germany and the U.S. Global roll-out continues with launches taking place in over 40 countries FDA approval received for flexible administration 	487	87.1%
	<ul style="list-style-type: none"> Became the No. 1 sulfonylurea in Japan in February 2003 and continues to grow strongly Maintained No. 1 position in Germany, capturing a 25% share of the generic-dominated market for oral antidiabetic agents 	596	14.8%
	<ul style="list-style-type: none"> The <i>Insuman</i> family of human insulins maintains its popularity as a traditional brand among patients in Germany 	176	4.5%
CARDIOLOGY/THROMBOSIS			
 	<ul style="list-style-type: none"> Maintained No. 1 position in worldwide sales in low-molecular-weight heparin category Increased sales growth in the U.S. and Europe in key growth driver indications – cardiology and medical prophylaxis 	1 659	21.3%
 	<ul style="list-style-type: none"> Blockbuster status achieved for the first time Results of HOPE-TOO point to sustained prevention of cardiovascular disease and incremental reductions in both heart attack and the development of diabetes 	1 066	20.6%
HUMAN VACCINES ⁽²⁾			
Influenza vaccines	<ul style="list-style-type: none"> Approximately 43 million doses of <i>Fluzone</i> are shipped to customers for the 2003-4 influenza season with initial shipment of vaccine beginning one month ahead of schedule Position as the largest supplier of influenza vaccine in the U.S. 	479	17.7%
Pediatric combination vaccines	<ul style="list-style-type: none"> Sales of <i>Daptacel</i> increase after successful U.S. launch in 2002 Sales of <i>ActHib</i> rise thanks to reliable supply situation 	527	16.2%

*Excluding currency translation effects

Therapeutic Area	Key Developments	2003 Key Figures	
		Sales (in € million)	Activity Variance*
RESPIRATORY/ALLERGIES			
 	<ul style="list-style-type: none"> Telfast 30 mg tablets receive EU approval for pediatric use (6-11 years) A New Drug Application for Allegra-D 24 hour tablet is submitted to the FDA in December 	1736	1.1%
	<ul style="list-style-type: none"> Patient preference study confirms that Nasacort AQ is preferred by patients 2 to 1 over competing products based on sensory attributes Nasacort aerosol nasal inhaler removed from the market in July 2003 in compliance with the Montreal Protocol 	278	-0.7%
ANTI-INFECTIVES			
	<ul style="list-style-type: none"> Approved and launched in Canada, Japan and Turkey Achieves status as best antibiotic launch in France, Mexico, Belgium, Greece, Turkey and Finland 	115	135%
	<ul style="list-style-type: none"> Submitted in the UK (EU-RMS) (4) for the treatment of prostatitis Approved in the UK (EU-RMS) for the treatment of uncomplicated urinary tract infections 	216	-12.3%
	<ul style="list-style-type: none"> Approved for pediatric use in Japan Leading antibiotic for the treatment of serious Gram-positive infections in Japan and the UK 	207	-1.1%
ARTHRITIS/OSTEOPOROSIS			
	<ul style="list-style-type: none"> New 35 mg once-weekly formulation successfully launched in major European and International markets Differentiation achieved by establishing bone quality as a key measure of bone health 	194	81.4%
	<ul style="list-style-type: none"> Receives FDA approval for additional indication to improve physical function in rheumatoid arthritis Approved and launched in Japan 	255	8.3%
CENTRAL NERVOUS SYSTEM			
	<ul style="list-style-type: none"> Launched in French pharmacies in September 2003 Continued excellent market penetration in Europe Fastest-growing multiple sclerosis therapy worldwide 	617	27.3%

Important notice: The therapeutic indications mentioned in this document do not necessarily correspond to the exact indications registered in every country where the relevant pharmaceutical products are marketed and sold. The products identified in this document are only a selection of the total product offering of Aventis.

(1) Licensed from Yakult Honsha (not sold by Aventis in the United States)

(2) Includes sales by the joint venture Aventis Pasteur MSD, which is accounted for using the equity method

(3) Licensed from Daiichi (not sold by Aventis in the United States)

(4) EU-RMS = European Union Reference Member State

(5) Sold in cooperation with Procter & Gamble Pharmaceuticals; sales consolidated by Aventis

(6) Sold in cooperation with Teva Pharmaceutical Industries

Life can't wait... expresses our appreciation for the value of a healthy life. We are driven by the urgency of health challenges and the pressing needs of patients and are dedicated to developing pharmaceutical products to protect, prolong and improve life. As we work towards helping people across the globe, we never lose sight of the precious span of time given to each of us. We want to help our partners in life to embrace that gift and seize every moment in the best of health.

Contents

Letter to Shareholders	2
Report of the Supervisory Board	6
<i>Oncology</i>	<i>10</i>
<i>Metabolism/Diabetes</i>	<i>16</i>
<i>Human Vaccines</i>	<i>22</i>
<i>Cardiology/Thrombosis</i>	<i>28</i>
<i>Respiratory/Allergies</i>	<i>34</i>
<i>Other Strategic Brands</i>	<i>40</i>
<i>Pipeline Overview</i>	<i>42</i>
Aventis People	44
Sustainable Healthcare	46
Key Financials for 2003	48
Corporate Governance	54
Your Contacts	55
Dates & Publications	56

Letter to Shareholders

Dear Shareholders,

Every day millions of people around the world rely on innovative pharmaceutical products. Serious and life-threatening diseases such as cancer, diabetes or cardiovascular conditions, to name just a few, still cannot be cured. On the contrary, they are even on the increase. Other conditions, linked to aging, such as Alzheimer's or arthritis, are also becoming more widespread as average life expectancy continues to rise in both the industrialized world and developing countries. It is our aspiration at Aventis to help people around the world with innovative pharmaceutical products to prevent, treat and cure disease – because “Life can't wait.”



From left to right: Thierry Soursac, Richard J. Markham, Heinz-Werner Meier, Igor Landau, Frank L. Douglas, Patrick Langlois, Dirk Oldenburg

I am pleased to report to you on the conclusion of another successful year. Our 2003 earnings results are very strong and form a solid basis for future accelerated growth. We achieved double-digit earnings growth despite the rapid appreciation of the euro against other currencies and the negative impact of European healthcare reforms on sales of non-strategic products. We continued to invest in the future. Aventis is now better positioned for sustained future organic growth than ever before. These achievements were made possible by the commitment, dedication and expertise of the 75 000 employees of Aventis around the world. On behalf of the Management Board, I extend my sincere gratitude for their contribution to our success in 2003.

Key Achievements in 2003

- Core business sales rose 5.9% on an activity basis to €16.791 billion. Strong activity growth (+ 17%) of our strategic brands and human vaccines was offset by the negative impact of non-strategic brands, which declined by 10.6%.
- EBITA (operating income and equity in earnings of affiliated companies before goodwill amortization) at €4.595 billion rose 2.0% compared to 2002, equating to 27.4% of sales. Excluding currency impact, EBITA grew + 16.9%.
- Net income for the core business rose 17.5% to €2.444 billion.
- We improved our core business EPS by 18.6%, from €2.62 in 2002 to €3.11 in 2003, at the higher end of our market guidance. This is one of the strongest earnings growth rates in the industry.

- Free cash flow at €1.025 billion – after payment of €1.5 billion towards fulfillment of our pension obligation in Germany – is the best ever for Aventis. This improved our credit rating to A+.
- Our regulatory achievements in 2003 were impressive: We received approvals for five new products and 11 line extensions. At the same time, we submitted five new chemical entities and vaccines and four line extensions for regulatory approval.
- We made significant progress with the divestment of the last major non-core business interests by completing the disposal of Clariant, selling a 9.9% stake in Rhodia and agreeing the sale of Aventis Behring to CSL Ltd of Australia.

Where We Stand Today

Having met our sales and earnings targets despite the weaker sales growth for *Allegra/Telfast* and the 10% decline in sales of non-strategic products, we are confident that we are well-positioned to move ahead in this rapidly changing and more challenging environment.

Our Product Leadership Strategy, through which we are maximizing the performance and the potential of our strategic brands, is delivering results in both the U.S. and Europe. Strategic brands and human vaccines now account for 65% of core business sales, up from 59% in 2002. We generated 38% of total core business sales in the U.S., compared to only 28% in 2000.

In 2003 we reinforced our strategic competitiveness in our key disease areas. The following achievements illustrate our progress to remain or become a dominant company in three of these areas – oncology, diabetes and vaccines:

The oncology franchise, founded on the continued success of *Taxotere*, is set to grow through further indications, the expected approval in 2004 of the targeted cancer therapy *Genasense*, which has been granted a priority review by the FDA, the new taxanes in development, the in-licensing of Regeneron's VEGF Trap – an innovative inhibitor of the growth of new blood vessels to block tumor growth – as well as the collaboration with ImmunoGen to discover, develop and commercialize novel antibody-based cancer therapeutics.

We continued to strengthen our diabetes franchise, which is growing from the successful launches of *Lantus* in over 40 countries. 2003 saw the submission of *Apidra* (in EU and U.S.), a rapid-acting insulin, the progression of *Exubera*, an inhaled insulin which we are developing with Pfizer and Nektar, and the in-licensing of AVE-0100 from Zealand Pharma of a novel approach to treat diabetes by a GLP-1 receptor agonist of the exendin class.

Aventis Pasteur is building on its leading position in flu and pediatric vaccines and submitted *Menactra*, the first quadrivalent conjugate vaccine to prevent the most virulent form of meningococcal meningitis. In addition, Aventis Pasteur is preparing for a 2004 U.S. submission of *Adacel*, the first trivalent booster against diphtheria, tetanus and pertussis and is pushing forward with the research and development of potential vaccines for SARS and HIV among others.

Meeting Future Challenges

The sustained strength of the euro, our reporting currency, will continue to affect our reported earnings. Further cost-containment measures within Europe and the U.S. will exert increased pressure on healthcare spending, hastening the decline in sales of older products.

Nevertheless, we expect our future earnings and sales growth to be fueled by our strategic brands and introduction of new products. We will continue to enhance the effectiveness of our sales and marketing activities and pursue additional line extensions to expand the range of indications for existing core strategic brands. At the same time, we are preparing for launches of recently submitted products, e.g. *Genasense* (U.S.), *Ketek* (U.S.), *Apidra* (EU; U.S.), *Alvesco* (U.S.), *Menactra* (U.S.) and *Sculptra* (U.S.). By partnering or divesting non-strategic products, representing sales of up to €1.5 billion in 2004, we will further reduce their declining contribution to, and limitation of, our future growth.

By pursuing a focused disease area strategy, we aim to generate the mid- to long-term growth necessary to achieve global leadership in the pharmaceutical industry. In each of our selected disease areas, this will be achieved by the acceleration of internal development projects and continued aggressive in-licensing of products with novel and commercially attractive mechanisms of action, complementary to our existing portfolio. We currently have more than 90 prescription drug candidates and human vaccines in development, including 14 products in late-stage development and over 40 products in early-stage clinical development. This year alone, we advanced four potential blockbuster compounds from early-stage to late-stage development.

Having the best people in all positions and development plans in place to continuously strengthen the quality and depth of our talent pool is crucial to our long-term success. At the same time we are focusing on differentiation in reward and recognition of outstanding achievement to continue to build a high-performance organization.

Corporate Responsibility

Working always in a responsible and sustainable manner is very important for us at Aventis. We have long been committed to sustainability as evidenced by the implementation of various policies and protocols including the Sustainable Healthcare Policy and the Environment Health Safety Policy. This year we have crystallized our commitments in a single overarching Sustainability Policy, which aligns our current programs and enables us to strategically map our path forward.

Along with our Annual Report, our Sustainability Report outlines our continued efforts and contributions towards a better future. Focusing on selected activities at the global level, we decided to commit ourselves to involvement in projects to treat global problems, but which have an immediate impact at a local level. As partners in the Global Alliance for Vaccines and Immunization (GAVI) we actively promote immunization in developing countries ensuring the treatment of global immunization

problems by local approaches. At the same time we are also fully involved in fighting both tuberculosis (TB), working with the Nelson Mandela Foundation, and sleeping sickness (trypanosomiasis) with WHO.

Conclusion and Outlook

- In 2003, Aventis delivered strong earnings growth for the fourth consecutive year and built a solid platform for future growth.
- In 2004, Aventis is expecting sales growth of 6 to 7% with earnings per share growth in the mid teens.
- The launch of four new products is planned in 2004.
- Sales growth should be further enhanced by the disposal of a significant share of our non-strategic products (representing sales of up to €1.5 billion).
- Sales between 2005 and 2007 are targeted to grow 10 to 11% annually. Over this time earnings per share should grow by 13 to 15% due to the sales growth, continuous productivity improvement measures and the implementation of a new share buyback program of €2 to 3 billion in 2004 and 2005.

In January 2004 Sanofi-Synthelabo launched a hostile bid for control of Aventis. The Management Board has unanimously rejected this unwelcome offer. The Supervisory Board supports the Management Board in its rejection of this offer. This offer does not reflect the full value and future potential of Aventis. The Management Board is committed to secure the best future for the employees, and shareholders of Aventis.

Creating and sustaining value for shareholders, patients, employees and society at large is the essence of our strategy. We are therefore firmly committed to delivering increasing value. In this way, we will offer our employees the challenging and rewarding environment of a high-performance organization and patients around the world the therapeutic innovations of the future.

On behalf of the Management Board I would like to thank you all for your current and future support and interest in Aventis.



Igor Landau
Chairman of the
Management Board



Report of the Supervisory Board

Dear Shareholders,

In 2003, Aventis concentrated on its strengths and took another positive step towards its goal of becoming a pharmaceutical industry leader. 2003 was a successful year in terms of both earnings and investments in the future of the company. Aventis is now, more than ever before, solidly positioned for organic growth.

Business Environment and Strategy

In order to build further on this success, Aventis is putting in place the foundations for future growth and value creation. Aventis strategic initiatives are targeting three areas:

- Accelerating top-line growth
- Establishing a strong position in our chosen disease areas
- Fielding the best teams.

Continuous improvements in business processes and productivity will allow the necessary reallocation of resources to fund these initiatives. This will enable Aventis to realize the successful marketing and development of innovative products while delivering above-average annual earnings growth.

Aventis 2003 Results

The Supervisory Board reviewed the financial results of 2003 presented by the Management Board.

Aventis core business sales rose 5.9% on an activity basis to €16.791 billion. Strong growth (+ 17%) of our strategic brands and human vaccines was offset by the negative impact of declining non-strategic products (- 10.6%).

Core EBITA at €4.595 billion rose 2.0% compared to 2002, equating to 27.4% of sales, a change of 1.8 percentage points over 2002.

Core EPS improved by 18.6% from €2.62 (2002) to €3.11 (2003).

Aventis consolidated group sales were €17.815 billion in 2003 compared to €20.622 billion in 2002. The 2002 sales figure included contributions from Aventis CropScience and Aventis Animal Nutrition, which were divested during the first half of 2002. Group net income was €1.901 billion in 2003 compared to €2.091 billion in 2002, which included the net gain related to those divestments.

The Supervisory Board notes that consolidated basic earnings per share (EPS) in 2003 were €2.42 compared to €2.64 in 2002.

