

Item 4. Information on the Company

General

Aventis is a stock corporation (*société anonyme*) organized under French Commercial Law. According to our by-laws, our corporate existence shall run through July 17, 2030 except in the event of earlier dissolution or extension by our shareholders. Formed in December 1999 through the business combination of former pharmaceutical-chemical conglomerates Hoechst of Germany and Rhône-Poulenc of France, Aventis today is a major pharmaceutical industry player that discovers, develops, manufactures and commercializes prescription drugs for important therapeutic areas such as oncology, cardiology, diabetes, respiratory/allergy, as well as human vaccines.

Our registered office is at 67917 Strasbourg, France, cedex 9, our telephone number is +33 388 99 11 00. Our principal U.S. office is Aventis Pharmaceuticals Inc., 300 Somerset Corporate Boulevard, Bridgewater, NJ 08807-2854. Other principal operating subsidiaries include: Aventis Pharma S.A. in Antony, France, Aventis Pharma Deutschland GmbH in Bad Soden, Germany, and Aventis Pharma Ltd. in Tokyo, Japan. Our global human vaccines business Aventis Pasteur, is headquartered in Lyon, France. In western Europe, commercial operations of the human vaccines business are conducted by Aventis Pasteur MSD, a 50-50 joint venture with Merck & Co.

In 2002, Aventis generated sales of € 17.59 billion, invested € 3.14 billion in research and development and employed approximately 71,000 people worldwide in its core business.

Major corporate developments since the formation of Aventis in 1999

December 15, 1999

Aventis is officially formed following an extraordinary meeting of Rhône-Poulenc shareholders who approved by an overwhelming majority (97.1%) the final steps to complete the business combination of Hoechst and Rhône-Poulenc. On December 20, Aventis shares begin trading under the symbol "AVE" on the Paris and Frankfurt stock exchanges and in the form of American Depositary Shares on the New York Stock Exchange (NYSE).

May 24, 2000

Aventis holds its first Annual General Meeting, shareholders approve a dividend of € 0.45 per share.

June 23, 2000

Aventis and Millennium Pharmaceuticals sign a major strategic agreement to jointly develop and commercialize anti-inflammatory drugs. As part of the alliance, Aventis agrees to purchase US\$ 250 million in Millennium Pharmaceuticals stock and invest up to US\$ 200 million in technology transfer agreements.

November 15, 2000

Aventis announces plans to divest the agriculture segment to focus exclusively on pharmaceuticals.

May 2, 2001

Sale of industrial gases affiliate Messer Griesheim GmbH closes.

May 21, 2001

The Annual General Meeting of Shareholders approves € 0.50 per share dividend for fiscal 2000 and elects four employee representatives to the Supervisory Board.

February 20, 2002

Aventis and Bayer AG sign a non-binding letter of intent to combine their respective global therapeutic proteins activities, Aventis Behring and Bayer Biological Products, in a new, jointly owned business.

April 3, 2002

Sale of Aventis Animal Nutrition to CVC Capital Partners closes.

May 14, 2002

The third Annual General Meeting of Aventis shareholders approves changes in the corporate governance structure of Aventis. A new, seven-member Management Board is formed consisting of Igor Landau as Chairman, Richard J. Markham and Patrick Langlois as Vice Chairmen, Frank L. Douglas, Heinz-Werner Meier, Dirk Oldenburg and Thierry Soursac. Jürgen Dormann and Jean-René Fourtou are appointed Chairman and Vice Chairman, respectively, of the Aventis Supervisory Board. See “Item 6. Directors, Senior Management and Employees” for further information.

June 3, 2002

Sale of Aventis CropScience to Bayer AG closes for an enterprise value of € 7.25 billion. Aventis received total consideration of around € 5.7 billion in cash and debt deconsolidation for its 76% interest in this business. See “—Non-Core Businesses—Aventis CropScience,” below.

January 31, 2003

Aventis and Bayer end negotiations concerning the formation of a therapeutic proteins joint venture.

February 18, 2003

Aventis and CSL Limited enter into preliminary discussions on a potential acquisition of Aventis Behring.

For information on our principal capital expenditures and divestitures, see “Item 5. Other Material Financial Elements.”

The net sales and operating income of Aventis broken down by business segment are presented in Note 26 of the Aventis Consolidated Financial Statements included in Item 18 of this report.

Business Overview

Aventis is a global pharmaceutical company that discovers, develops, manufactures and markets branded prescription drugs and human vaccines to protect and improve the health of patients around the world. Our therapeutic innovations rank among the leading treatments for lung and breast cancer, thrombosis, seasonal allergies, diabetes and hypertension.

Our core business comprises our activities in branded prescription drugs and human vaccines as well as our 50% interest in the animal health joint venture Merial with Merck & Co., and corporate activities. We do not consolidate sales of Merial, however our 50% interest in its earnings is included under the equity method.

As of 2002, the therapeutic proteins business Aventis Behring is no longer considered “core” as we intend to exit from this business. Other non-core businesses, i.e. those that we expect to divest in the near future, include Rhodia, Wacker and DyStar. The divestments of two former non-core businesses, Aventis Animal Nutrition and Aventis CropScience, closed in April and June of 2002, respectively. Both businesses have been deconsolidated as of their respective divestment closing dates.

Strategy

The vision to which Aventis aspires is to be recognized as a pharmaceutical industry leader – valued by patients and healthcare providers, sought after as an employer, and respected by the scientific community and by our competitors.

The strategy that we are pursuing to realize this vision and create sustainable value for patients, healthcare professionals, shareholders and employees centers around products. We want to rapidly develop, launch and market innovative prescription drugs and human vaccines that not only satisfy unmet medical needs in large patient populations, but also help lower the overall cost of healthcare.

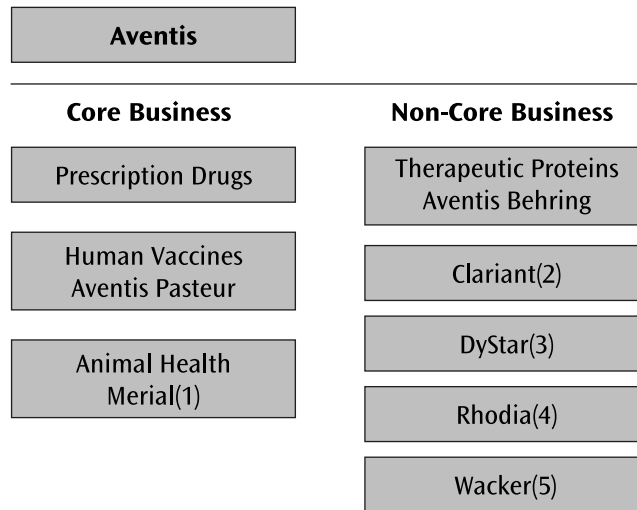
Our strategic priorities have evolved from managing and effecting a successful integration to strengthening and focusing on the core pharmaceutical business and establishing a track record of achievability. Going forward, our strategic goal is to maintain this successful track record by delivering sustainable growth in a changing environment. In order to remain one of the fastest-growing multinational pharmaceutical companies, our strategic imperative is product leadership by discovering, developing and supplying those products that offer the greatest therapeutic benefit to patients.

Our strategy to achieve our goal of product leadership includes:

- Focusing discovery efforts and development resources on core disease areas to introduce a steady stream of innovative and value-adding prescription drugs and vaccines
- Aggressively deploying a targeted in-licensing and alliance strategy to supplement organic growth and enhance our vigorous in-house R&D efforts with high-value, late-stage products
- Maximizing the value of existing and recently launched global brands through commercial investments and by continually expanding their utility through proactive life-cycle management
- Working to increase our share of sales in the United States and for key strategic brands
- Building an industry-leading position in the application of cutting-edge scientific tools
- Recruiting and retaining the best scientists with passion to discover and develop innovative therapies.

As our financial results for 2002 show, our strategy for growth is working. We were one of the fastest-growing multinational pharmaceutical companies in terms of both sales and earnings in 2002. This is due not least to the performance of our strategic brands, which now account for 55% of prescription drug sales compared to 47% in 2001. Our sales in the U.S., the world’s largest pharmaceutical market, grew 21% on an activity basis and now represent 39% of our global core business sales. We have succeeded in narrowing the profitability gap with our peers, having increased gross margin from 73.3% in 2001 to 74.1% in 2002. We intend to close this gap further by resolutely focusing on the significant remaining growth potential of our currently marketed products.

The Organizational Structure of Aventis as of December 31, 2002



(1) 50% owned by Aventis, 50% owned by Merck & Co.

(2) 11.8% interest owned by Aventis.

(3) 35% interest owned by Aventis.

(4) 25.2% interest owned by Aventis.

(5) 49% interest owned by Aventis.

Major Business Developments in 2002

January

Actonel (2.5 mg once daily risedronate sodium tablets) is approved in Japan for the treatment of osteoporosis.

Aventis Pharma Japan submits a New Drug Application (NDA) for the anti-infective *Ketek* (telithromycin) for use in adults.

Ketek is launched in Italy and Spain.

March

Aventis and Coley Pharmaceutical Group expand their existing collaboration to include a drug discovery program to screen and evaluate second-generation immunomodulatory CpG product candidates for the treatment of asthma and allergic rhinitis.

Aventis Pasteur donates 88.5 million doses of smallpox vaccine to the U.S. government.

April

Delix (ramipril) approved in Germany for use in stroke and heart attack prevention.

Ketek is launched in Brazil.

Allegra (60 mg twice daily) approved in Japan for the treatment of itching associated with dermatological diseases.

Aventis joins forces with the Nelson Mandela Foundation to combat tuberculosis in South Africa in a five-year, € 15 million agreement.

Aventis and Genta Inc. enter into a worldwide partnership to develop and commercialize *Genasense*, an oncology drug candidate in multiple phase II and phase III clinical trials.

An NDA is submitted for *Lantus* (insulin glargine) in Japan.

Aventis and Vertex announce plans to expand clinical development of the interleukin-1 beta converting enzyme inhibitor pralnacasan.

May

Interim results of a landmark study reported at the Annual Meeting of the American Society of Clinical Oncology (ASCO) suggest the use of *Taxotere* in early-stage breast cancer.

The U.S. Food and Drug Administration (FDA) rejects *Picovir*, for common colds, from ViroPharma and Aventis.

The FDA approves *Daptacel*, a new acellular pertussis based combination vaccine from Aventis Pasteur.

The FDA approves a new, 35 mg once-weekly dosage strength of *Actonel* for the prevention and treatment of postmenopausal osteoporosis.

Actonel (2.5 mg once-daily risedronate sodium tablets) is launched in Japan.

June

Aventis launches its second Horizon program, a worldwide stock purchase plan for employees.

Third annual Aventis R&D Day is held in London and New York.

A European mutual recognition procedure is successfully completed in 13 European countries for *Repevax*, a booster vaccine for adults.

July

Aventis terminates enrollment in a global Phase III EXPEDITION study evaluating cariporide in coronary artery bypass graft surgery patients.

Aventis and Peptor enter into a licensing, development and commercialization agreement for *DiaPep277*, for the prevention and treatment of latent autoimmune diabetes in adults and type 1 diabetes.

A European mutual recognition procedure is successfully completed in 16 European countries for *Viatim*, a vaccine that protects against hepatitis A and typhoid fever.

August

The FDA accepts for filing the complete response to the agency's June 1, 2001 approvable letter for *Ketek* tablets (800 mg oral dose once daily) for the treatment of community-acquired pneumonia (CAP), acute bacterial exacerbation of chronic bronchitis (AECB), and acute bacterial sinusitis (ABS).

A new ramipril production plant is inaugurated in Germany.

Lantus is launched in the United Kingdom.

Risedronate (*Actonel/Optinate*) is approved in Sweden for once-a-week use in treating and preventing postmenopausal osteoporosis. Sweden will now serve as the reference member state for a European Union mutual recognition procedure for risedronate once-a-week.

A New Drug Application (NDA) is filed in Japan for an additional indication of *Taxotere* in esophageal cancer.

The September 2001 agreement to co-develop and co-promote *Picovir* (pleconaril) with ViroPharma Incorporated is terminated by mutual decision of the parties.

Based on the disappointing outcome of Phase II trials, clinical development of the ACE/NEP inhibitor M100,240 in hypertension is terminated.

September

Ketek (telithromycin) is launched in France.

Aventis announces plans to focus research programs to achieve leadership positions in key disease areas.

The FDA approves *Fluzone* Preservative-free Pediatric Dose, an influenza virus vaccine from Aventis Pasteur.

October

Aventis and Pfizer affirm commitment to *Exubera*, and an expanded clinical program is underway.

November

Aventis launches a cash tender offer on all of its bonds exchangeable into Rhodia shares.

Aventis discloses details of most extensive research program on *Allegra*.

Aventis Pasteur announces plans to increase its industrial capacity with a US\$ 150 million investment.

A U.S. District Court grants final approval of a settlement agreement with a class of approximately 100 direct purchasers in the *Cardizem* CD antitrust multidistrict litigation.

December

The U.S. FDA approves *Taxotere* in combination with cisplatin for first-line treatment of non-small-cell lung cancer.

Lantus is granted marketing authorization by the European Commission (EC) for flexible administration at any time of day.