The Supervisory Board acknowledges the results of the statutory financial statements of Aventis, i.e. the results of the Aventis holding company, amounting to a net profit of €847 million in 2003 compared to €1.145 billion in 2002.

Corporate Governance

The Supervisory Board met five times in 2003 and carefully reviewed the work of the Aventis Management Board. There was ongoing contact with the Management Board in order to follow the development of the company. The Management Board provided the Supervisory Board and its committees with detailed written and oral information and allowed for sufficient opportunity to discuss all major strategic decisions, the development of Aventis and the industry as a whole, in accordance with the Internal Rules of the Supervisory Board and Management Board.

Supervisory Board Committees

The **Strategy Committee** held two meetings in 2003 with an attendance rate of 100%. In 2003, the Committee reviewed and discussed an extensive analysis, prepared by the Management Board, of the current and anticipated future trends in the global pharmaceutical industry and its regulatory and economic environment, the competitive position of Aventis as well as the opportunities and risks faced by the company. In conclusion, the Committee approved the strategy proposed for Aventis by the Management Board on the basis of a series of scenarios and options on how to respond to these factors and to secure growth and value creation.

The Committee also reviewed the initial results of the ongoing development of the Aventis disease area strategy, which is aimed at building and securing competitive leadership positions for Aventis in market segments that are believed to remain highly attractive in the future because of large unmet medical needs and emerging new therapeutic approaches. Strategies were presented for oncology, diabetes and vaccines, and consolidated recommendations for all core disease areas will be reviewed in 2004. Another focus was the progress of the Aventis pipeline in 2003 and measures taken by the DI&A leadership team to further improve productivity and innovation quality.

The **Finance and Audit Committee** held regular five meetings in 2003, with an attendance rate of 100%.

The Finance and Audit Committee reviewed the Aventis financial statements and annual report including the auditors' report, the pro forma off-balance sheet items and non-consolidated companies and the proposed resolutions to the Annual General Meeting of Shareholders in April 2003. It also reviewed the company budgets and objectives, the business plan, the productivity enhancement initiatives, various divestitures or reorganizations and financing topics.

The Committee examined contingencies and litigation, made proposals on stock options and equity-based compensation and reviewed the launch of the employee stock purchase program (Horizon 2003).

The Committee reviewed the company's credit ratings, the renewal of the authorizations to be given to the Management Board, the liability of directors and officers of the company, property and business interruption insurance, and pension funding in Germany.

Apart from examining enterprise risk management, internal audit activities (follow-up of implementation of audit recommendations), the Committee approved the audit plan, reviewed audit activities and reports, and discussed the Corporate Governance topics in connection with new U.S., French and German rules and recommendations for the year 2003.

The **Nomination and Compensation Committee** held five meetings in 2003 with an attendance rate of 90%. In 2003, the Nomination and Compensation Committee worked on the following subjects:

- Determination of the variable part of the 2002 compensation paid to the members of the Management Board. The Committee reviewed the results and proposed to the Supervisory Board a recommendation for 2002. As in previous years, common 2003 objectives linked to the company's performance, also in relation to pharma competitors, e.g. Aventis share price evolution, earnings per share, strategic action plans, were determined at the beginning of 2003. At the same time, a set of proposed objectives for each Management Board member was recommended for 2003.
- 2003 compensation of Management Board members. As in previous years, the Committee reviewed a market analysis prepared by an outside compensation consulting company, reviewed the compensation of each Management Board member and made a recommendation to the Supervisory Board.
- Review of the 2002 professional expenses of the Management Board members.
- Review of the Talent Management program. A review was organized with the two-fold aim of checking whether the present incumbents of key positions of the company have the necessary competencies and checking whether the company has a sufficient number of potential successors for the mid-term.
- Stock option December 2003 grant. The Aventis long-term incentives policy is to attract and retain quality managers in an industry where long-term incentives are used widely. Based upon market surveys conducted by an outside consulting company, the Committee reviewed the December 2003 plan and recommended to the Supervisory Board to continue to grant stock options.
- Governance. The Committee examined and made proposals for the governance of the company. The proposals will be presented for the approval of Aventis shareholders during the Annual General Meeting of Shareholders.

The Supervisory Board supported the draft resolutions as proposed by the Management Board that will be put to vote at the next Annual General Meeting of Shareholders.

The Supervisory Board thanks the management and all employees for their dedication and accomplishments in 2003.

Recent Events

After having reviewed and considered the terms and conditions of the unsolicited exchange offer put forward by Sanofi-Synthélabo on January 26, 2004, the Supervisory Board unanimously concluded that this offer would not be in the best interest of Aventis shareholders and employees. On January 28, 2004 the Supervisory Board gave a mandate to the Management Board to explore alternative scenarios offering a stronger industrial and social rationale for both the shareholders and employees of Aventis.

Jürgen Dormann

Jürgen Dormann
Chairman of the
Supervisory Board



Jean-René Fourtou

Jean-René Fourtou
Vice Chairman of the
Supervisory Board





ONCOLOGY

Soraya heard the news in 2000, just before the young Latina singer-songwriter was to leave for a concert tour to promote her third album. “It came out of nowhere and shot through my heart,” she recalls in her recent ballad, ‘No One Else.’ “Time stood still as my world fell apart. Four simple words turned me upside-down.” You have breast cancer. Soraya had previously lost her mother, grandmother and aunt. Now an aggressive stage III breast cancer threatened her life, at age 31. And Soraya’s whole focus shifted to surviving. “Women need to know that breast cancer is not the death sentence it once was and medicine has come a long way,” Soraya says.

“The options available helped me battle breast cancer. My medical team and I decided on a holistic approach that included dietary changes, radiation, surgery and a chemotherapy regimen, all of which contributed to my recovery.” In the battle, she relied on support from family, friends and faith. “This is my reality,” Soraya says. “I had – and have – only one choice, and that’s to fight.” Soraya sprang back into the spotlight in 2003 with her fourth album. Her single “Casi,” a song that rocks with the emotion of her fight against cancer, hit #1 on the Latin Billboard charts. She toured the United States and Latin America, as well as Germany. Soraya’s skilled guitar playing and rich, lilting voice serve an expanded mission now: educating women, particularly Latinas, about breast cancer. Another avenue for her activism is her role as a spokesperson for Aventis and its Web site www.livingwithit.org

Soraya feels good about her direction in life. As she sings: “Now I’m breathing once again. And time has shown me the power of my strength. This journey is an ever-winding road, and I will walk it proud, tall and strong. And as I’m standing face to face with myself, I thank the Lord I’m no one else.”



“This is my reality. I had – and have – only one choice, and that’s to fight.”

Medical Background

Cancer develops when cells in a part of the body begin to grow out of control. This can happen when DNA is damaged and not repaired. People can inherit damaged DNA or a person's DNA can become damaged by environmental factors, such as smoking. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Cancer cells can form a mass of tissue commonly referred to as a tumor. Metastasis occurs when cancer cells move via the bloodstream or lymph vessels to other parts of the body and begin to grow and replace normal tissue. Not all tumors are cancerous. Benign tumors do not spread to other parts of the body (metastasize) and are rarely life-threatening.

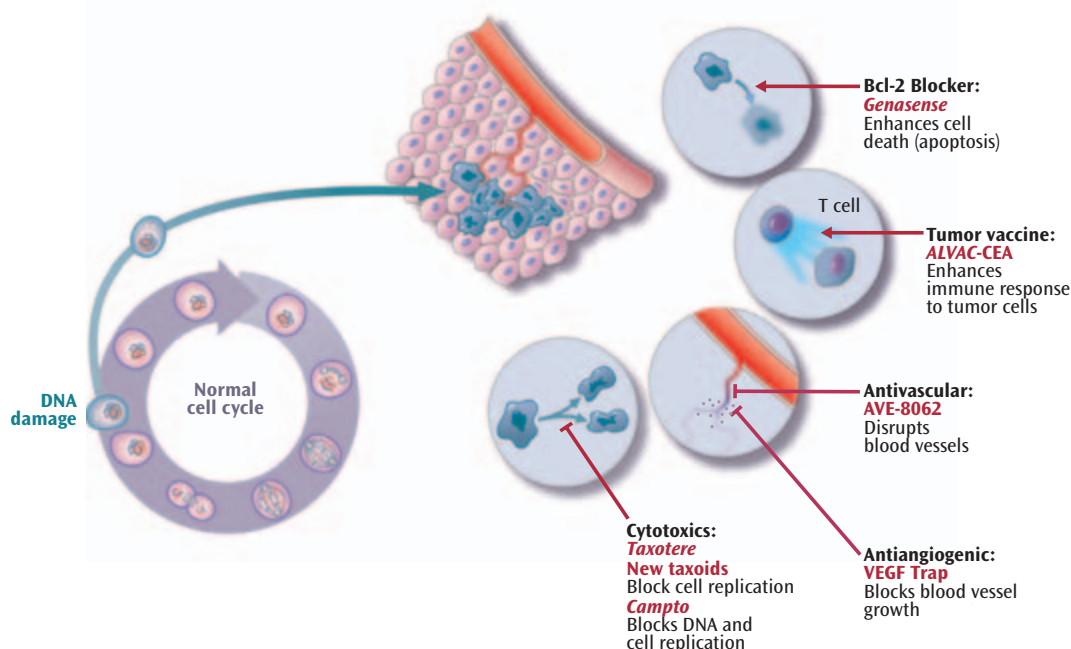
Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments.

Breast cancer is the second leading cause of cancer deaths among women in the major pharmaceutical markets. More than 80% of patients

are diagnosed with early-stage disease (stages I and II). While the exact causes of breast cancer are unknown, research has shown that women with certain risk factors such as age or a personal or family history of breast cancer are more likely than others to develop the disease. Yet most women who develop breast cancer have no family history of the disease. 80% of women with breast cancer have no known risk factors. More than 20% of breast cancers are diagnosed in women under the age of 50.

It is estimated that there are currently nearly 3.1 million people worldwide with lung cancer, with 80% of these patients having a diagnosis of non-small-cell lung cancer (NSCLC). Lung cancer is the leading cause of cancer deaths, as it is generally diagnosed only after it has reached an advanced stage. The development of NSCLC is most often associated with a long history of smoking, and men are several times more likely than women to develop the disease. Nearly 75% of patients diagnosed with NSCLC are considered either stage IIIB or IV.

Aventis approaches to treat cancer



A better understanding of the cancer process has led to the identification of many new targets that regulate the growth, survival, invasion, and spread of cancer cells. Aventis is committed to the development of cancer agents that selectively target one or more processes that give rise to cancer, such as overexpression of proteins that prevent cancer cell death, waning tumor immune response and tumor vascularization, as shown here.

Aventis Strategic Brands



Taxotere (docetaxel) is a chemotherapy agent primarily used to treat metastatic breast cancer and non-small-cell lung cancer (NSCLC). Launched in 1995, *Taxotere* is the foundation of our oncology franchise and is being studied extensively in early-stage breast, prostate, head and neck and gastric cancers.

Approved indications

- Second-line treatment of locally advanced or metastatic breast cancer and non-small-cell lung cancer
- First-line treatment of non-small-cell lung cancer in combination with cisplatin (U.S., Europe, Japan)
- Gastric, ovarian, and head and neck cancer (Japan)

Major markets

Taxotere is marketed in over 86 countries, and is used widely throughout Europe, the U.S. and Japan.

Product features

- Most widely used taxane in the U.S.
- Only agent approved in Europe for use in combination with doxorubicin for first-line treatment of locally advanced or metastatic breast cancer
- *Taxotere* has demonstrated an impressive tumor response rate in locally advanced or metastatic breast cancer after failure of cytotoxic therapy, as well as prolonged patient survival
- *Taxotere* was the first taxane approved in the United States for treatment of locally advanced or metastatic breast cancer after failure of prior chemotherapy
- Well-differentiated from paclitaxel



Campto (irinotecan), first approved in 1995, is a chemotherapy agent and the current standard of treatment for advanced colorectal cancer. We market *Campto* under a license from Yakult Honsha.

Approved indications

- First-line treatment of advanced colorectal cancer in combination with 5-fluorouracil (5-FU) and folinic acid (FA)
- Second-line treatment of advanced colorectal cancer (CRC) in monotherapy

Major markets

Aventis markets *Campto*, primarily in Europe, Asia and Africa and its major markets are Germany, France, Italy and the United Kingdom. We do not market this product in North America, Japan or South America. *Campto* is available in more than 40 countries.

Product features

- First and only drug to demonstrate a survival benefit in advanced CRC over 5-FU/FA in randomized phase III trials
- *Campto* in combination with 5-FU/FA is the current standard in first-line treatment of advanced colorectal cancer

Research and Development

Making a True Difference in the Lives of People with Cancer

Almost everyone knows someone who's been up against some form of cancer – a relative, a friend, a neighbor, or a co-worker. A diagnosis that was more often than not equated with a terminal illness is gradually losing its stigma. Cancer awareness campaigns and regular screening are enabling people to identify the disease and seek treatment early. Medical science is also making significant strides in the fight against cancer. The results of recent research studies show that Aventis is playing a major role in the development of promising new treatments for patients with this disease.

Already recognized as a leading treatment for metastatic breast cancer and non-small-cell lung cancer, *Taxotere* is the subject of numerous clinical trials exploring the safety and efficacy in early treatment and several other forms of cancer. In 2003, several clinical studies involving *Taxotere* yielded positive results, confirming the significant potential of this life-saving therapy.

One of the highlights of the San Antonio Breast Cancer Symposium in December 2003 was the detailed assessment of the impact of *Taxotere* when used together with an anthracycline-containing treatment regimen in the treatment of women with early-stage, node positive breast cancer.

This exciting data will serve as the basis of the FDA and EMEA submissions of *Taxotere* for adjuvant breast cancer in 2004.

The value of *Taxotere* has been underscored in a number of other studies. At the 2003 European Cancer Conference (ECCO), results from a randomized phase III study demonstrated that women with metastatic breast cancer who were treated with *Taxotere* showed a statistically significant improvement in overall survival and time to disease progression compared to those who were treated with paclitaxel, a rival drug.



Production of docetaxel, the active ingredient of *Taxotere*, at Aventis in Vitry, France

Taxotere is also being studied extensively for its efficacy in the treatment of other forms of cancer, such as gastric and hormone-refractory prostate cancer. The preliminary results of the largest international study ever conducted in the treatment of patients with advanced stomach (gastric) cancer suggest that *Taxotere*-based chemotherapy has the potential to improve overall response and survival rates among patients with this often fatal disease.

These encouraging results are testimony to the progress Aventis is making in the battle against cancer. As we continue to develop existing brands such as *Taxotere* and seek new treatments and potential cures, we are both strengthening our oncology portfolio for the future and helping to save thousands of lives.

Expert Opinion on Oncology

Professor David Khayat is the Head of the Oncology Department at Pitié-Salpêtrière Hospital in Paris and a permanent advisor for the interministerial campaign to overcome cancer.



How much progress have we made in the battle against cancer?

The evidence shows that cancer is still a major public health problem. According to the WHO, in 2000, there were 10 million new cases each year and 6 million deaths. These figures will rise to 20 million new cases resulting in 10 million deaths by 2020. In most developed countries, cancer has become the primary cause of death before the age of 65.

What are the challenges facing us before we can reverse the situation?

There are several stakes in so far as cancer is concerned: scientifically, obviously, because we must understand the underlying mechanisms: why does a cell become malignant one day? There are also medical stakes since we have to find the tools and resources to counter the life-threatening tumor. In addition, social, political and economic aspects are also at stake. Smoking is a perfect illustration. Thanks to action taken by the French government, there were 1.5 million fewer smokers in the last quarter of 2003, which will mean 350 000 fewer deaths due to lung cancer over the next twenty years. Breast cancer in women over the age of 50 is another example. If every woman were to have a mammogram every two years, an additional 3 000 lives would be saved every year in France.

What role do taxanes play in the current therapeutic arsenal?

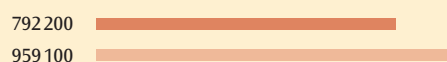
Taxanes play a key role. These molecules have allowed major advances to be made in the treatment of the most aggressive tumors: breast, lung, head and neck, bladder, ovary and stomach, etc. Their spectrum of activity largely covers the field of oncology. Moreover, they are either the or one of the two most effective drugs in term of remission. More patients should have greater access to these new treatments.

Can the emerging target treatments eventually replace traditional chemotherapies and radically modify the approach to cancer treatment?

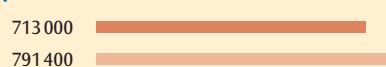
No, the target treatments will undoubtedly be combined with more conventional, systemic chemotherapies that are effective over the entire body. The latter act by bombarding the cancerous cells, regardless of where they hide, with cytotoxic products, but they also partly affect healthy cells. The new target drugs act as real missiles fitted with homing devices. The malignant cells dispersed throughout the body are detected and neutralized without affecting the healthy cells. This brings us to an intelligent, extraordinarily multi-faceted approach since the cancerous cell involves a countless number of gene-controlled mechanisms that have to be overcome.

Number of diagnosed prevalent cases of breast cancer

United States



Europe



Japan



Estimates for Europe cover France, Germany, Italy, Spain and the UK.
Source: Decision Resources, Inc. Waltham, MA.



METABOLISM / DIABETES

Marie Armelle knew nothing about diabetes while she was growing up. Her father had the disease and eventually died from it. Her father's brothers had diabetes. So did her mother's sister. But the subject was taboo. It was not until Marie herself was diagnosed at age 34 that she began to learn how to live with diabetes. And it was not to be an easy journey.

Marie's first reaction to the news was shock. A lifelong disease? No. Starting out on oral antidiabetic agents, she did not strictly follow her treatment plan. After six months, Marie's blood sugar level was still dangerously high. Her doctor then explained the long-term complications: With uncontrolled diabetes, she could face progressive nerve damage, kidney disease, loss of vision, risk of amputation, cardiovascular events, death.

Now, more than two decades later, the mother of three and grandmother of five has a more optimistic outlook. At 56, she enjoys tending her garden in La Wantzenau, France, doing water gymnastics and working as a bookkeeper.

Early on, four insulin injections a day helped, but became burdensome. Marie stopped insulin for several years, but her diabetes became unstable. In 2002, Marie's specialist in nearby Strasbourg offered a chance to join a clinical trial for an innovative insulin treatment – offering 24-hour blood sugar control with a single daily injection. Her average blood sugar, or A1C, is on target now. Marie has fewer hypoglycemic episodes. And with her glucose under control, she is less afraid of long-term complications.

Yes, the disease is always there, but Marie now knows diabetes can be managed.



“I have realized that having diabetes is not my fault, but keeping it from getting worse is my responsibility.”

Medical Background

Diabetes mellitus is a condition where the body does not produce, or properly use insulin, the hormone needed to convert glucose (sugar) into energy. In a healthy, non-diabetic person, insulin acts to convert glucose (created when sweet and starchy foods are digested) into the energy needed to perform daily tasks. People with diabetes do not have enough insulin and/or are insulin-resistant and are thus unable to make this necessary conversion into energy. They therefore have high levels of unused glucose in their system, which is referred to as high blood glucose or hyperglycemia.

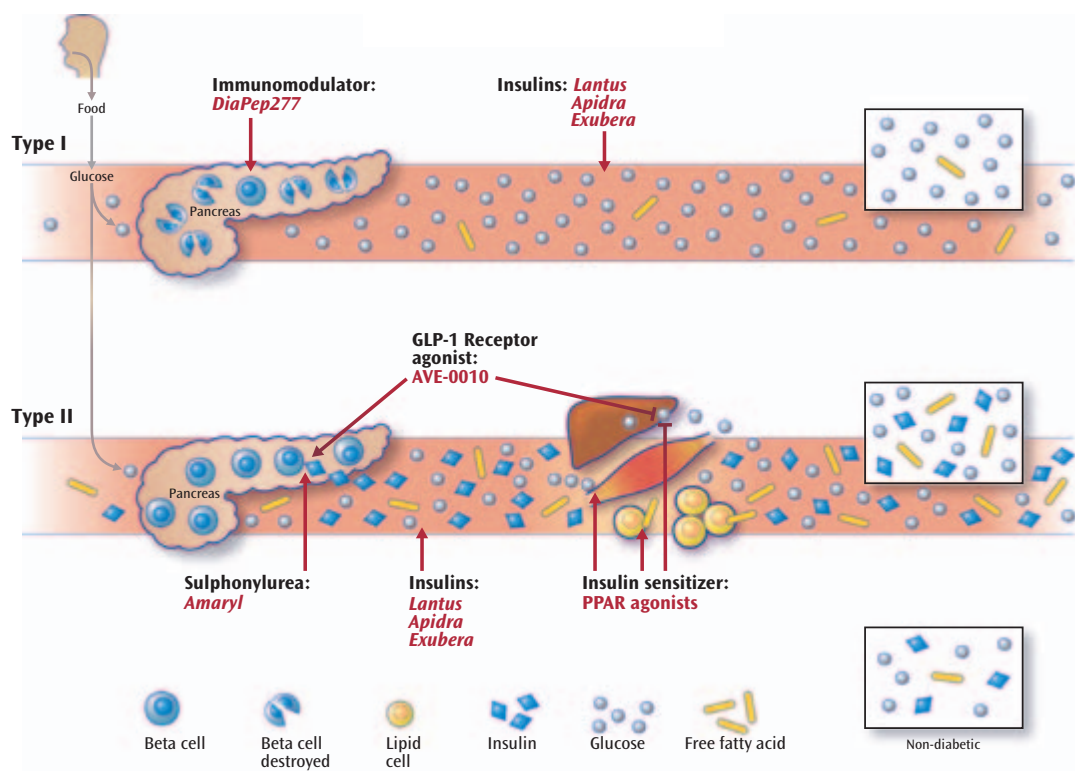
In type 1 diabetes there is a complete deficiency in insulin production and secretion. Impaired insulin secretion occurs when a person's immune system attacks and destroys the beta cells in the pancreas. Therefore, type 1 diabetes is called an autoimmune disease. People with type 2 diabetes have a condition referred to as relative insulin deficiency. While the pancreas is making insulin, there is not enough insulin being produced to adequately control glucose levels.

With insulin resistance, pancreatic beta cells continue to produce insulin at varying rates but the body is unable to effectively use the insulin. Insulin resistance is associated with many medical problems seen with type 2 diabetes.

Although diabetes cannot be cured, it can be treated or controlled very effectively. The aim of diabetes treatment is to maintain blood glucose levels as close to normal, non-diabetic levels as possible. One measure of control is glycated hemoglobin or HbA1C (A1C), an assessment of blood glucose levels over a two- to three-month period. A person without diabetes will have an A1C level between 4-6%, meaning only 4-6% of glucose has attached to hemoglobin.

If a person with diabetes has blood glucose levels which are persistently above the normal range ('uncontrolled diabetes') they are at high risk of developing many serious health problems, such as blindness, kidney failure, heart attacks, strokes, impotence and amputation.

Aventis approaches to treat diabetes



Type 1 diabetes is an autoimmune disease which destroys the insulin-producing beta-cells of the pancreas. Patients suffer from absolute insulin deficiency. It is characterized by a rapid onset in young age. Type 2 diabetes develops over time through a deterioration in insulin signaling. Typically in patients beyond age 40, chronic hyperlipidemia and hyperglycemia then counteract insulin-mediated glucose uptake and hepatic regulation of glucose output.

Aventis Strategic Brands



LANTUS®
insulin glargine [rDNA origin] injection



Amaryl®
Glimepiride



insuman®
HUMAN INSULIN

Lantus (insulin glargine) is the world's first long-acting insulin analogue that provides 24-hour insulin coverage through a once-daily injection with no pronounced peak of action.

Approved indications

- Once-daily subcutaneous administration in the treatment of adult patients with type 2 diabetes mellitus who require basal (long-acting) insulin for the control of hyperglycemia and for adult and pediatric (age six and older) patients with type 1 diabetes mellitus
- Flexible dosing, i.e. at any time of the day, in patients with types 1 and 2 diabetes mellitus (U.S./EU)

Major markets

Approved worldwide, *Lantus* is the most frequently prescribed medication for newly diagnosed type 1 cases in the U.S. and Germany. The global roll-out continued in 2003, with launches taking place in over 40 countries, including France and Japan.

Product features

- *Lantus* is the only once-daily insulin analogue that is proven to lower basal glucose levels for a full 24 hours
- Delivers excellent basal glucose control in combination with oral hypoglycemic agents or as part of a regimen with short-acting regular insulin

Amaryl (glimepiride) is a once-daily, new-generation sulfonylurea that lowers the body's blood glucose level primarily by helping the body produce more insulin.

Approved indications

Treatment of type 2 diabetes when diet and exercise are no longer sufficient to control hyperglycemia, either as a monotherapy or in combination with insulin or metformin.

Major markets

Amaryl is marketed in over 60 countries. Its main markets are the U.S., Europe, Japan and Korea.

Product features

- Position as leading first-line therapy and partner of choice in combination with other oral diabetes treatments
- Convenient and effective once-daily dosing may be a key factor in patient compliance and offers an advantage over certain commonly prescribed agents of the same class
- Improves predominantly insulin secretion and also action, helping to attain recommended glycemic control with a reduced risk of hypoglycemia and minimal weight gain

Insuman (human insulin)

Approved indications

Treatment of patients with type 1 or type 2 diabetes mellitus who require insulin for the maintenance of normal glucose levels.

Major markets

Insuman was approved in the EU in 1997 and launched in Germany in 1999. *Insuman* is available throughout western and eastern Europe as well as Latin America. Aventis does not sell this product in the U.S. or Asia.

Product features

The *Insuman* family of recombinant human insulins comprises:

- *Insuman* Basal 100 u/ml suspension for injection, an intermediate-acting, isophane insulin suspension
- *Insuman* Rapid 100 u/ml solution for injection, a fast-acting, neutral insulin solution
- *Insuman* Comb 25 100 u/ml suspension for injection which provides a combination of both intermediate- and fast-acting insulins

Production and Manufacturing

Meeting the Challenges of Insulin Supply

Millions of people around the world rely on insulin to manage their diabetes – an illness that WHO statistics predict will affect more than 300 million people worldwide by 2025. As a leading global developer and producer of innovative diabetes therapies, Aventis is helping improve the daily lives of diabetes patients all over the world.

In 2003, Aventis took its insulin production capabilities to new heights. In a project orchestrated by Aventis Industrial Operations (IO), the company inaugurated the world's most modern biotech insulin production plant in Frankfurt, Germany in September. The €160 million facility produces the active ingredient for *Lantus* (insulin glargine). The plant will be able to meet the insulin needs of more than two million people with diabetes worldwide.

The Frankfurt plant, which has created 220 jobs, is just one part of the company's insulin development strategy. A further €100 million is currently being invested in a new *Lantus* manufacturing facility, now under construction. When it opens, this building will manufacture the finished *Lantus* products from the active ingredients facility.



Inauguration of the new *Lantus* plant in Frankfurt, Germany

The production of insulin has come a long way since Hoechst, an Aventis predecessor company, became the first company in Europe to manufacture insulin around 80 years ago. While today's insulins are produced in large volumes through biotechnological processes, in the early days, insulin was derived from cow and pig pancreases and was produced in limited amounts.

Today, at the state-of-the-art production facility of Aventis in Frankfurt, cutting-edge systems and highly-trained, specialized staff ensure the manufacture of compliant products. The process for producing *Lantus* begins with the cultivation of *E. coli* bacteria equipped with the gene for human insulin. When the bacteria have sufficiently multiplied, they are destroyed using a disinfectant.

Then, the cell walls of the bacteria are broken to extract the insulin hormone in the form of long strands of protein, which are then folded in exactly the same way nature intended for a perfect insulin molecule. The next stage is the purification of the correctly folded proteins via the chromatographic process that separates out insulin-like attendant materials and high molecular impurities from the pure hormone. Finally, the insulin undergoes high pressure liquid chromatography (HPLC), crystallization and drying processes under aseptic conditions. The end result is an insulin of the highest purity.

Aventis IO is constantly working to meet the challenges of insulin production. A great deal of process knowledge is required for the handling and storage of insulin to ensure its quality and consistency, from optimizing purification techniques to creating stronger packaging systems.

With the number of diabetes patients growing each year, keeping a smooth supply chain going is also a central concern of Aventis IO. Stockpiling insulin is not an option due to the sensitivity of the process, so cutting-edge electronic systems are employed to maintain an optimized supply chain. The seamless supply of insulin pens and syringes is also carefully coordinated with the production of the insulin itself.

Beyond helping Aventis to manage and grow *Lantus*, Aventis IO is playing a key role in supporting the manufacture of the company's other diabetes therapies. From the recombinant human insulin *Insuman*, the oral antidiabetic agent *Amaryl* and the new rapid-acting insulin analogue *Apidra*, Aventis IO is helping Aventis expand its position as a global leader in diabetes therapies.

Expert Opinion on Diabetes

Philip Home, Professor of Diabetes Medicine at the University of Newcastle upon Tyne, UK is a former President of the International Diabetes Federation Europe (IDF), and Chairman of WorldWIDE, an initiative for professional education in diabetes.



What is the status of diabetes treatment and control today?

Poor recognition and management of diabetes in the past have resulted in it being a costly problem. Even in countries with a low prevalence of the condition, one in 17 of the population dies from a diabetes-related condition, and it is a major cause of heart attacks, strokes, kidney failure, blindness, and amputation.

Thanks to recent advances in medical technology and improved diagnostic and therapeutic practices, we have a far better understanding of how to manage diabetes than we did a decade ago. Managing diabetes is not just about glucose lowering; it's also about blood pressure and blood lipid management, and screening for early complications. However, the number of people with diabetes is expanding faster than our current resources can cope. Thus, even in the industrialized world, we are under-using blood pressure and blood glucose management tools, and under-screening patients' eyes. Meanwhile in the developing world, there is a vast gap between our knowledge of diabetes and our ability to treat and prevent it.

Looking ahead, how do you foresee our ability to effectively manage diabetes?