Subsequent to a cash tender offer for all of its 45,211,662 outstanding 3.25% bonds exchangeable into shares of Rhodia, Aventis acquires 98.6% of the bonds initially issued.

The EU Committee For Proprietary Medicinal Products (CPMP) issues a positive opinion for *Lantus* administration in children of six years or above with diabetes.

Actonel 35 mg once-a-week dosing is approved in the EU.

January 2003

Taxotere receives European approval as first-line treatment for non-small cell lung cancer.

Aventis receives an approvable letter from the U.S. Food and Drug Administration (FDA) for *Ketek* tablets for the treatment of acute exacerbations of chronic bronchitis, acute bacterial sinusitis and community-acquired pneumonia. In the approvable letter, the FDA has requested additional information and analysis but has not required additional clinical studies before considering further our application for marketing approval. The FDA will have up to six months to respond after we submit the requested information.

Aventis exercises early redemption rights and acquires the remainder of its bonds exchangeable into shares of Rhodia.

Key Marketed Products

Prescription Drugs

The following table presents the strategic brands of our prescription drugs business:

Therapeutic area	Strategic brand	First launch	Main markets served by Aventis	Sales 2002 (in € million)	Country/Ranking/Market Share ⁽¹⁾
Respiratory & Allergy	Allegra/Telfast fexofenadine	1996	U.S./Japan/Europe Latin America, Asia	2,030	U.S.: #2/23% (Allegra) #5/6% (Allegra-D) Japan: #2/13.3% (Allegra)
	Nasacort triamcinolone acetanide	1997	U.S., Canada, France, Germany and Italy	329	U.S.: #3/11% (Nasacort AQ); #5/3% (Nasacort) France: #2/22% Canada: #3/11% (Nasacort AQ); #5/3% (Nasacort)
Thrombosis/ Cardiology	Lovenox/Clexane enoxaparin sodium	1987	96 countries worldwide	1,563	U.S.: #1/86% France: #1/55% Germany: #1/31%
	Delix/Tritace ramipril	1989	UK, Germany, France, Italy, Canada	923	Germany: #1/15% Canada: #1/25% UK: #2/19%
Oncology	Taxotere docetaxel	1995	U.S., Europe, Japan, Asia	1,261	U.S.: #1/24% France: #2/23% Japan: #3/12%
	Campto(2) irinotecan	1995	Europe, Asia	241	France: #2/36% Germany: #2/35% Italy: #2/36%
Metabolism/ Diabetes	Amaryl glimepiride	1996	U.S., Europe	578	U.S.: #8/4% Germany: #1/25% Japan: #4/7%
	Insuman human insulin	1999	Europe, Japan	172	Germany: 25% France: 3% Austria: 17%
	Lantus insulin glargine	2000	U.S., Germany, UK	299	U.S.: 9% Germany: 9% UK: 3.2%
Arthritis/ Osteoporosis	Actonel(3) risedronate	1999	U.S., Europe, Japan	539	U.S.: #4/10% France: #1/29% Germany: #2/22%
	Arava leflunomide	1998	U.S., Europe Latin America	271	Germany: 12% U.S.: 9%
Anti-infectives	Targocid teicoplanin	1986	Italy, Japan, France, Germany, UK, Spain and Brazil	222	Italy: #1/84% Japan: #3/15% UK: #1/59%
	Tavanic(4) levofloxacin	1998	Europe, Middle East, Africa, Latin America	257	Germany: #3/4% Italy: #9/3% Spain: #8/3%
	Ketek telithromycin	2001	Europe, Latin America	52	Germany: #17/1.4% Italy: #33/0.6% France: #55/0.4%
Central nervous system	Copaxone(5) glatiramer acetate	1996	Europe	554	Germany: #4/12% Canada: #3/20% Australia: #2/28%

(1) Market share percentages and ranking derived from sales figures (IMS Health), except for France (GERS). Data based on one moving annual total (MAT) ending September 2002.

(2) Licensed from Yakult Honsha (not sold by Aventis in the United States or Japan).

(3) Sold in cooperation with Procter & Gamble Pharmaceuticals; combined sales for Procter & Gamble and Aventis.

(4) Licensed from Daiichi (not sold by Aventis in the United States or Japan).

(5) Marketed in Europe together with Teva Pharmaceutical Industries.

Respiratory/Allergy

Allegra/Telfast (fexofenadine), the top-selling product of Aventis in 2002, is an effective, fast-acting, 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. In April 2002, *Allegra* was approved in Japan for the treatment of itching associated with dermatological diseases. *Allegra/Telfast* is one of the world's most widely studied antihistamines, with more than four billion patient days of therapy recorded to date.

Nasacort (triamcinolone acetonide) Nasal Inhaler is indicated for the nasal treatment of seasonal and perennial allergic rhinitis symptoms in adults and children six years of age and older. **Nasacort AQ** Nasal Spray is an unscented, water-based metered-dose pump spray formulation unit containing a microcrystalline suspension of triamcinolone acetonide in an aqueous medium. It 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.

Thrombosis/Cardiology

Lovenox/Clexane (enoxaparin sodium) is the world's leading low-molecular-weight heparin (LMWH) and has the broadest range of indications of all anticoagulants. Sold as *Lovenox* in the United States and in France, and as *Clexane* in most countries in the rest of the world, this drug has been used to treat more than 108 million patients in 96 countries since its launch in 1987. *Lovenox/Clexane* is indicated for the prevention of post-surgical deep vein thrombosis (DVT), to treat and prevent DVT with or without pulmonary embolism, to treat unstable angina and non-Q-wave myocardial infarction, and to prevent DVT in critically ill medical patients. *Lovenox/Clexane* is the first LMWH marketed in the U.S. for unstable angina and non-Q-wave myocardial infarction. In March 2002, the 5,800 patient EXCLAIM trial began to study the safety and efficacy of prolonged administration of *Lovenox/Clexane* versus placebo in preventing blood clots in acutely ill medical patients. In May 2002, we announced the ExTRACT study to examine the safety and efficacy of *Lovenox/Clexane* versus unfractionated heparin in heart attack patients.

Delix/Tritace (ramipril) is an ACE (angiotensin converting enzyme) inhibitor for the treatment of hypertension and congestive heart failure after myocardial infarction. *Delix/Tritace* is the best-selling ACE inhibitor outside the U.S. and Japan and is today recognized as one of the leading treatments 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 use of *Delix/Tritace* for prevention of cardiovascular events has increased dramatically since 2000 when results of the landmark HOPE study (Heart Outcomes Prevention Evaluation) were reported. According to a study published in the American Journal of Cardiology in November and data from over 50,000 heart attack patients included in the MITRA PLUS heart attack registry from 1992–2002, *Delix/Tritace* is superior to all other ACE inhibitors in preventing death after myocardial infarction. *Delix/Tritace* is the market leader in Germany, France, Italy and Canada. The U.S. rights were sold in 1998.