Over the next decade, the incidence of diabetes will continue to increase, particularly in the U.S., China, and Japan, where type 2 diabetes is becoming more prevalent. Many will develop diabetes at a young age, the complications then disrupting their most productive years. In parallel however, we will see more insulins and insulin-delivery tools, and other new pharmaceuticals working in novel ways, on the market. There may even be drugs to protect directly against diabetes complications, such as damage to the retina of the eye or the filtering mechanism of the kidneys.

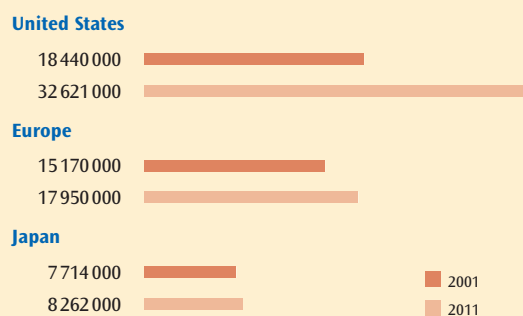
Why is effective glucose control important and how might early insulinization be beneficial?

Glucose is a fuel, and like other fuels such as nuclear and gas, it is only safe as long as it is controlled. High-energy substances can be dangerous in the wrong conditions or in excessive quantities. Because glucose is toxic, if it reaches higher than normal levels, it can damage the body's blood vessels causing strokes, eye problems and the like. We can control people's glucose with insulin in a way that is not possible with other drugs, and it can be used in combination with them. Early insulin use is central to this.

What is the greatest challenge facing diabetes healthcare professionals in the 21st century?

With the number of diabetes cases doubling every 20 years, our biggest challenge is preventing childhood obesity. Educating people about healthy lifestyles is known to help delay and prevent diabetes.

Number of prevalent cases of type 2 diabetes



Estimates for Europe cover France, Germany, Italy, Spain and the UK.
Source: Decision Resources, Inc. Waltham, MA.



HUMAN VACCINES

Dr. Bonnie Word recalls a rare case: the first patient she saw with measles. “The child had recently come to the U.S. from Africa. One of the mothers said, ‘This looks like measles.’ And one of our smartest residents said, ‘Oh no, ma’am, that can’t possibly be measles.’ The vaccine had eliminated the disease in this country,” Dr. Word says. “It took a more senior physician, who had actually seen measles before, to see the child and confirm the diagnosis.”

Vaccination of young children is a success story in U.S. health care. As director of the infectious disease clinic at Texas Children’s Hospital, the largest pediatric hospital in America, Dr. Word is a leading advocate for immunization – and she knows the satisfaction of participating in the eradication of diseases. “A recent example is the bacteria *Haemophilus influenzae*, which at one time was the No. 1 cause of meningitis in children. The vaccine was introduced in 1987, and I have not seen a case in over five years,” says Dr. Word. “Like physicians who saw the introduction of the vaccines against polio and measles, I have now seen a disease eliminated during my lifetime. That is just amazing.”

Enormous challenges remain in infectious diseases. In less fortunate regions of the world, vaccines are not widely available. Even in the U.S., an estimated 35 million adolescents have slipped through the cracks of immunization efforts. And adults face disparities in their protection against influenza and pneumococcal disease. Some pathogens have so far eluded the development of safe, effective vaccines – AIDS, rotavirus, HPV and group B streptococcus are at the top of Dr. Word’s list. But



the pediatrician says what gives her hope is knowing that millions of children will not get measles, Hib or various other diseases because of innovative vaccines.

“I have now seen a disease eliminated during my lifetime. That is just amazing.”

Medical Background

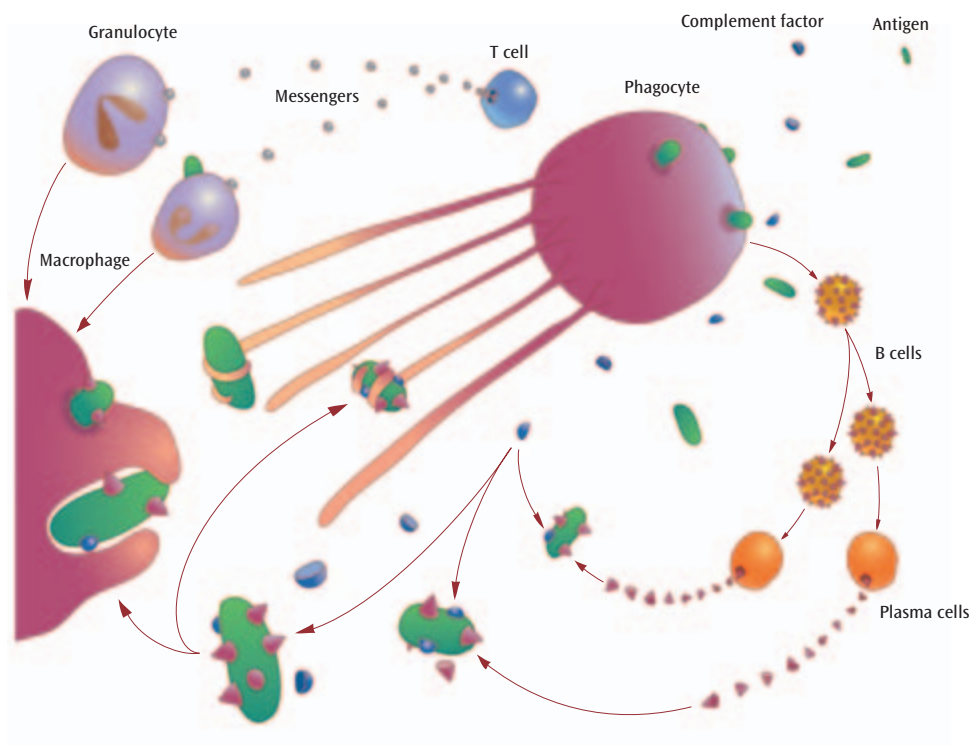
Immunization primes the body's own immune system to prevent diseases caused by specific viruses and bacteria. It helps the immune system to build its defenses against these organisms so that when an immunized person is exposed to the disease, the immune system can mobilize quickly and effectively to prevent infection.

Immunization works by exposing the body to vaccines, usually by injection. Vaccines contain tiny amounts of material that stimulate the immune system to produce antibodies and special cells aimed at a specific virus or bacteria. The immune system stores this information. Later, even many years later, when the immunized person is exposed to that virus or bacteria, the immune system remembers how to respond. It can then produce the appropriate antibodies and cells quickly and in large amounts. This prevents the virus or bacteria from becoming established in the body and causing infection.

There are several different types of vaccine. Some, such as measles, mumps and rubella, are live, attenuated vaccines which means the virus has been weakened so that it stimulates antibody production, but does not cause the disease. Others such as inactivated polio and influenza vaccines use an inactivated, or killed, virus that still triggers an immune response. Tetanus toxoid (TT), the vaccine that protects mothers and newborns from tetanus, is a detoxified version of the toxin (poison) that causes the disease. A fourth variety of vaccine, such as that for *Haemophilus influenzae* type b (Hib) and acellular pertussis, uses only the components of the virus or bacteria that provoke an immune response.

Vaccination is considered one of the most cost-effective and efficient ways to protect public health. Yet when adults are not properly immunized, they too run the risk of contracting and spreading vaccine-preventable diseases such as pertussis (whooping cough), tetanus, meningitis and influenza.

The microcosmos of the immune system



Phagocytes surround bacteria with their “tentacles” and ingest them. B cells – carrying antibodies on their surfaces – begin to divide and produce copies of themselves. Most develop into plasma cells that can create antibodies. The antibodies attach themselves to passing antigens. When they cling to a bacterium, they activate other immunological agents, so called complement factors. Phagocytes like macrophages or granulocytes are also activated by T cells, which send out messengers.

Aventis Human Vaccines



Pediatric combination vaccines

The components of these vaccines vary because of diverse immunization schedules throughout the world. Protecting against up to six diseases, this group of products is anchored by acellular pertussis components in general and by the trivalent vaccine *Daptacel* in particular. *Daptacel*, which also protects against diphtheria and tetanus, was launched in 2002 and has become a strong sales contributor due to its synergy with immunization schedules. *Pentacel*, a new vaccine against five diseases that has been a standard of preventive care in Canada since its launch in 1997, is registered in nine countries. *Tripedia*, also for the prevention of pertussis, diphtheria and tetanus, and *ActHib* for the prevention of *Haemophilus influenzae* type b, are two further important growth drivers within the pediatric product line. *Pediacel*, another acellular pertussis-based pentavalent vaccine, was registered in the UK in 2002 and is expected to be launched in this country and parts of Latin America and east Asia in 2004.

Influenza

With a 38% share of the €1.2 billion influenza vaccine market, Aventis is the world leader in the production and marketing of flu vaccines. Since 1998, sales of the flu vaccines *Fluzone* and *Vaxigrip/Mutagrip* have nearly tripled and production capacity was recently doubled to 165 million doses to better meet demand.

Polio

Aventis is the world's major manufacturer of inactivated polio vaccine (IPV), known as *IPOL* in the U.S. As the aim of global polio eradication approaches, the use of IPV vaccines will increase. As a result, Aventis Pasteur is expanding its production capacity to meet this growing demand. The worldwide polio eradication initiative of the WHO and UNICEF has positioned Aventis Pasteur as a global preferred partner with both oral polio vaccine and IPV vaccines.

Adult and adolescent boosters

The incidence of pertussis ("whooping cough") is on the rise globally, affecting both children and adults. Its resurgence, combined with an increased awareness of the dangers of vaccine-preventable diseases, have led to higher sales of this product group in recent years. We expect to submit *Adacel*, which will be the first

trivalent booster against diphtheria, tetanus and pertussis, for U.S. approval in 2004. This booster vaccine, which uses acellular pertussis technology, is already marketed in Canada and Germany.

Meningitis

Targeting meningococcal meningitis, arguably the most deadly form of meningitis, our product range includes a polysaccharide AC vaccine and the quadrivalent polysaccharide vaccine *Menomune*. Our new conjugate vaccine *Menactra*, which was submitted for U.S. approval in December 2003, is expected to offer a longer-lasting immune response against four serogroups (A/C/Y/W-135).

Travelers/endemic area

Offering the widest range of vaccines in the industry, Aventis Pasteur's product offering includes vaccines for typhoid, rabies, yellow fever, Japanese encephalitis and cholera.

Research and Development

Exploring New Frontiers in Vaccine Technology

Immunization is the global community's most effective way to prevent disease. With a wide range of vaccines protecting against 20 bacterial and viral diseases, Aventis Pasteur is on the front line in the battle to keep children and adults all over the world healthy and safe from some of the most life-threatening diseases. Every year, our vaccines protect more than 500 million people worldwide, a tremendous source of pride for us.



Gene protein analysis at Aventis Pasteur

The R&D efforts of our human vaccines unit are focused on building on existing core assets in pediatric combinations, adult boosters, meningitis and influenza vaccines as well as pursuing new targets against diseases such as Respiratory Syncytial Virus (RSV), dengue, SARS, HIV and cancer. Our pipeline is rich and diversified, both in terms of new agents as well as improvements to existing products.

At the end of 2003, we filed for regulatory approval in the U.S. for *Menactra*, a conjugate vaccine that protects against meningococcal disease in people aged 11 to 55. Submissions for children below the age of 11 will follow. In 2004, we plan to submit *Menactra* for ages 2-55 in Europe. Meningitis vaccines, which include our successful polysaccharide vaccine *Menomune*, are expected to become a significant growth contributor due to their anticipated future use in infants under age 2.

We also plan to submit *Adacel*, the first trivalent booster against diphtheria, tetanus and pertussis, for U.S. regulatory approval in 2004. This product

will play an important role in efforts to better control pertussis by not only preventing the disease in adolescents and adults, but thereby breaking the cycle of transmission impacting infants too young to be immunized or only partially vaccinated.

Longer term, we are working on a number of innovative projects. We are seeking to be the first to the market with a vaccine to fight Respiratory Syncytial Virus (RSV), which causes severe and sometimes fatal respiratory infections. This project is now in phase II. Currently in phase I, Aventis Pasteur is also working on a vaccine for dengue fever, targeted at high-risk areas such as Africa, Asia and Latin America as well as travelers to those regions.

In the area of therapeutic vaccines, we are exploring the combination of chemo- and active immunotherapy in the treatment of colorectal cancer and melanoma through synergies between the human vaccines and prescription drugs business.

Widely acknowledged as a pioneer in the field of Human Immunodeficiency Virus (HIV) vaccine development, we are exploring both prophylactic and therapeutic approaches to developing vaccines to combat HIV, the virus that causes AIDS. A phase III trial for a prophylactic vaccine in Thailand was launched in late 2003, while phase II trials are underway for a therapeutic vaccine. The U.S. government-sponsored Thailand study will run for five years and is the largest clinical trial of an HIV vaccine ever fielded. A prophylactic vaccine using the prime-boost approach, is the object of a partnership agreement with Merck & Co.

We are also at the forefront in the battle against the global threat of SARS. Using technology that we developed for our inactivated polio vaccine, in September we agreed to develop a SARS vaccine candidate in cooperation with the National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. National Institutes of Health (NIH).

Expert Opinion on Immunization

Carol Bellamy is Executive Director of the United Nations Children's Fund since 1995. The immunization of every child is one of her major priorities.



What role has immunization played in public health?

One hundred years ago, infectious diseases were the world's leading cause of death. Today, immunization is a global public health success story. In 1979, as a result of the first worldwide immunization campaign, smallpox was certified to be eradicated. In the 1980s, immunization coverage against diphtheria, pertussis and tetanus rose from less than 20% of the global population to more than 70%. In the 1990s, deaths from measles and tetanus sharply declined. Today, eradication of polio is just around the corner. Immunization has saved millions and has enabled others to lead longer, healthier lives.

What is the global situation?

The advances have not reached all parts of the globe equally. More than 30 million children in the world are unimmunized either because vaccines are unavailable, because health services are poorly provided or inaccessible, or because families are uninformed or misinformed about when and why to bring their children for immunization. In sub-Saharan Africa, only about 50% of children are immunized during their first year of life. In Eastern Europe and the Commonwealth of Independent States, immunization rates declined dramatically following the political and economic upheaval that accompanied independence from the Soviet Union. As a result, more than 2 million children die unnecessarily each year. The battle against infectious diseases must go on.

What is UNICEF doing in this respect?

The highest priority for UNICEF is "to ensure sustainable immunization services that regularly reach all children with all appropriate vaccines and vitamin A supplements, as part of the overall commitment to strengthen primary health care systems."

Child survival lies at the heart of everything UNICEF does and we believe every child has the right to grow to adulthood in health, peace and dignity. In 2002 more than half of our annual expenditure went to programs focused on child health and survival in the earliest years of life.

How will the situation develop in the coming years?

Advances in science and technology mean that vaccines against certain types of diarrhea and pneumonia will be available in the next five to seven years. Research is also under way on vaccines against HIV/AIDS and improved vaccines are being developed against other infectious diseases. Strengthening health systems now is essential to ensuring that all children can benefit from these new vaccines once they are approved for use.



CARDIOLOGY/THROMBOSIS

Georg Müller has helped patients through many emergencies, but the physically fit 52-year-old never expected an acute medical emergency to nearly take his own life. Georg Müller is a family physician in a village of 2000 near Wetzlar, Germany. Besides seeing dozens of patients a day, he practices emergency medicine by riding in an ambulance once a week. He works out. And he travels.

Georg Müller's trouble began on a weekend trip to a medical meeting in India: "On Thursday, we started from Frankfurt, and on Sunday I got back on a plane to Germany, to return to my patients by Monday." Each way, the physician folded his 1.96-meter (6 foot 5 inch) frame into an economy-class seat. Long flights are a risk factor for blood clots in the legs, or deep vein thrombosis, but the danger can attack stealthily. "After I came back, I was visiting a patient and had a little problem getting air. I thought I was just tired," Georg Müller says.

Three weeks later, he went to the Austrian Alps to go cycling with his teenage son. Overcome by fatigue, he had to turn back. Then, after a driving trip, "I started feeling very bad ... This time, I thought I was going to die, I was so short of breath." Finally he went to the hospital. Diagnosis: pulmonary embolism, an often-fatal condition in which blood clots enter the lungs and block arteries. Dangerously low on oxygen, he also had a dilated right ventricle in his heart. Georg Müller received the same urgent care he had often given others. Anticoagulant medication cleared up the clots, and the crisis passed. Now back to active practice, he spends free time boxing and riding his racing bike. "It is a medical miracle," he says, "that I am alive today."



"More people die from thrombosis after flying on airplanes than from any crash – my interest is to warn people to be safe."

Medical Background

Deep vein thrombosis (DVT) occurs when a blood clot develops in the deep veins of the legs. A blood clot in the deep veins poses the risk of detaching from the vessel wall and migrating towards the heart and entering the lungs. If the embolus gets lodged in a pulmonary artery or one of its branches, it can interrupt further blood flow and cut off oxygen supply to the body, leading to a life-threatening condition known as pulmonary embolism.

DVT/PE is often associated with

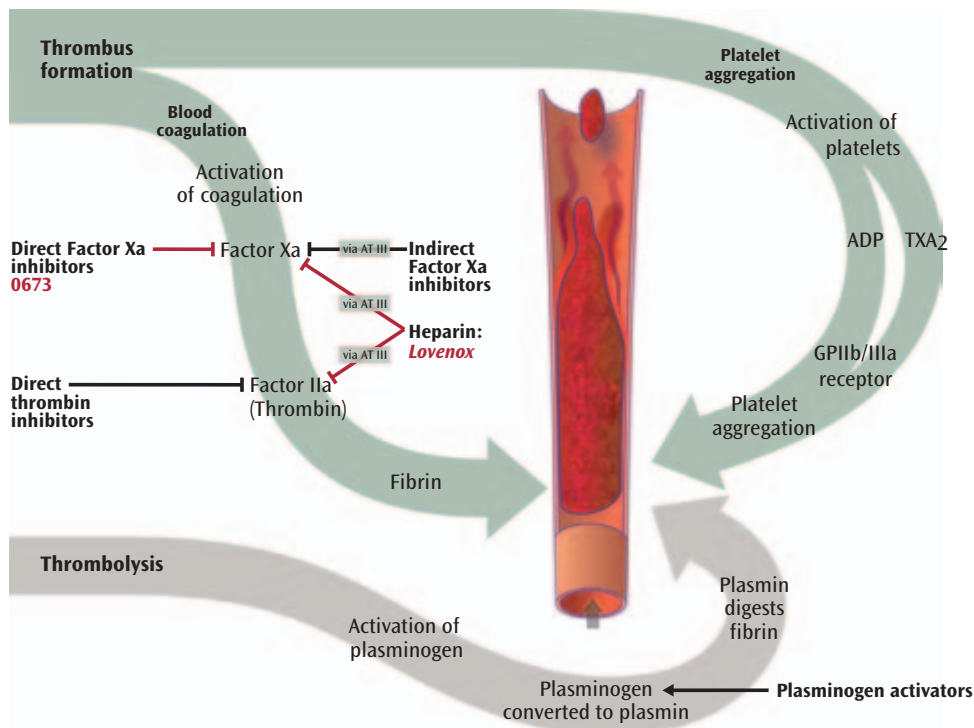
- Long periods of immobility
- Cancer
- Hypercoagulation, as a result of hereditary factors or illness
- Abdominal or orthopedic (knee, hip replacement) surgeries.

Deep vein thrombosis/pulmonary embolism (DVT/PE) is a major cause of morbidity and mortality in hospitalized patients. Failure to diagnose and administer prophylaxis for DVT/PE has made it the most common cause of unexpected death in hospitalized patients.

While DVT is preventable, it remains an underestimated, underdiagnosed and undertreated public health threat. One out of every 2000 adults is at risk of developing DVT; complications from DVT kill more people each year in the U.S. than AIDS and breast cancer combined.

Thrombosis can also occur in arteries. Acute coronary syndromes involve the formation of blood clots in the arteries that supply blood to the heart, leading to a reduction in the supply of oxygen to the heart. These conditions include unstable angina, non-Q-wave or non-ST-elevation myocardial infarctions and acute myocardial infarction (heart attack).

Aventis approaches to treat thrombosis



Thrombus formation is a hemostatic process in which blood coagulation and platelet aggregation are tightly interwoven to prevent major blood loss after injury. Endogenous thrombolysis limits this process to regions of vascular damage and dissolves the clot when wound healing begins.

Aventis Strategic Brands



Lovenox®
Enoxaparin sodium

CLEXANE®
Enoxaparin sodium



Delix®

TRITACE®
Ramipril

Lovenox/Clexane (enoxaparin sodium) is the most widely studied and used low-molecular-weight heparin (LMWH) in the world. It has been used to treat an estimated 118 million patients in 96 countries since it was first introduced in 1987 and is approved for more clinical indications than any other LMWH.

Approved indications

- Prophylaxis of deep vein thrombosis, which may lead to pulmonary embolism
 - in medical patients with severely restricted mobility during acute illness
 - in patients undergoing abdominal, hip or knee replacement surgery
- Prophylaxis of ischemic complications of unstable angina and non-Q-wave myocardial infarction, when concurrently administered with aspirin
- Treatment of acute deep vein thrombosis

Major markets

Lovenox/Clexane is a market leader in all major countries, including U.S., France, Germany, Italy, Spain and UK.

Product features

- Approved for more indications than any other anti-thrombin therapy
- *Lovenox/Clexane* with aspirin is more effective than and as safe as unfractionated heparin in reducing the incidence of death and myocardial infarction in patients with unstable angina (UA) and non-Q-wave myocardial infarction (NQMI)

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

Approved indications

- Treatment of mild to moderate essential hypertension
- Heart failure
- Post-myocardial infarction heart failure
- Nephroprotection
- Prevention of cardiovascular events in high-risk patients and people with diabetes

Major markets

Aventis sells *Delix/Tritace* in more than 70 countries, excluding Japan and the U.S. *Delix/Tritace* is a market leader in Canada, Germany, France, Spain and the UK. The U.S. rights were sold in 1998.

Product features

- *Delix/Tritace* is one of the best-selling ACE inhibitors outside the U.S. and Japan and is today recognized as a standard in cardiovascular prevention beside statins and acetylsalicylic acid
- *Delix/Tritace* is the only ACE inhibitor approved for the prevention of stroke, heart attack and cardiovascular death in people at high risk for cardiovascular events
- The results of the HOPE-TOO (HOPE – The Ongoing Outcomes) study presented in September 2003 showed that *Delix/Tritace* provided sustained prevention of cardiovascular disease, while also offering increased reductions over time in the risk of new onset of type II diabetes and new onset of heart failure

The Power of Evidence-Based Medicine

Having recently joined the elite club of blockbuster pharmaceutical products with sales of more than €1 billion, *Delix/Tritace* (ramipril), is a fine example of how clinical superiority is driving sales and market share growth. Now the leading angiotensin converting enzyme (ACE) inhibitor for the prevention and treatment of cardiovascular disease, *Delix/Tritace* has been going from strength to strength since that pivotal moment in 1999 when the results of a landmark study were published in the New England Journal of Medicine.

The results of the HOPE (Heart Outcomes Prevention Evaluation) study demonstrated a 22% reduction in the risk of cardiovascular deaths, myocardial infarction and stroke in at-risk patients. The findings were so remarkable that it was considered unethical to proceed with the placebo arm of the trial.

Since 1999, many countries have received regulatory approval for a new indication to support the use of *Delix/Tritace* not only for the treatment of hypertension but also for the prevention of cardiovascular events in patients at high risk. The efforts of the cross-functional MAX team to leverage the product's outstanding properties have been fundamental in helping *Delix/Tritace* achieve its vast potential. The performance of the drug in Canada, where it is sold under the brand name *Altace*, is a case in point.

By maximizing awareness of the HOPE trial and the importance of managing patients at increased risk of cardiovascular events, Canada successfully grew the ACE (inhibitor) prevention market and clearly positioned the product as the gold standard. *Delix/Tritace* moved from 9% market share in 1999 to 43% in 2003. Physicians in Canada now treat their patients earlier and more aggressively to prevent heart attacks, stroke and death, having moved treatment objectives from mere blood pressure control to prevention.

Delix/Tritace has become the market leader in its class and is today the most prescribed cardiovascular agent and the third most prescribed product in the Canadian pharmaceutical market. According

to the Canadian Diabetes Association's most recently issued guidelines, vascular protection through the use of an ACE inhibitor should be the first treatment goal in all patients with diabetes.

But the good news doesn't stop there. The results of a three-year follow-up study to HOPE, HOPE-TOO, have indicated the benefit of *Delix/Tritace* in the prevention of new onset of both heart failure and type 2 diabetes over time. Further studies to promote the superiority of *Delix/Tritace*, both as a single agent and in combination with other compounds, are currently underway.



The Aventis plant in Laval, Quebec, which produces all the *Altace* (*Delix/Tritace*) sold in Canada

In close partnership with Industrial Operations, the MAX team is now concentrating its efforts on lifecycle management and ways to maximize the return on investment from *Delix/Tritace*. With Aventis losing market exclusivity in some European countries in 2004, pursuing *Delix/Tritace* sales aggressively as well as identifying potential *Delix/Tritace*-based combination products will help secure a strong future for this life-saving therapy.

Expert Opinion on Cardiovascular Diseases

Salim Yusuf is director of cardiology at McMaster University, Hamilton, Ontario. Dr. Yusuf holds a research chair at the Heart and Stroke Foundation of Ontario and is a senior scientist of the Canadian Institutes of Health Research. His accolades include the 2001 Prix Galien Canada Research Award and the Lucian Award for Cardiovascular Research in 2002.



What is the status of the treatment and control of cardiovascular diseases today?

Our approach to understanding, preventing and treating cardiovascular disease, the world's leading cause of mortality with 8 - 10 million related deaths worldwide per year, has greatly changed over the last 50 years. While cardiovascular disease has decreased in the developed world, 80% of cardiovascular disease today occurs in developing countries. By 2020, 85 - 90% of cardiovascular disease cases will occur in the developing world.

Lifestyle changes in different parts of the world are a fundamental driver in the prevalence of cardiovascular diseases. The industrialization of poorer countries has led to a decrease in activity, and people are eating richer food and smoking more. This has led to an increase in obesity, high blood pressure and high lipids. Meanwhile, with many people in richer nations changing towards healthier lifestyles, the risk of cardiovascular disease is decreasing.

What important new developments in the field will we see looking ahead?

The next few decades will present some interesting challenges. Today there are a wide number of effective treatments for cardiovascular disease from ACE inhibitors and Beta blockers to simple aspirin. Going forward, we need to ask which combinations of the available therapies work best, and, most importantly, how cost effective they are. This will be the biggest challenge facing the pharmaceutical industry.

We will also need to concentrate our efforts on finding ways to reduce the care gap to ensure that proven treatments are used widely and appropriately.

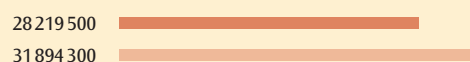
How far have we come in cardiovascular risk prevention?

As recently as the mid-1960s, there were no effective ways to treat cardiovascular disease. But over the last 40 years we have made tremendous progress, from controlling blood pressure to cholesterol lowering. Crucially, we are making headway towards preventing the onset of cardiovascular disease in younger segments of the population.

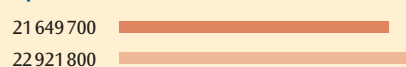
The main challenge we face today is that most of our efforts to treat cardiovascular disease are based on rearguard actions; they do not treat the root causes of the disease: obesity, high blood pressure and high lipids. We need to focus on preventing the spread of cardiovascular disease through societal policies to promote activity and a healthy diet and curb tobacco consumption and fatty foods.

Number of candidate events for DVT/PE prophylaxis

United States



Europe



Japan



Estimates for Europe cover France, Germany, Italy, Spain and the UK.
Source: Decision Resources, Inc. Waltham, MA.



RESPIRATORY/ALLERGIES

Michinari Teramae faces two opponents on the football field – the other team, and his allergies. He has learned how to win against both. Teramae plays American-style football as a defensive back on the Goyo-kensetsu Pirates. Fast-paced, physical and intense, American football has a small but enthusiastic following outside the U.S. In Japan, amateur teams in the top-level X league, including the Pirates, compete every bit as fervently as any American team. “The moment of winning a game is the most exciting,” says Teramae. “As a sales representative for an advertising agency, I work from morning till around 8 p.m. on weekdays. That is satisfying, but playing American football offers an excitement that work could never provide. My goal is to win the Japanese championship.”

But Teramae’s winning ambitions – at work and on the field – can be threatened by seasonal allergies, especially to cedar and Japanese cypress pollen. “When I wake up in the morning, I cannot stop sneezing. I work outside in the daytime, and when I come back to the office, I have a runny nose,” says Teramae. “As a sales representative, I meet my clients every day. With a runny nose and watery eyes, I am afraid I give a poor impression. And when I am out playing football, I cannot stop sneezing. My nose runs and my eyes fill with tears, so it is hard to concentrate. The medicine I used to take was not very effective, and it made me sleepy.” Teramae took his problem to the doctor, who prescribed a newer antihistamine that relieves symptoms without causing drowsiness. “I cannot even imagine my life without this,” Teramae says. “Pollen allergy is an irritating condition. Nothing is more im-

portant for me than controlling it.” Now the skilled defender stays on top of his game, regardless of the season.



“Pollen allergy is an irritating condition. Nothing is more important for me than controlling it.”

Medical Background

An allergy is an overreaction or hypersensitivity of the body's immune system to specific substances or allergens. These substances may include pollens, molds, house dust mites, animal dander and insect bites.