Oncology

Taxotere (docetaxel) is a chemotherapy agent primarily used to treat metastatic breast cancer and non-small-cell lung cancer in over 86 countries. Launched in 1995, Taxotere is the foundation of our oncology franchise and a standard of care in the treatment of locally advanced or metastatic breast cancer. Results from the first planned interim analysis of the TAX 316 study presented at the Annual Meeting of the American Society of Clinical Oncology (ASCO) in May 2002 showed that a *Taxotere*-based treatment regimen improves survival and reduces the risk of breast cancer relapse in early-stage breast cancer. *Taxotere* was approved in early 2000 for second-line use in treating non-small cell lung cancer (NSCLC) in the U.S. and the EU. *Taxotere* is also indicated for the treatment of gastric, ovarian, and head and neck cancer in Japan. In August, a New Drug Application (NDA) was filed in Japan for esophageal cancer. In November, the FDA approved *Taxotere* for the first-line treatment of non-small-cell lung cancer in combination with cisplatin. In January 2003, *Taxotere* was approved for the same indication in the EU. *Taxotere* is thus the only drug indicated for previously treated non-small cell lung cancer as a single agent and for newly diagnosed non-small cell lung cancer in combination with cisplatin.

Campto (irinotecan) is the current standard of treatment for advanced colorectal cancer. Indicated in first-line treatment of advanced colorectal cancer in combination with 5-fluorouracil (FU) and folinic acid (FA), *Campto* is also used as second-line treatment of colorectal cancer in monotherapy. Several studies are underway to evaluate the use of *Campto* in adjuvant chemotherapy in colorectal cancer, advanced gastric cancer, small cell lung cancer and non-small-cell lung cancer. Aventis markets *Campto*, which was first

launched in 1995 under a license from Yakult Honsha, primarily in Europe, Africa and Asia. We do not market this product in the United States or Japan.

Diabetes

Lantus (insulin glargine) is a once-daily long-acting human insulin analog for type 1 and type 2 diabetes. *Lantus* provides 24-hour basal insulin coverage, with no pronounced peak concentrations through a once-daily injection. The “treat-to-target” campaign is helping to position *Lantus* as one of the most effective ways to help patient achieve target A1C levels.

A New Drug Application for *Lantus* was submitted in Japan in April. *Lantus* was launched in the UK and Ireland in August 2002 and the global roll-out of *Lantus* will continue in 2003. In May 2002, the results of a study were presented at the American Academy of Clinical Endocrinologists (AACE) annual meeting showing patients treated with *Lantus* achieved A1C control (< 7% A1C) with fewer episodes of hypoglycemic symptoms compared with NPH insulin, particularly nocturnal hypoglycemia. In September 2002, two further clinical studies presented at the annual meeting of the European Association for the Study of Diabetes (EASD) in Budapest supported previously reported studies in type 2 diabetes which demonstrated that patients uncontrolled with oral anti-diabetic agents achieved an A1C target below 7% while being associated with a reduced incidence of hypoglycemia versus NPH. In December 2002, *Lantus* was granted marketing authorization by the European Commission (EC) for flexible administration at any time of day.

Amaryl (glimepiride) is a once-daily sulfonylurea for the oral treatment of type 2 diabetes as an adjunct to diet and exercise. *Amaryl* reduces the body’s blood sugar level primarily by helping the body produce more insulin. According to a study presented at 2002 meeting of the American Diabetes Association (ADA), *Amaryl* is associated with a reduced risk of hypoglycaemia and less weight gain than other sulfonylureas. *Amaryl* is the first oral diabetes drug in its class to receive three indications: either as a monotherapy or in combination with insulin or metformin, another oral diabetes treatment, in all 15 EU countries, the U.S., and in more than 23 other countries around the world.

Insuman (human insulin) is a biosynthetic insulin identical to that produced by the human body and is used for treatment of type 1 and type 2 diabetes. *Insuman* is marketed throughout Europe, with the largest markets in terms of sales being Germany and Austria. It was approved in August 2001 in Japan, where it is registered as *Isuhuman*. Aventis does not sell this product in the United States.

Arthritis/Osteoporosis

Actonel (risedronate sodium) is a novel bisphosphonate approved for treatment and prevention of postmenopausal osteoporosis and for the treatment of glucocorticoid-induced osteoporosis. It is also approved for treatment of Paget’s disease, a rare bone disorder. *Actonel* is the only bisphosphonate that has shown rapid clinical vertebral fracture reduction in just one year and has shown sustained fracture reduction of up to five years. *Actonel* is being co-developed and co-marketed in partnership with Procter & Gamble Pharmaceuticals through the Alliance for Better Bone Health. The 5 mg once-daily formulation received U.S. and EU approval in 2000 and is currently approved in 77 countries worldwide. In Japan, risedronate sodium was approved in January and launched for the treatment of osteoporosis in May. It is being marketed there jointly through two channels under two brand names, “*Actonel* 2.5 mg tablets” from Ajinomoto (manufacturer) and Aventis (distributor) and “*Benet* 2.5 mg tablets” from Takeda.

Actonel was approved in a 35 mg once-weekly formulation in the U.S. in May and in the European Union in December. Once-a-week risedronate has also been approved in Argentina, Brazil, Egypt, Guatemala, New Zealand and Switzerland. New data presented at a meeting of the American Society for Bone and Mineral Research on September 20 showed that a 5 mg dose of *Actonel* daily significantly reduced moderate and severe vertebral fracture risk by 70% within one year of treatment in women with postmenopausal osteoporosis.

Arava (leflunomide) is an oral disease-modifying anti-rheumatic drug (DMARD) for first-line treatment of rheumatoid arthritis. It is the first drug to be indicated to reduce the signs and symptoms of rheumatoid arthritis and to retard structural damage, such as erosions and joint-space narrowing, as evidenced by X-ray. Two studies presented at the American College of Rheumatology (ACR) 66th Annual Meeting in October 2002 demonstrate the consistent efficacy and safety of *Arava* in treating rheumatoid arthritis. *Arava* offers once-daily dosing and can be used in both early and late stages of the disease.

Anti-Infectives

Ketek (telithromycin), the first of a new class of antibiotics known as the ketolides, was designed to deliver an optimal spectrum of activity for the first line treatment of upper and lower respiratory tract infections including those caused by resistant pathogens – with less propensity to induce resistance – and a short treatment regimen.

In Europe, *Ketek* was approved in July 2001 for the treatment of patients 18 years and older for community-acquired pneumonia (CAP), mild or moderate; acute exacerbation of chronic bronchitis (AECB); acute sinusitis; and tonsillitis/pharyngitis caused by Group A beta streptococci, as an alternative when beta lactam antibiotics are not appropriate, in patients 12 years and older. *Ketek* was launched in October 2001 in Germany. In 2002, *Ketek* was launched in Spain, Italy and France and in all the major markets of Latin America. Over one million patients worldwide have been treated with *Ketek* since its launch. A New Drug Application (NDA) was filed in January 2002 for *Ketek* in Japan, the second largest antibiotic market worldwide.

In January 2003, the U.S. Food and Drug Administration (FDA) issued an approvable letter for *Ketek* for the treatment of acute exacerbations of chronic bronchitis, acute bacterial sinusitis and community-acquired pneumonia. The FDA has requested additional information and analysis but has not required additional clinical studies before considering further our application for marketing approval. The FDA will have up to six months to respond after we submit the requested information.

Targocid (teicoplanin) is an injectable glycopeptide antibiotic for treatment of infections caused by susceptible Gram-positive bacteria, including those resistant to other antibiotics such as methicillin and cephalosporins.

Tavanic (levofloxacin) is an IV/oral broad-spectrum fluoroquinolone antibiotic in-licensed from Daiichi. This fast-acting bactericidal antibiotic offers once-daily dosing for the treatment of community acquired pneumonia, acute exacerbations of chronic bronchitis, acute sinusitis, complicated urinary tract infections and skin and soft-tissue infections. We do not market *Tavanic* in Japan or the U.S.

Central Nervous System

Copaxone (glatiramer acetate) is the first non-interferon, non-steroidal agent indicated for reduction of the frequency of relapses in patients with relapsing-remitting multiple sclerosis (MS). *Copaxone* has demonstrated continued efficacy in reducing relapse rates over eight years, and has shown a significant effect on Magnetic Resonance Imaging (MRI) monitored activity and burden of disease. *Copaxone* received marketing approval for all EU countries in August 2001. In September 2002, seven-day room temperature *Copaxone* was approved across sixteen European countries. In Europe, *Copaxone* is marketed by Teva Pharmaceutical Industries Ltd. and Aventis. In North America, *Copaxone* is marketed by Teva Neuroscience.

Human Vaccines

Aventis Pasteur is a world leader in vaccines, offering the broadest range of products in the industry. With a heritage dating back to Louis Pasteur, our vaccines unit provided 1.4 billion doses of vaccines in 2002, protecting almost 500 million people against 20 serious diseases in 150 countries. In terms of sales, we account for nearly one-quarter of the global market for vaccines, which has enjoyed a compounded annual growth rate of 14% during the past 10 years.

Aventis Pasteur contributed sales of € 1,580 million in 2002, an increase of 10.9% (+16.3% activity variance) over sales of € 1,425 million in 2001. The strong growth was due mainly to higher sales in the United States, particularly for pediatric combination vaccines and adult boosters (tetanus-diphtheria).

Aventis Pasteur holds a leading position in most countries. In the United States, which accounts for 40% of the worldwide vaccines market, higher sales during the last two years have positioned Aventis Pasteur as one of the top two vaccine companies. In Europe, commercial operations are conducted by Aventis Pasteur MSD, a 50–50 joint venture between Aventis Pasteur and Merck & Co., providing vaccines to 19 countries. Aventis Pasteur MSD, which is accounted for using the equity method, had total net sales of € 577 million in 2002 compared to € 556 million in 2001. In emerging countries, which account for 80% of the world population, Aventis Pasteur has established a leading position, notably in Latin America and increasingly in Asia, where we have been expanding our presence. We are also very active in donors' markets such as UNICEF and Pan-American Health Organization.

Leading Brands

Influenza vaccines: Our top-selling products are vaccines against influenza, a field in which we are the leader with nearly 50% of the world market. Immunization is considered one of the most cost-effective interventions available for preventing influenza. Our principal products are *Vaxigrip*, *Fluzone* and *Mutagrip*.

Pediatric combination vaccines: The components of these vaccines vary depending on needs in various parts of the world. Different combinations protect against up to six diseases: diphtheria, tetanus, pertussis (whooping cough), polio, hepatitis B and *Haemophilus influenzae* type b (Hib) to protect against meningitis. Our most innovative product is *Hexavac*, a new vaccine approved in 2000 in Europe and under registration in various international markets. Developed in cooperation with Merck & Co., it is the only fully liquid pediatric combination vaccine that protects against six diseases. Other principal combinations include *Pentacel* and *Tetravac*.

Travelers/endemic area vaccines: This range of products is intended for travelers going to endemic areas, meaning regions with a constant or periodic occurrence of a disease, as well as for the local populations living in the affected areas. *Viatim/Vivaxim*, a new combination vaccine against hepatitis A and typhoid fever, was launched in the United Kingdom in 2001 and is being introduced in other European countries. Other principal products include *Typhim Vi*, *Avaxim*, *Verorab*, *JE-VAX*, *YF VAX* and *Stamaril*.

Meningitis vaccines: We have three vaccines against meningitis caused by three different pathogens.

- The first is the ActHib vaccine protecting against *Haemophilus influenzae* type b. This vaccine belongs to our pediatric combination range.
- The second one, a polysaccharide AC vaccine, protects against strains of meningitis present in Africa.
- The third, *Menomune*, A/C/Y/W135, is a quadrivalent meningococcal combination vaccine that has become increasingly important as global epidemiology has changed for meningococcal disease over the past decade. This vaccine has been important in protecting U.S. college students against meningococcal C and Y, which are most common serogroups causing disease among adolescents and college students. Globally, *Menomune* has been used to vaccinate travelers such as pilgrims going to Mecca or to certain African regions/countries where an increase in serotype W135 has been observed over the past two years.

Boosters: The tetanus and diphtheria combination (Td) is the prime booster product used throughout the world to “boost” protection against these diseases. *Repevax*, commercialized in some European countries, is a booster product that includes an inactivated polio and pertussis vaccine along with tetanus and diphtheria. Both products can be used for different age groups, from children to adults, and are integrated into vaccine calendars according to national guidelines and recommendations.

Polio vaccines: Polio vaccines continue to be one of our major growth drivers. The worldwide polio eradication initiative from WHO and UNICEF has positioned Aventis Pasteur as a global preferred partner with the injectable/inactivated vaccines *IPOL* and *Imovax Polio* as well as the Oral Polio Vaccine (OPV), which is still being used in emerging countries. After eradication, the injectable form may be included in national immunization recommendations for polio vaccination for at least another decade, while the oral polio vaccine may be removed from immunization calendars. The injectable polio vaccine is becoming a pivotal antigen in new pediatric combinations that we offer.