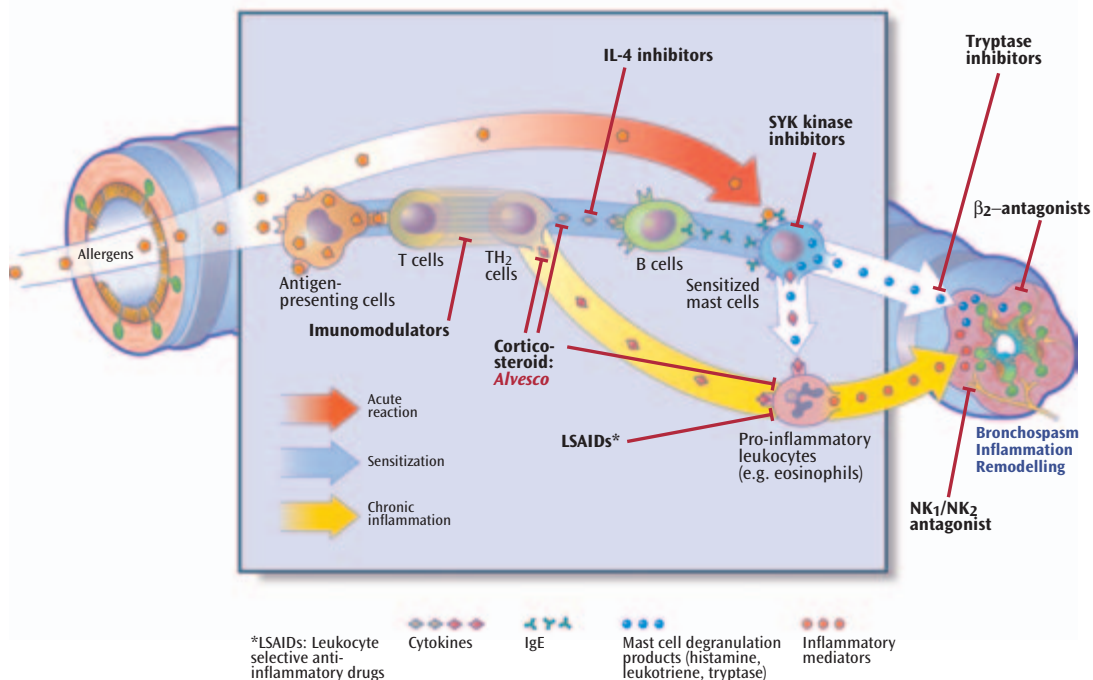
A healthy immune system fights illness by attacking harmful invaders, such as bacteria, viruses, and parasites. But in people with allergies, the immune system mistakes a harmless substance such as pollen or dust for a harmful substance it must destroy. When a person with allergies is exposed to a specific allergen, the immune system creates antibodies to fight the dangerous invader. The antibodies specifically associated with allergies are called IgE antibodies.

IgE stands for the substance immunoglobulin E, a protein in the immune system that acts like a

signal. IgE antibody is always specific for a particular allergen. IgE antibodies attach themselves to the allergen as well as two different types of cells: mast cells or basophils. Once this binding has occurred, chemicals including histamine are released, which may cause allergic symptoms such as inflammation in the nose and airways or elsewhere in the body. What began as an innocent case of mistaken identity is now an allergic reaction.

IgE antibodies may cause many kinds of allergic responses, from hives to allergic rhinitis (hay fever), asthma symptoms, or very severe allergic attacks called anaphylaxis. Symptoms commonly associated with allergies include: sneezing, stuffy or runny nose, coughing, watery or itchy eyes, itchy throat and nose, post-nasal drip, itchy skin or rash and hives.

Aventis approaches to treat asthma



The development of allergic disease and asthma involves first the process of sensitization to inhaled allergens. On re-exposure to the same allergens, an acute allergic response will develop, caused by degranulation of mast cells. The release of various cytokines from activated TH₂ cells and mast cells will also cause the recruitment of pro-inflammatory leukocytes to the airways and their local activation to produce inflammatory mediators leading to chronic inflammation.

Aventis Strategic Brands



allegra
fexofenadine

Telfast
fexofenadine



Nasacort AQ
(triamcinolone acetonide) Nasal Spray



Ketek
TELITHROMYCIN

Allegra/Telfast (fexofenadine), is an effective, long-lasting and powerful non-sedating prescription antihistamine for the treatment of seasonal allergic rhinitis (SAR or hay fever) and the skin condition chronic idiopathic urticaria (CIU or hives). Aventis also offers *Allegra-D*, a combination product with an extended release decongestant for effective non-drowsy relief of seasonal allergy symptoms, including nasal congestion.

Approved indications

- Relief of symptoms associated with seasonal allergic rhinitis (SAR) and chronic idiopathic urticaria (CIU) (hives/wheals)
- Treatment of itching associated with dermatological diseases (Japan)

Major markets

Allegra/Telfast is marketed in more than 55 countries worldwide, led by the U.S. and Japan.

Product features

- *Allegra/Telfast* offers rapid onset of action along with safe, effective and continuous relief throughout the recommended dosing period
- *Allegra/Telfast* has been clinically demonstrated to be non-sedating and non-impairing
- Excellent safety profile: The side-effect profile of *Allegra/Telfast* is similar to that of placebo in clinical trials

Nasacort AQ (triamcinolone acetonide) nasal Spray is an unscented, water-based metered-dose pump spray formulation containing a microcrystalline suspension of triamcinolone acetonide in an aqueous medium.

Approved indications

Nasacort AQ Nasal Spray is indicated for the treatment of the nasal symptoms of seasonal and perennial allergic rhinitis in adults and children six years of age and older.

Major markets

Nasacort AQ is available in 44 countries worldwide, and its most important markets are the U.S., France, Canada, Germany and Italy.

Product features

- Nondrowsy and nonhabit-forming
- Unscented, contains no alcohol
- Convenient once-daily dosing
- Preferred by patients 2 to 1 over competing products based on sensory attributes

Ketek (telithromycin) is an antibiotic designed to deliver an optimally targeted spectrum of activity for upper and lower respiratory tract infections (RTIs), including those caused by resistant pathogens – with less propensity to induce resistance – and a short treatment regimen.

Approved indications

- Community-acquired pneumonia (CAP), mild or moderate in patients 18 years and older
- Acute exacerbation of chronic bronchitis (AECB)
- Acute sinusitis
- Tonsillitis/pharyngitis
- Infections caused by erythromycin A- and penicillin-resistant pathogens (as evidenced by in vivo studies)

Major markets

Since its first approval in 2001, *Ketek* has been used to treat more than 5 million patients in 40 countries. In 2003, *Ketek* was approved in Turkey, Canada and Japan.

Product features

- World's first ketolide antibiotic
- Convenient and efficacious once-daily treatment regimen
- Excellent spectrum of activity, offering coverage against common and atypical respiratory pathogens
- Short-course therapy (5 days), except for community-acquired pneumonia (7-10 days)

Sales and Marketing

Turning Challenges Into Opportunities

An innovative product originating in Aventis laboratories, *Ketek* is the first of a new class of antibiotics called ketolides and a revolutionary new treatment for respiratory tract infections caused by pathogens that are becoming increasingly resistant to older antibiotics. On the market since 2001, *Ketek* has been a classic example of overcoming the hurdles of introducing a global product locally.

The *Ketek* story started back in 1987 when it was developed by researchers in France. Clinical trials were conducted in the late 1990s and EU approval



Coated *Ketek* tablets, produced at Aventis in Kansas City, U.S.

was granted in 2001. Germany was the first country to launch in 2001, followed by Italy, Spain, France and Latin America in 2002. In 2003, further important *Ketek* approvals were granted in Turkey, Canada and Japan. To date, *Ketek* has been used to treat over 5 million people in nearly 40 countries. The product's performance in France, Mexico, Belgium, Greece, Turkey and Finland has earned it the status of being the most successful new antibiotic launch in these countries, an achievement that would not have been possible without the concerted efforts of the team behind *Ketek*.

Thinking globally while acting locally

Preparing to launch *Ketek* in France, Europe's largest antibiotic market, the *Ketek* team saw challenges mounting. New government regulations were en-

couraging the use of generic products and a government-sponsored public education campaign advocated more judicious use of antibiotics.

The *Ketek* team addressed concerns about appropriate antibiotic use very directly, positioning *Ketek* consistently during pre-launch and launch as the ideal first-line choice and a solution designed to tackle the growing problem of resistance in common respiratory infections without contributing to the problem of future resistance. Market share increased quickly and *Ketek* became France's most successful antibiotic launch. The same strategy has produced positive results in other markets.

The approval of *Ketek* in Japan, the world's second-largest antibiotic market, represented another important milestone for the *Ketek* team. With national standards making the development of special 300 mg tablet necessary, experts in the various countries pooled their experience and knowledge to meet the challenge and deliver the highest standards of quality. In December, only two months after approval, *Ketek* was launched on behalf of Aventis by Sankyo and Fujisawa.

Next in line for approval is the United States. Having recently submitted a complete response to a second approvable letter from the FDA, the *Ketek* team is preparing the groundwork for a successful launch in the second half of 2004.

The importance of networking

Winning approval and preparing national launches for a new drug class requires exceptional planning and regular optimization. As a global product, *Ketek* has generated important insights into the value of leveraging early launch lessons to ensure and enhance the success of subsequent launches. The engagement, commitment and cooperation of the entire *Ketek* team are certain to ensure the drug's future success on the world market.

Expert Opinion on Infectious Diseases

John G. Bartlett is Professor of Medicine and Chief of the Division of Infectious Diseases at Johns Hopkins University School of Medicine. With special interests including HIV and anaerobic infections, Dr. Bartlett has served on the editorial boards of professional journals since the 1970s as well as many AIDS-related committees at state and national levels.



What is the current status in the treatment and control of bacterial infections?

The three most common respiratory infections – sinusitis, pneumonia and middle-ear infections – account for 75% of all outpatient antibiotic prescriptions. But the trouble with bugs is that it's very hard to know where they will land. Diseases can explode out of nowhere, occurring both inside and outside of hospitals. So far, we've more or less been able to keep up with infectious diseases. However, bacteria constantly develop resistance to antibiotics and it's impossible to predict when resistance will occur.

So our greatest concern right now is the availability of new antibiotics to combat diseases as they appear or develop increased resistance to existing treatments. Additionally, we would also benefit from more treatments for SARS, influenza and other viral – as opposed to bacterial – diseases.

What is your view on the new class of antibiotics known as “ketolides”?

Any new class of antibiotics that helps solve the problem of resistance is welcome. The good safety profile and oral delivery of these drugs make them especially practical, which would not be the case if we had to inject them or if they had bad side-effects.

How would you assess the chances of therapeutic progress in this field?

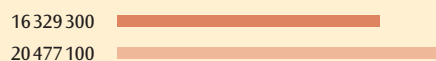
The rate at which bacteria will develop resistance to antibiotics will increase. But the pipeline is drying up because pharmaceutical companies are not developing as many new antibiotics as previously. Existing drugs like *Ketek*, for example, are very effective in the fight against bugs, but new, useful treatments are becoming increasingly scarce.

Looking ahead, pharmaceutical companies are likely to focus on developing anti-infectives for illnesses such as Hepatitis and HIV. Drugs for these diseases are potentially more profitable because patients take them over the course of many years, whereas minor infections can generally be cured within a week of antibiotic treatment.

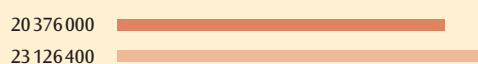
It's hard to persuade drug companies to develop antibiotics. The mechanisms we have in place to guarantee the safety of drugs are arduous and expensive; it currently costs \$ 800 million to get a drug to the market. With that level of investment, developing a cholesterol-lowering drug seems more attractive than working on an antibiotic for sinusitis.

Number of total incident episodes of acute exacerbations of chronic bronchitis

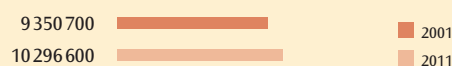
United States



Europe



Japan



Estimates for Europe cover France, Germany, Italy, Spain and the UK.
Source: Decision Resources, Inc. Waltham, MA.

Other Aventis Strategic Brands

Apart from our leading brands for the therapeutic areas of diabetes, oncology, cardiovascular diseases, respiratory/allergies and human vaccines, we

also market five additional products belonging to the group of products that we refer to as strategic brands.



Actonel (risedronate) is a third-generation bisphosphonate that prevents bone loss by inhibiting bone resorption.

Approved indications

- Treatment and prevention of postmenopausal osteoporosis (PMO) and glucocorticoid-induced osteoporosis
- Treatment of Paget's disease

Major markets

Actonel is co-marketed by Procter & Gamble Pharmaceuticals and Aventis in Europe, the U.S. and Canada through the Alliance for Better Bone Health. In Japan, we market *Actonel* under a license from Ajinomoto. We market *Actonel* in other parts of the world under a license agreement with Procter & Gamble Pharmaceuticals. *Actonel* once-a-day (5 mg) is currently approved in 82 countries and the new once-weekly formulation (35 mg) has been approved in 68 countries.

Product features

- The only bisphosphonate to offer rapid and sustained vertebral and non-vertebral fracture protection
- Helps preserve bone microarchitecture
- Excellent gastrointestinal tolerability
- Available in 5 mg daily and 35 mg weekly dosage forms

Arava (leflunomide) is an oral disease-modifying anti-rheumatic drug (DMARD) for use in both early and established rheumatoid arthritis.

Approved indications

- Treatment of active rheumatoid arthritis in adults to reduce signs and symptoms and to inhibit structural damage
- Improvement of physical function in adults with active rheumatoid arthritis

Major markets

Arava is currently available in over 70 countries worldwide, following its U.S. launch in 1998 and European launch in 1999.

Product features

- Effectively reduces the signs and symptoms of rheumatoid arthritis and has been shown to slow down progression of the disease
- Significantly improves patient's functional abilities
- Demonstrates an early and sustained response and is a once-daily oral medicine



TARGOCID[®] IM/IV
[teicoplanin]



TAVANIC[®]
Levofloxacin



COPAXONE[®]
Glatirameracetat

Targocid (teicoplanin) is a consistent and reliable agent that targets the growing problem of hospital-based infections.

Approved indications

Potentially serious infections caused by susceptible Gram-positive bacteria, including those resistant to other antibiotics such as penicillins and cephalosporins.

Major markets

Targocid is available throughout Europe, Asia and Latin America. Aventis does not sell this product in the U.S.

Product features

- *Targocid* is useful in the therapy of serious staphylococcal infections in patients who cannot receive or who have failed to respond to the penicillins and cephalosporins, or who have infections with staphylococci resistant to other antibiotics
- Effective in range of infections, including skin and soft tissue infections, urinary tract infections, lower respiratory tract infections, joint and bone infections and septicaemia

Tavanic (levofloxacin) is a broad-spectrum fluoroquinolone antibiotic.

Approved indications

- Community-acquired pneumonia (CAP)
- Acute exacerbations of chronic bronchitis (AECB)
- Acute sinusitis
- Complicated urinary tract infections
- Skin and soft-tissue infections (STI)

Major markets

Aventis sells this drug, which is licensed from Daiichi, mainly in Europe, the Middle East, Africa and Latin America. We do not sell this drug in the U.S. or Japan.

Product features

- Once-daily dosing
- Good efficacy against Gram-positive pathogens, particularly *S. pneumoniae*, while maintaining good Gram-negative and atypical coverage
- Excellent risk-/benefit profile

Copaxone (glatiramer acetate) is a non-interferon, disease-modifying therapy for patients with relapsing-remitting multiple sclerosis.