Merial

Merial, a 50–50 joint venture with Merck & Co. is the world’s leading animal health company dedicated to providing products and solutions that enhance the health, well-being and performance of a wide variety of animals. The company is also a market leader in the development of poultry breeding stock. Operational headquarters are located in Duluth, Georgia, U.S. With approximately 6,500 employees in 150 countries, Merial offers a comprehensive line of veterinary pharmaceuticals and vaccines to prevent and treat a wide range of animal diseases.

Merial’s products help veterinarians, food producers, pet owners and governments worldwide to improve and maintain the health of animals and thereby of humans. In addition, the joint venture participates in the development and implementation of international agreements on animal health and is especially involved in the development and implementation of efficient epidemiological monitoring systems.

The product range of Merial includes *Frontline* (fipronil), their number-one product and the world’s best-selling topical anti-parasitic for the treatment and prevention of fleas and ticks in cats and dogs.

Other significant products include avermectin-based products, led by the paratitocides *Ivomec* (ivermectin) and *Eprinex* (eprinomectin) for the treatment of beef and dairy cattle as well as sheep and swine.

Research and Development

As an innovation-driven supplier of prescription drugs and human vaccines, Aventis invests substantial human and financial resources in research and development. In 2002, our research and development spending on prescription drugs and human vaccines totaled € 3.14 billion.

Prescription Drugs

Research and development of branded prescription drugs is the responsibility of our Drug Innovation & Approval organization, which consists of approximately 5,700 people working at four main locations in France, Germany, Japan and the United States. The key objectives of the global Drug Innovation & Approval function are to:

- Deliver the pipeline
- Increase innovation and productivity and
- Optimize the value of our products

The activities of Drug Innovation & Approval are organized around a value chain that performs time-critical activities in parallel instead of sequentially, and follows a network-centric approach. Drug discovery is conducted by sites in France, Germany and the U.S. The sites act as entrepreneurial units responsible for managing the project portfolio of the assigned disease groups from the exploratory stage to phase IIa clinical testing. This is achieved by the combined efforts of site-based disease groups and expertise from the global functions Lead Generation and Lead Optimization. Late-stage development and approval is conducted globally, and is managed out of the Global Drug Development Center in Bridgewater, New Jersey.

The following global functions support site-based as well as global project teams:

- Lead Generation (LG) works with the disease groups to identify and validate targets, identify and modify leads, and generate early development compounds. LG is organized into five centers of expertise located at sites in France, Germany and the U.S. The technology provided by LG is critical to manage the portfolio through phase IIa.
- Lead Optimization (LO) bridges development from the preclinical to the clinical phase. The key objective of this function is to establish proof of concept in man so that the candidates with the greatest chance of success can be selected for phase IIb and phase III studies. LO comprises four centers of expertise and their scientists work in project teams at the four sites.
- Product Realization (PR) is responsible for managing late-stage clinical projects worldwide in phase IIb and phase III as well as optimizing the value of strategic brands by delivering new therapeutic indications and commercially attractive dosage forms. Clinical studies are conducted using state-of-the-art Web-based clinical trial management and reverse planning tools.
- Global Regulatory Approvals & Marketing Support (GRAMS) interfaces with regulatory agencies and directs simultaneous submissions of global dossiers to obtain approvals in major markets. State-of-the-art electronic document management technologies are used to bring drug candidates through the regulatory approval process. GRAMS also maintains these approvals and ensures surveillance of safety profiles for all Aventis compounds (both in development and marketed).

New disease area focus announced

In September 2002, we announced plans to focus our research activities on certain key disease areas in which we intend to build leadership positions. We have decided to reinforce our efforts in the therapeutic areas of oncology, diabetes and thrombosis. In addition, we will focus our research efforts in areas such as Alzheimer's disease, asthma, coronary heart disease, multiple sclerosis, rheumatoid arthritis, schizophrenia and chronic viral infections, as we believe these areas will provide opportunities for us to leverage existing in-house scientific expertise, and to develop innovative therapies which address critical medical needs. In parallel, research will be focused on the vaccine and immunological approaches currently conducted at Aventis Pasteur. For the anti-bacterial and anti-fungal research activities, Aventis plans to create a partnership to leverage and further develop existing expertise in this area.

In July, our bone research and development activities located at the Romainville site near Paris, France were transferred to ProSkelia, a newly created pharmaceutical research and development company

specializing in bone diseases. ProSkelia's capital is held by U.S. venture capital firm Warburg Pincus (58%) and Aventis (42%). ProSkelia employs approximately 90 people.

We plan to establish a Business and Technology Center at Romainville, which will be home to the new anti-infectives partnership and ProSkelia. The new center will provide technology companies with an attractive and competitive infrastructure that caters to their research and development needs and is expected to create new employment opportunities.

Reinforced alliance strategy

In order to supplement our organic growth and support our principal goal of bringing innovative, new prescription drugs and human vaccines of high medical importance to the market, we are actively pursuing a targeted in-licensing and technology alliance strategy. We are also aiming to complement our strengths in select therapeutic areas by entering into co-development and co-commercialization agreements with biotechnology firms and other pharmaceutical companies. Several promising drug candidates for key therapeutic areas such as oncology, diabetes and asthma have been added to the portfolio during the last two years. They include:

DiaPep277, a new diabetes therapy that has shown promising results in phase II clinical trials. *DiaPep277* is being developed for the prevention and treatment of latent autoimmune diabetes in adults (LADA) and type 1 diabetes. We entered an exclusive worldwide license agreement with Peptor Ltd. for this new drug in July.

Genasense, an antisense drug candidate currently in multiple phase II and phase III clinical trials to test its ability to enhance the effectiveness of chemotherapy in patients with both hematologic cancers and solid tumors. This compound is being developed and commercialized jointly by Aventis and Genta Inc.

Alvesco (ciclesonide) is an inhaled corticosteroid for the treatment of asthma. Currently in phase III trials, *Alvesco* is demonstrating excellent efficacy without corticosteroid-associated systemic side effects. We are developing *Alvesco* in collaboration with Altana Pharma and will co-commercialize the product in the U.S.

Major strategic partnerships include:

<u>Compound</u>	<u>Partner</u>	<u>Indication</u>
<i>Actonel</i>	Procter & Gamble	Osteoporosis
<i>Alvesco</i>	Altana Pharma	Asthma
Anti-inflammatory compounds	Inflazyme	Asthma
AVE-8062	Ajinomoto	Cancer
<i>Campto</i>	Yakult	Cancer
CpG immunomodulators	Coley	Asthma and allergic rhinitis
<i>Copaxone</i>	Teva Pharmaceuticals	Multiple sclerosis
CRF-1 antagonists	Neurogen	Anxiety/depression
<i>DiaPep277</i>	Peptor	Diabetes
Dynepo	Transkaryotic Therapies	Anemia
<i>Exubera</i>	Pfizer	Diabetes
<i>Genasense</i>	Genta	Cancer
Nicotinic agonists	Targocept	Alzheimer's disease
Pralnacasan	Vertex	Arthritis (RA and OA)
SERM	ProSkelia	Bone diseases
<i>Tavanic</i>	Daiichi	Bacterial infections

In order to increase the productivity of our in-house drug innovation and approval efforts, we leverage external know-how, technologies and innovation by collaborating on preclinical research, development and technology projects with biotechnology companies, other pharmaceutical companies and scientific institutions. We currently have more than 300 collaborations with academic institutions and biotechnology companies worldwide.