Approved indications

First-line treatment for the reduction in frequency of relapses in patients with relapsing-remitting multiple sclerosis.

Major markets

Copaxone is approved in 42 countries worldwide, including the U.S., Canada, Australia, Israel and all the European countries. In Europe, *Copaxone* is marketed by Teva Pharmaceutical Industries Ltd., and Aventis. In North America, *Copaxone* is marketed by Teva Neuroscience.

Product features

- First non-interferon agent for MS
- Only MS drug that delivers sustained efficacy and good tolerability
- Ten-year MS trial shows that patients treated with *Copaxone* have an unchanged or improved condition

Pipeline Overview

Preparing to Deliver a New Wave of Innovation

During 2003, the efforts of our research organization to enhance innovation and productivity made substantial progress. We moved four compounds from early-stage to late-stage development and strengthened our highly promising early-stage pipeline. We now have more than 30 human drug and vaccine candidates in pre-clinical, over 40 in early-stage and 14 in late-stage development. At the same time, we submitted five new products for regulatory approval, and expanded the range of indications for many of our strategic brands through broad life-cycle management programs.

Through a well-defined disease area strategy, we intend to maintain and expand our leadership position in diabetes, oncology, thrombosis, human vaccines and other select key therapeutic areas.

Consequently, we are channelling our research and development investments, which totaled €2863 million in 2003, into promising in-house projects and attractive in-licensing opportunities in disease areas with significant unmet medical needs and thus opportunities for strong and sustainable growth.

In 2003, we added several promising drug candidates to our pipeline, including AVE-0010, a GLP-1 (glucagon-like peptide-1) receptor agonist of the exendin class from Zealand Pharma, the Vascular Endothelial Growth Factor (VEGF) Trap, an anti-angiogenesis compound from Regeneron, and AVE-3933, an antidementia agent in-licensed from Dainippon. We also entered into a collaboration agreement with ImmunoGen to discover, develop and commercialize novel antibody-based anti-cancer products.

Key Compounds in Late-Stage Clinical Development

PROJECT ⁽¹⁾	DISEASE	STATUS
<i>Alvesco</i> ⁽²⁾ (U.S.)	Asthma	Submitted
<i>Apidra</i>	Type 1 and 2 diabetes	Submitted
<i>Genasense</i> ⁽³⁾	Malignant melanoma	Submitted
<i>Ketek</i>	Respiratory tract infections	Submitted ⁽⁴⁾
<i>Menactra</i>	Meningitis (vaccine)	Submitted
<i>Sculptra</i>	Facial lipoatrophy	Submitted
<i>Adacel</i> (U.S.)	Booster vaccine for adults and adolescents	Phase III
<i>Exubera</i> ⁽⁵⁾	Type 1 and 2 diabetes	Phase III
<i>Pentacel</i> (U.S.)	Pediatric combination vaccine	Phase III
Teriflunomide	Multiple sclerosis	Phase III
109,881	Cancer	Phase III
0673 (Factor Xa inhibitor)	Acute coronary syndrome	Phase IIb
100,907	Sleep disturbance	Phase IIb
Pralnacasan (on hold)	Rheumatoid arthritis	Phase IIb

(1) New chemical/biological entities (NCE/NBE) only

(2) Cooperation with ALTANA Pharma

(3) Cooperation with Genta Inc.

(4) In response to the second FDA approvable letter of January 2003,

Ketek is approved in Europe, Canada, Japan, Latin America

(5) Cooperation with Pfizer

Key Regulatory Achievements in 2003/4

PRODUCT	INDICATION	ACHIEVEMENTS
<i>Allegra</i> (LE)	Pediatric exclusivity	Approved in the U.S. (Jan. 2003)
<i>Allegra</i> (LE)	Pediatric tablets	Approved in the UK (EU-RMS) (April 2003)
<i>Allegra-D</i> (LE)	Once-daily administration	Submitted in the U.S. (Dec. 2003)
<i>ActHib</i>	Hib meningitis vaccine	Submitted in Japan (March 2003)
<i>Alvesco</i> (NCE)	Asthma	Submitted in the U.S. (Dec. 2003)
<i>Apidra</i> (NCE)	Diabetes	Submitted in the U.S. and the EU (June 2003)
<i>Arava</i> (LE)	Rheumatoid arthritis – improvement of physical function	Approved in the U.S. (May 2003)
<i>Arava</i> (NCE)	Rheumatoid arthritis	Approved in Japan (April 2003)
<i>Genasense</i>	Malignant melanoma	Submitted in the U.S. (Dec. 2003)
<i>Ketek</i> (NCE)	Respiratory tract infections	Approved in Japan (Oct. 2003)
<i>Ketek</i> (NCE)	Respiratory tract infections	Response to 2 nd FDA approvable letter submitted in the U.S. (Oct. 2003)
<i>Lantus</i> (NCE)	Diabetes	Approved in Japan (Oct. 2003)
<i>Lantus</i> (LE)	Flexible dosing	Approved in the U.S. (May 2003)
<i>Lantus</i> (LE)	Pediatrics	Approved in the EU (March 2003)
<i>Lovenox</i> (LE)	300 mg multidose vial	Approved in the U.S. (Jan. 2003)
<i>Menactra</i>	Meningococcal meningitis (A,C, Y and W-135)	Submitted in the U.S. (Dec. 2003)
<i>Sculptra</i>	Facial lipoatrophy	Submitted in the U.S. (Dec. 2003)
<i>Targocid</i> (LE)	Pediatrics	Approved in Japan (Jan. 2003)
<i>Tavanic</i> (LE)	Prostatitis	Submitted in the UK (EU-RMS) (May 2003)
<i>Tavanic</i> (LE)	Uncomplicated urinary tract infections	Approved in the UK (EU-RMS) (May 2003)
<i>Taxotere</i> (LE)	1 st line NSCLC	Approved in the EU (Jan. 2003)
<i>Taxotere</i> (LE)	Hormone-refractory prostate cancer	Submitted in the U.S. (Jan. 2004) and the EU (Feb. 2004)
<i>Taxotere</i> (LE)	Esophageal cancer	Approved in Japan (Jan. 2004)
<i>Taxotere</i> (LE)	Endometrial cancer	Submitted in Japan (Nov. 2003)

EU-RMS = European Union Reference Member State
for Mutual Recognition Procedure

NCE = New Chemical Entity

LE = Line Extension

NSCLC = Non-small-cell lung cancer

Achieving Alignment with Business Goals: Focus on Performance and Talent Management

Having the right people in the right positions at the right time is crucial to the success of a global company. In order to ensure that Aventis has the best teams in place to meet the challenges of a changing industry environment, we are focusing on attracting, developing and retaining top talent and building a high-performance culture. In 2003, we drove these efforts much further into the organization by aligning performance more closely with company objectives and enriching and deepening the talent pipeline with a steady flow of potential future leaders.

In 2003, we made significant progress in establishing common processes and criteria for talent management, thus ensuring consistency of assessment and the availability of a global talent pool. Through international and cross-functional moves, we want to increase the early identification and development of high-potential and top-performing employees. At the same time, we are encouraging our managers to sharpen their leadership and business skills through global development programs. To strengthen the link between talent and performance management, we are continuing to refine grading and reward systems that address technical careers and cross-functional positions.

Promoting a high-performance culture

The performance of Aventis is a direct reflection of the abilities, achievements and ambition of our employees. Rewarding and recognizing dedicated people who contribute decisively to company goals is therefore a key objective. To underscore the impor-

tance of achieving alignment of individual employee performance with business goals, we are promoting a pay-for-performance approach based on differentiation at all levels. We want to reward those people who perform to the highest standards. As a key element of performance management, the SMART goal-setting process is being used to review and measure progress on a quarterly basis and to determine the individual performance component of the annual bonus of more than 10 000 managers company-wide.

Offering employees the opportunity to acquire company shares at preferred conditions has become part of our corporate culture. In 2003, 6 523 employees in 55 countries purchased Aventis shares through the third Horizon stock purchase plan. By promoting employee stock ownership, we want to increase motivation and loyalty among our people. Our annual stock option grants for eligible senior executives are another important tool to motivate and retain key talent and align them with the long-term goals of the company.

Investing in people

An innovation-driven company relies on the expertise and the leadership qualities of its people. Through effective career path planning and leadership development programs, we want to motivate and train promising young managers to become business leaders.

To retain top scientific and technical talent and to enable employees to continue to advance their career at Aventis, whether they follow the managerial or scientific-technical career paths, Aventis has introduced the Dual Career Ladder. In 2003, this new career management system was successfully rolled out in the U.S. and Japan for scientific-technical employees in our Drug Innovation & Approval organization. It will be rolled out in France and Germany beginning in 2004, making it a fully global career management program.

The first Global Business Leader program was conducted with the Wharton-INSEAD Alliance. The

Employees by Region

	2003	2002
Europe	39 443	40 297
North America	18 046	19 495
Asia-Pacific	9 938	9 780
Central/South America	5 214	5 509
Africa/Middle East	2 926	3 018
Total	75 567	78 099



Ute Herzog,
Corporate Human
Resources, and
Stéphanie Camus,
Corporate
Communications

program is designed to enable Aventis managers around the world to improve their strategy execution capabilities through leadership. Senior Aventis executives co-teach cases, share business experiences, and link learnings with real-world business scenarios.

To build a culture of coaching and mentoring within Aventis, the Leadership Development Network was successfully implemented worldwide for our top talent in 2003. This tool provides rigorous individual leadership assessment, development and

networking opportunities for future business leaders, and it institutionalizes good coaching skills in the Aventis culture.

Furthering open and transparent leadership communication

In order to promote transparency throughout the organization and help employees better understand and execute the Aventis strategy and business priorities, high importance is attached to proactive and open leadership communication. Besides global online communication activities, employees are given many opportunities to meet face-to-face with management. In 2003, members of the Management Board participated in over 50 management/ townhall meetings around the world to discuss the Aventis strategy and key business issues as well as address employee questions.

At European level, regular meetings with the European works council promote a social dialogue and the exchange of information between employee representatives and management.

Employees by Function

	2003	2002
Sales & Marketing	34 105	34 559
Production & Manufacturing	24 180	25 226
Research & Development	6 956	6 923
Corporate & IT	3 557	3 516
Total Prescription Drugs & Human Vaccines	68 798	70 224
Other Core Business	372	511
Total Core Business	69 170	70 735
Non-Core Business	6 397 ⁽¹⁾	7 364 ⁽¹⁾
Total	75 567	78 099

(1) mainly Aventis Behring

Sustainable Healthcare

Rising to the Challenge: Sustainable Healthcare in Practice

As one of the world's leading global pharmaceutical companies, our business objective is to discover, develop, manufacture and commercialize innovative pharmaceuticals and human vaccines that satisfy unmet medical needs in large patient populations. Yet this objective also poses a tremendous responsibility to conduct our operations in a manner that is responsible, equitable and acceptable to both the company and society.

In order to better understand and manage these expectations and the impact of our activities on society, we are deepening our commitment to Sustainable Healthcare. This means strengthening our efforts to promote access to healthcare, finding new ways to balance the short- and long-term interests of our stakeholders, and walking the talk

when it comes to the ethical and technological issues confronting our industry. To meet the business challenge of Sustainable Healthcare, in 2003 we took concerted action to engage our key stakeholders along the pharmaceutical value chain.

Improving access to healthcare through public-private partnerships

Around the world, people rely on access to effective medicines. Yet often there is a gap between demand and ability to access life-saving treatments. To help close this gap, Aventis is partnering with institutions and non-governmental organizations. In the second year of our five-year partnership with WHO to combat sleeping sickness in sub-Saharan



Africa, we supplied 60 000 vials of effornithine, 100 000 vials of melarsoprol and 100 000 vials of pentamidine. Through the Aventis Foundation, we are working with the Nelson Mandela Foundation to combat tuberculosis in South Africa. Our human vaccines business continues to play a pivotal role in the Global Polio Eradication Initiative and has reinforced its commitment to strengthening vaccination systems in developing countries through EPIVAC.

Pharma scenarios and the business case for sustainable healthcare

The pharmaceutical industry is facing a set of issues that have the potential to significantly alter the current business model. It is thus essential to anticipate key future developments through a strong, flexible and durable policy framework. With this aim in mind, in 2003 we advanced the “Pharma Scenarios for Sustainable Healthcare” project. By describing the landscape in which future challenges, dilemmas and opportunities could play themselves out, the project aims to facilitate new ways of looking at established paradigms and develop strategies to position the company for a sustainable future.

Addressing sustainability issues

With a view to both effectively managing and shaping business-critical topics, we actively participate in industry and political dialogues. In 2003, company experts continued to work closely with patient groups, legislators and non-governmental organizations on issues such as timely and equitable access to products and information for patients, restoring the competitiveness of the research-based pharmaceutical industry in Europe and intellectual property protection.

To track and report annual progress on our environment, health and safety Journey to EHS Excellence, an annual scorecard was introduced in 2003.



Vaccination session at the Nanoro village health district medical center, Burkina Faso

Every quarter, the scorecard reflects the progress of each business function in achieving their annual goals. To further develop and strengthen an EHS culture throughout Aventis, EHS leadership training was introduced for line management and global programs to improve safety performance across all functions were launched.

Triple bottom-line reporting

Sustainability reporting took on a new level of importance at Aventis in 2003 with the publication and third-party verification of the first Aventis Sustainability Report. Previously limited to environment, health and safety variables, sustainability reporting now also encompasses detailed accounts of the company's social performance. Socially responsible investors are increasingly integrating values and societal concerns with investment decisions, and assessing companies according to the social and environmental dimensions of their business performance.

For more information, please visit the Sustainability Forum at www.aventis.com/sustainability and access a copy of the Aventis Sustainability Report for 2003.

Key Financials for 2003

Driving Profitability through Sales Growth and Enhanced Operational Effectiveness

In a challenging economic and political environment, we are striving for sustainable growth driven by our marketed products, our products in development in key therapeutic areas, and by enhanced operational effectiveness. We are thus focusing our efforts on our strategic brands in order to maximize their commercial potential and to optimize our product mix. Additionally, we are expanding our sales base in the U.S. Our research activities are focused on selected disease areas for which we anticipate strong growth potential and aim to maintain or achieve sustainable leadership positions in these franchises.