Major technology alliances include:

<u>Partner</u>	<u>Area of collaboration</u>
Affymetrix	Gene chips
Celera	Genomics data base and Cathepsin S for inflammatory diseases
Incyte Pharmaceuticals	Genomics data base
Millennium Pharmaceuticals	Inflammatory diseases and technology transfer
PPD Discovery	Cancer functional genomics
ProCorde	Cardiovascular functional genomics

Human Vaccines

The research and development efforts of our human vaccines business Aventis Pasteur are focused on developing preventive and therapeutic vaccines, improving existing vaccines and simplifying administration methods.

The research and development organization of Aventis Pasteur comprises approximately 1,000 scientists located at three research and development centers in Marcy l'Etoile, France, Toronto, Canada and Swiftwater, Pennsylvania, U.S. Aventis Pasteur devotes 17% of its sales to research and development of new vaccines.

Research and development efforts at Aventis Pasteur are currently concentrated on six major programs:

- **New pediatric combination vaccines:** New combinations incorporating an acellular pertussis valence are in development to protect children against multiple diseases with a limited number of injections. We are also working on a vaccine protecting against five diseases (diphtheria, tetanus, polio, whooping cough and Hib meningitis) for the U.S. market called *Pentacel*.
- **Booster vaccines:** These vaccines offer a response to the growing needs of adolescents and adults by extending protection against diphtheria, tetanus, polio and pertussis, with an increasing incidence of pertussis being noticed in this population.
- **Respiratory tract infections:** New vaccines are being developed against respiratory viral infections (Respiratory Syncytial Virus, influenza, etc.) as well as bacterial infections (*S. pneumoniae*, etc.).
- **Vaccines for travelers and for endemic zones:** Phase I clinical trials are underway for the prevention of Dengue fever, a major public health problem in Asia and South America.
- **Blood-borne diseases:** ALVAC-HIV vaccine candidates are currently being developed in prophylactic and therapeutic approaches. In 2003, a prophylactic vaccine is scheduled to begin phase III trials in Thailand. A new approach with a recombinant Tat toxoid protein is in phase I as a therapeutic vaccine.
- **Therapeutic vaccines for certain types of cancer:** Tumor-associated antigens are being used to elicit tumor-specific responses. The multi-antigen candidate vaccines are targeting melanomas and colorectal cancers (Phase I/II).

In addition, we are developing the quadrivalent conjugate vaccine *Menactra* to protect adolescents and infants against meningitis caused by a broad range of serogroups of *N. meningitidis*.

In support of research and development projects to improve the efficacy of its vaccines, Aventis Pasteur also develops new technologies, e.g. new adjuvants and administration methods, live vectors (viral and bacterial), and genomics-based approaches to identify target antigens. A number of other targets are being investigated through internal research and development and business development agreements, giving Aventis Pasteur a very promising pipeline.

Strong scientific and business alliances

Aventis Pasteur has an established international network of collaborations:

- Cancer vaccines: Therion (U.S.), Aphton Corporation (U.S.), Ludwig Institute for Cancer Research (U.S.), National Cancer Institute (U.S.), Karolinska Institute (Sweden), Leiden University (the Netherlands), National Research Council (Canada).

- Genomics approach: Incyte Pharmaceuticals, Inc. (U.S.), EOS Technologies, Inc. (U.S.), Millennium Pharmaceuticals, Inc. (U.S.).
- Dengue fever vaccine (hemorrhagic fever): Acambis (UK).
- New anti-bacterial vaccines based on lipopolysaccharides: National Research Council (Canada), Oxford University (UK), BioSynth (Italy), University of Stockholm (Sweden).
- AIDS vaccines: Pasteur Institute (France), ANRS (France), National Institutes of Health (U.S.), Walter Reed Institute (U.S.), Eurovac (EU).
- In addition to our relationship with Merck & Co., we have long-standing ties with the Pasteur Institute with respect to certain vaccine research programs.

Pipeline

We currently have more than 40 compounds in clinical development, including over 25 in early-stage clinical development and more than 15 in late-stage development. By taking early data-driven decisions, we want to optimize and prioritize our compound portfolio so as to increase the success potential and thus the value of our pipeline. In addition, we are actively pursuing attractive in-licensing opportunities and alliances to strengthen our leading positions in disease areas such as oncology, diabetes, thrombosis and vaccines.

The following charts are a current snapshot of the Aventis pipeline, with the new products set out below having the highest priority among all our products currently in development. The nature of drug discovery and development is such that not all products can be expected to fulfill expectations or meet with favorable regulatory response, so it is possible that some projects in clinical development will not result in marketable products.

Key Compounds in Phase III Clinical Development

Project(1)	Disease	Status	Planned submission(2)
<i>Alvesco</i> (ciclesonide)(3)	Asthma	Phase III	2003 (U.S.)
<i>Cariporide</i>	Coronary artery bypass graft surgery	Phase III	2003
<i>Genasense</i> (4)	Cancer	Phase III	2003
<i>Glulisine</i> (1964)	Type 1 and 2 diabetes	Phase III	2003
<i>Menactra</i>	Meningitis (vaccine)	Phase III	2004
<i>Pentacel</i>	Pediatric combination vaccine	Phase III	2004 (U.S.)
<i>Exubera</i> (5)	Type 1 and 2 diabetes	Phase III	Tbd

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

(2) United States and European Union (except as otherwise noted).

(3) Cooperation with Altana Pharma.

(4) Cooperation with Genta Inc.

(5) Cooperation with Pfizer.