Our core business comprises activities that we consider to be strategic to the Group's pharmaceutical operations and intend to retain:

- Prescription drugs
- Human vaccines
- Our 50% equity interest in Merial (animal health); accounted for under the equity method
- Corporate activities (mainly insurance entities)

In 2003, consolidated net sales decreased 13.6% to €17 815 million from €20 622 million in 2002, due mainly to the divestitures of Aventis Animal

Aventis Group – Statements of Operations

(in € million, except per share information in €)

	2003	2002
Net sales	17 815	20 622
Co-promotion income	252	161
Production costs and expenses	(5 377)	(6 578)
Selling, general and administrative expenses and other operating income (expenses)	(5 365)	(6 866)
Research and development	(2 924)	(3 420)
Restructuring expenses	(251)	(68)
Goodwill amortization	(480)	(1 021)
Operating income (loss)	3 670	2 830
Equity in earnings of affiliated companies	(107)	51
Interest (expense) income – net	(151)	(309)
Miscellaneous non-operating income and expenses – net	(501)	1 120
Income (loss) before taxes and minority interests	2 911	3 692
Provision for income taxes	(929)	(1 430)
Minority interests in net income of consolidated subsidiaries	(29)	(86)
Preferred remuneration	(52)	(85)
Net income (loss)	1 901	2 091
Average number of shares outstanding (in million shares)	786	793
Basic earnings (loss) per share in €	2.42	2.64
Basic earnings (loss) before goodwill amortization per share in €⁽¹⁾	3.03	3.92
Operating income and equity in earnings of affiliated companies before goodwill amortization⁽¹⁾	4 044	3 901

(1) These columns and lines are unaudited and non-GAAP financial measures.

Nutrition and Aventis CropScience in 2002. In addition, sales were negatively impacted by currency translation, which reduced reported net sales by approximately 9.4%, principally due to the decline of the U.S. dollar and of Latin American currencies relative to the euro.

The ongoing strong performance of strategic brands and vaccines were the primary drivers of the core business sales performance in 2003. Sales of strategic brands (brand-name pharmaceuticals that we believe have significant commercial potential and on which we focus our marketing efforts) and human vaccines totaled €10851 million, a 17.0%

activity increase compared to €10448 million in 2002 and accounted for 64.6% of total core business sales in 2003 compared to 59.4% in 2002.

Four of the strategic brands – *Allegra/Telfast*, *Lovenox/Clexane*, *Taxotere*, and *Delix/Tritace* – generated sales of more than €1 billion each in 2003, meaning that they are considered “blockbuster drugs” by industry standards. *Delix/Tritace* reached this level of sales for the first time in 2003.

Allegra/Telfast sales increased 1.1% on an activity basis, mainly driven by the good performance in Japan. Sales growth in the U.S. was essentially flat, primarily as a result of the market entry of new

Aventis Group – Balance Sheet

(in € million)

	2003	2002
Marketable securities, short-term deposits, cash	1 125	1 299
Other current assets	7 469	8 347
Assets held for sale	1 182	-
Investments and other assets	4 763	5 828
Property, plant and equipment	4 130	4 455
Intangible assets	9 608	11 144
Total assets	28 277	31 073
Current liabilities	6 839	7 513
Liabilities held for sale	391	-
Long-term liabilities	5 361	7 225
Debt	5 085	4 752
Minority interests	167	159
Amortizable preferred securities	-	89
Stockholders' equity	10 434	11 335
Total liabilities	28 277	31 073

over-the-counter (OTC) branded and generic loratadine (*Claritin*) allergy products since *Claritin* became an OTC product in November 2002, and a weak spring allergy season. *Allegra/Telfast* sales in Japan were driven by growth in allergic rhinitis and skin disease, resulting from focused sales force and professional education efforts aimed at enhancing brand credibility with physicians.

Global sales of *Lovenox/Clexane* grew 21.3% on an activity basis due to strong sales performance in the U.S. and Europe. *Lovenox/Clexane* remains the market leader in terms of sales value in each of the major European markets, achieving double-digit growth in 2003 and continuing to expand sales in the open care segment.

Taxotere sales grew 22.5% on an activity basis. This was due to strong performance in all markets, spearheaded by the U.S., where sales benefited from increased usage in metastatic breast cancer and first-line non-small-cell lung cancer (NSCLC). *Taxotere* sales in Germany were supported by the launch in first-line NSCLC and by increased sales force focus through our establishment of separate oncology sales lines and optimized customer targeting and segmentation. More than 250 abstracts on *Taxotere* presented at the 39th American Society of Clinical Oncology (ASCO) in June 2003 increased awareness of *Taxotere* within the medical community.

Delix/Tritace sales grew 20.6% on an activity basis to €1 066 million, achieving blockbuster status for the first time. *Delix/Tritace* outperformed all competing ACE inhibitors in terms of sales volume, growing by 24% in total prescriptions worldwide (excluding the U.S. and Japan) during the 12 month period from Q4 2002 through Q3 2003. Market share for *Delix/Tritace* increased in all key segments with particularly strong growth in diabetes and cardiovascular risk. Sales growth was primarily driven by strong performance in the UK, Canada and France. A key factor in the global sales growth of *Delix/Tritace* in 2003 was increased use of *Delix/Tritace* 10 mg, based on the clinical findings of the MITRA PLUS and HOPE studies that demonstrated its superiority over other ACE inhibitors.

Lantus sales rose 87.1% on an activity basis. This steep increase is the result of the successful global rollout with over 40 additional countries having launched *Lantus* in 2003. In the U.S., *Lantus* gained market share against major competitors and became the best-selling branded insulin in 2003 (IMS Health). In the UK, the introduction of *Lantus* in August 2002 was one of the most successful launches of any new prescription medicine. In Germany, *Lantus* became the best-selling branded analogue insulin in 2003 (IMS Health). In France, *Lantus* was launched in August 2003 and achieved a 7% monthly market share based on October sales. In Japan, *Lantus* was launched in December.

Ketek sales reached €115 million in 2003 as compared to €52 million in 2002. Since its first launch in October 2001, *Ketek* has been introduced in all major EU, Latin American and Middle-East markets. It was launched in Japan in December 2003.

Actonel generated combined sales of €766 million for Aventis and Procter & Gamble Pharmaceuticals in 2003 compared to €539 million in 2002. As per our alliance agreement with Procter & Gamble Pharmaceuticals, Aventis consolidates only part of the combined worldwide sales. *Actonel* sales were driven by the product's established benefits in offering both fast and sustained fracture reduction and by the new, convenient once-weekly formulation *Actonel* 35 mg, which has already been approved in 68 countries and launched in 58 of these.

Human Vaccines contributed €1 621 million to our consolidated sales in 2003, an activity increase of 16.6% from sales of €1 580 million in 2002. Human vaccines sales were mainly driven by strong growth in the U.S. and by the good performance of pediatric combination vaccines, influenza vaccines, and adult boosters, partially offset by declining sales of polio vaccines in the U.S.

In Europe, our human vaccines business is conducted by Aventis Pasteur MSD, a 50-50 joint venture between Aventis Pasteur and Merck & Co. Aventis Pasteur MSD, which we account for using the equity method, generated sales of €591 million in 2003 compared to €577 million in 2002.

Net Sales by Business ⁽¹⁾

(in € million, except percentages)

	2003	%	2002	%
Core business (total) ⁽²⁾	16 791	94	17 591	85
- Prescription Drugs	15 190	85	16 026	78
- Human Vaccines	1 621	9	1 580	8
- Eliminations	(20)		(16)	
Non-core business (total)	1 046	6	3 066	15
- CropScience			1 831	9
- Others	38	0	167	1
- Therapeutic Proteins	1 008	6	1 068	5
Eliminations (intragroup) ⁽³⁾	(22)		(35)	
Aventis (total)	17 815	100	20 622	100

Operating Income (Loss) by Business ⁽¹⁾

(in € million)

	2003	2002
Core business (total) ⁽²⁾	3 920	3 754
- Prescription Drugs	3 313	3 202
- Human Vaccines	465	444
- Corporate & Animal Health	141	108
Non-core business	(249)	(924)
Aventis (total)	3 670	2 830

(1) Unaudited

(2) Consists of our "Prescription Drugs", "Human Vaccines" and "Corporate" segments. Merial sales and operating income are not reflected since Merial is accounted for using the equity method.

(3) Elimination of sales between core and non-core businesses.

In the **United States**, the world's largest pharmaceutical market, sales increased 11.1% on an activity basis, driven by the ongoing strong performance of strategic brands and human vaccines, which accounted for 86.9% of total sales in the country in 2003 compared to 83.7% in 2002. *Taxotere*, *Lantus* and *Lovenox/Clexane* reported double-digit sales increases, helping to offset essentially flat sales of *Allegra/Telfast*.

An additional growth driver was the strong performance of U.S.-based Dermik, now conducting the North American prescription dermatology business of Aventis Dermatology. Dermik achieved sales of

€377 million in 2003, as compared with €391 million in 2002 (+ 15.0% activity growth).

The 4.7% sales decline in **France** resulted partially from the high base of sales in 2002 due to the acquisition of a safety stock of antibiotics by the French health authorities as a precaution against potential acts of bioterrorism. Excluding this one-time effect, sales would have decreased by approximately 1.1%. This decline is attributable to the implementation of policies to limit healthcare spending. Generic substitution, price cuts and introduction of reference pricing for some brands resulted in decreased sales of our non-strategic products, which

Abbreviated Consolidated Statements of Cash Flows

(in € million)

	2003	2002
Operating Activities:		
Net income (loss) (after income tax and before preferred remuneration)	1 953	2 176
Elimination of expenses and income without effect on cash	1 463	1 423
Increase/decrease in operating assets and liabilities (excluding net operating assets acquired)	(2 030)	(1 740)
Net cash provided by operating activities	1 386	1 859
Investing Activities:		
Net cash (used) provided by investing activities	(284)	3 239
Financing Activities:		
Net cash (used) by financing activities	(1 058)	(5 008)
Net effect of exchange rate changes on cash	(7)	(60)
Increase/(decrease) in net cash and cash equivalents	37	30
Cash and cash equivalents at beginning of year	756	814
Net effect of consolidation changes on cash and cash equivalents	35	(88)
Cash and Cash Equivalents at the End of Year	828	756

still constitute a significant part of our business in France. The range of antibiotics was negatively impacted by campaigns to limit inappropriate antibiotic prescriptions.

Sales in Germany declined by 0.7%. While our strategic brands *Taxotere*, *Lovenox/Clexane* and *Lantus* developed strongly, the ongoing health-policy discussions and cost containment measures, a new rebate system and new reference prices for ACE inhibitors such as *Delix/Tritace* impacted sales negatively. The out-licensing of the OTC business reduced sales by 2%. In addition, significant parallel imports for some strategic brands slowed down sales growth.

Sales in Japan increased 1.5% on an activity basis. Solid growth of our strategic brands was largely offset by a decline in non-strategic products, which represent more than 50% of total sales in Japan. In addition, sales growth was negatively impacted by some non-strategic products that had been divested and still generated sales in 2002 and 2003.

Core Business Sales by Country ^{(1) (2)}

(in € million, except percentages)

	2003	2002	Activity variance in %	Total variance in %
United States	6375	6859	11.1	-7.1
France	2 187	2 295	-4.7	-4.7
Germany	1 078	1 086	-0.7	-0.8
Japan	847	923	1.5	-8.3
Italy	640	628	1.9	1.8
United Kingdom	487	448	19.5	8.6
Canada	397	387	9.4	2.7
Spain	362	328	10.4	10.4
Mexico	344	396	13.7	-13.3
Brazil	239	287	-0.1	-16.5
Subtotal	12 956	13 639	6.5	-5.0
in % of total	77.2	77.5		
Other countries	3 835	3 952	4.0	-3.0
Total Net Sales	16 791	17 591	5.9	-4.5

(1) Core financial information is unaudited and non-GAAP.

(2) Does not reflect the Merial animal health joint venture and the Aventis Pasteur MSD human vaccines joint venture, which are accounted for using the equity method.

Corporate Governance and Management Team

Aventis is organized as a French stock corporation (société anonyme) with a Management Board (Directoire) and a Supervisory Board (Conseil de Surveillance).

The Supervisory Board

The Supervisory Board is responsible for appointing the Management Board, including its chairman and vice chairman, and for overseeing the management of the Aventis businesses by the Management Board.

- Jürgen Dormann
Chairman
- Jean-René Fourtou
Vice Chairman
- Joachim Betz*
- Werner Bischoff*
- Jean-Marc Bruel
- Alain Dorbais*
- Martin Frühauf
- Serge Kampf
- Hubert Markl
- Günter Metz
- Christian Neveu*
- Didier Pineau-Valencienne
- Seham Razzouqi
- Michel Renault
- Hans-Jürgen Schinzler
- Marc Viénot

*Employee representative

The Supervisory Board is supported by the work of three committees: the Strategy Committee, the Finance and Audit Committee and the Nomination and Compensation Committee.

The Management Board

The Management Board acts in the name of the company and is responsible for managing the business of Aventis, particularly in deciding general policy matters and determining the overall business and financial strategy of the company.

- Igor Landau
Chairman
- Richard J. Markham
Vice Chairman, Chief Operating Officer
- Patrick Langlois
Vice Chairman, Chief Financial Officer
- Frank L. Douglas
Executive Vice President, DI&A
- Heinz-Werner Meier
Executive Vice President, Human Resources
- Dirk Oldenburg
Executive Vice President, General Counsel
- Thierry Soursac
Executive Vice President, Commercial Operations

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Dates & Publications

Calendar of Events

First-quarter results:

April 29, 2004

Second-quarter results:

July 29, 2004

Third-quarter results:

October 28, 2004

Annual Report Order Service

This report is also available in French and German and may be obtained:

by phone: 00 800 40 53 43 40 (toll-free) or +49 6192 9 77 08 28 or by e-mail: Aventis@mt-w.de

It can also be downloaded from our Web site at www.aventis.com



Aventis Financial Reports
The “Document de Référence” and the Annual Report on Form 20-F present an extensive overview of our financial and business performance in 2003.

Other Publications

If you would like to find out more about Aventis, you can order the following publications or visit our Web site (see above).



Aventis Sustainability Report
The report documents our efforts and contributions towards a better tomorrow. Available in English, French and German.



Future
The Aventis magazine reports on news from the worlds of science, technology, society and medicine. Available in English, French and German.

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- *Claritin*, a trademark of Schering Corporation

Information Regarding Forward-Looking Statements

Statements in this annual report other than historical information are forward-looking statements subject to risks and uncertainties. The forward-looking statements in this document speak only of management's views as at March 1, 2004. Factors that could cause actual results to differ materially from those expressed or implied include, but are not limited to, impediments to the realization of integration cost savings as a result of labor or political issues or the difficulties of integrating large and complex businesses while continuing day-to-day operations, continued evolutions in the business and business environment, actions that may be taken by competitors or by regulatory authorities, unexpected negative results from research and development of current product candidates, the effectiveness of patent protection, the result of litigation and other risks and uncertainties that are difficult to predict. There can be no assurance that we will achieve the results set forth above. Additional information regarding risks and uncertainties is set forth in the current Annual Report on Form 20-F of Aventis on file with the U.S. Securities and Exchange Commission.

This report has been provided for information purposes only. Aventis prepares a legally binding annual report in the French language known as the "Document de Référence" prior to its Annual General Meeting of Shareholders as well as an annual report in the English language on Form 20-F pursuant to the U.S. Securities Exchange Act of 1934.

All reports can be ordered by phone: 00 800 40 53 43 40 (toll-free) or +49 6192 9 77 08 28

or by e-mail: Aventis@mt-w.de

They can also be downloaded from our Web site at www.aventis.com

Aventis, a stock corporation with a Supervisory Board and Management Board, and a share capital of €3 064 758 522.74 – 542 064 308
RCS Strasbourg