- ***Alvesco*** (ciclesonide) — An inhaled corticosteroid for the treatment of asthma, which Aventis is co-developing and co-promoting in the United States with Altana Pharma. Currently in Phase III trials, ciclesonide is a potentially important advance in asthma therapy due to its excellent efficacy, low side effects and long duration of action. Asthma is a growing market with about 20 million patients in the U.S. alone. Aventis is responsible for regulatory submission in the U.S., which is planned for the second half of 2003.
- ***Cariporide*** — A first-in-class heart muscle protectant targeted to reduce the incidence of heart attack and death in patients undergoing coronary artery bypass surgery. Enrollment in EXPEDITION, a phase III trial to determine the ability of cariporide to reduce death and myocardial infarction in patients undergoing coronary artery bypass surgery, was terminated in August 2002.
- ***Genasense*** is an antisense drug candidate currently in multiple phase II and phase III clinical trials to test its ability to enhance the effectiveness of chemotherapy in patients with both hematologic cancers and solid tumors. This compound is being developed and will be commercialized jointly by Aventis and Genta Inc.
- ***Glulisine*** — This fast-acting insulin analog for type 1 and type 2 diabetes is an important compound intended to broaden the Aventis diabetes portfolio. The international development program for glulisine is designed to achieve competitive labeling at launch, including flexible mealtime dosing and a pump application for continuous subcutaneous infusion. The product is on track for regulatory submissions in the U.S. and EU in 2003.
- ***Menactra*** — A quadrivalent conjugate vaccine against N. meningitis in adolescents and infants.
- ***Pentacel*** — A vaccine protecting against five diseases (diphtheria, tetanus, polio, whooping cough and Hib meningitis) for the U.S. market.

- **Exubera** — A novel approach to delivering insulin in a dry powder formulation by inhalation. *Exubera* is being developed for patients with type 1 and type 2 diabetes through a collaboration with Pfizer. Phase III efficacy trials have been completed and additional studies are underway to strengthen the long-term safety data. Regulatory filings in the U.S. and in Europe are under review pending more comprehensive data analysis.

Our early-stage pipeline (phase I/II) includes the following compounds:

Project	Disease
New-generation taxoids	Cancer
Flavopiridol	Cancer
AVE-8062	Cancer
ALVAC-CEA vaccine	Colorectal tumors
ALVAC-gp100 vaccine	Melanoma
ALVAC-HIV vaccine	HIV
RSV vaccine	Respiratory viral infections
Pralnacasan	Arthritis
AVE-7688	Hypertension
HP-184	Spinal cord injury
NV1FGF	Peripheral vascular disease
Teriflunomide	Multiple sclerosis
Anti-inflammatory compounds	Asthma
<i>DiaPep277</i>	Diabetes
Antiobesics	Obesity
Guanylate cyclase activators	Angina
100,907	Sleep disorders
CRF-1 antagonists	Depression/anxiety
SERM 3471	Postmenopausal osteoporosis
Factor Xa inhibitors	Thrombosis

- Two new-generation taxoids acting as chemotherapy agents have demonstrated a broad spectrum of antitumor activity in taxoid-resistant tumor cell lines. The safety profile of these novel cytotoxics appears similar to that of *Taxotere*. Phase II studies are underway.
- **Flavopiridol** — This innovative chemotherapeutic agent inhibits cyclin-dependent kinases through cell cycle arrest and cell death. Flavopiridol has demonstrated synergistic effects in combination with other cytotoxic agents and has also shown antitumor activity in early clinical studies. Aventis is initiating combination trials for flavopiridol with the chemotherapy agents *Taxotere* targeting lung cancer and *Campto* targeting colon cancer.
- **AVE-8062** is a novel compound for the treatment of cancer, which has demonstrated its potential efficacy in attacking tumor cells by cutting off a tumor's vital supply of blood. The worldwide rights to develop, manufacture and market AVE-8062 have been licensed to Aventis by Ajinomoto Co. Inc. of Japan.
- **ALVAC-CEA**, a therapeutic vaccine for colorectal cancer, is designed to induce T-cell and antibody responses directed against specific cancer cells bearing the tumor-associated antigen CEA. Phase I studies in patients with advanced colorectal cancer have demonstrated immune responses generated against CEA, and disease stabilization was observed in one-third of the patients studied over a two-year period. A second-generation vaccine is intended to target multiple antigens.

- **Pralnacasan**, a novel anti-inflammatory drug candidate has completed a phase II proof-of-mechanism trial in rheumatoid arthritis which demonstrated its ability to inhibit key mediators of joint inflammation and destruction by a novel mechanism of action. It has advanced into phase IIb. Proof-of-concept studies in osteoarthritis began in late 2002. Pralnacasan is being developed in cooperation with Vertex Pharmaceuticals Inc.
- **AVE-7688**, a new compound for the treatment of hypertension and congestive heart failure is currently in phase I.
- **HP-184** for improving function in chronic spinal cord injury. Data from preclinical trials have indicated improved nerve conduction and ambulation and Aventis expects that this compound will reduce neuropathic pain in patients.
- **NV1FGF** is a proprietary plasmid-based gene therapy that offers an innovative approach to induce the formation of new blood vessels. This compound is designed to help people who might otherwise face limb amputation due to lack of blood supply to the legs. Data from a phase I study demonstrated significant improvement in blood flow, healing of ulcerations, increasing skin oxygenation and pain reduction as well as formation of new blood vessels in arteriograms. Phase II trials are in progress.
- **Teriflunomide** is an orally active immunomodulator that is being developed for the treatment of multiple sclerosis.
- **Anti-inflammatory compounds** for asthma are currently in phase I/IIa, and have demonstrated high potency and a good pharmacokinetic profile. This new class of non-corticosteroid oral anti-inflammatory agents is being developed in cooperation with Inflazyme.
- **Anti-obesity drug candidates** are currently in phase I trials.
- **Guanylate cyclase activators** for the treatment of angina pectoris are currently in phase I to study their ability to relax blood vessels.
- **100,907** is a novel therapy for treatment of sleep disorders. As a selective serotonin (5-HT_{2a}) antagonist, 100,907 demonstrated benefit in a recently completed phase I study. While sleep-inducing drugs often lead to tolerance and “rebound” effects during the night, 100,907 could reduce the number of night-time awakenings. Phase IIa proof-of-concept studies are in progress.
- **CRF-1 antagonists** for the treatment of depression and anxiety are being developed in cooperation with Neurogen Corp.
- **SERM 3471** is a selective estrogen receptor modulator for the treatment and prevention of post-menopausal osteoporosis in cooperation with ProSkelia.
- **Factor Xa inhibitors** are novel agents for the treatment and prevention of arterial and venous thrombosis that very selectively inhibit the plasma coagulation Factor Xa. This new generation of agents offers the potential to inhibit coagulation without the unwanted side effect of bleeding often observed with other antithrombotics.

In addition to these primary development projects, several major line extensions are in clinical development. Line extensions are important elements of our growth, since many of our products are still in the early stages of their life cycle. We believe products such as *Lovenox*, *Taxotere*, *Lantus* and *Actonel* have significant growth potential ahead of them, and successful additional indications, formulations, market entries and line extensions would expand the breadth and depth of these products.

Key Line Extensions in Clinical Development

Product	Indication	Planned submission
<i>Allegra</i>	Perennial allergic rhinitis	2003 (U.S.)
	<i>Allegra-D</i> once-daily	2003 (U.S.)
	Orally disintegrating tablet	2003 (U.S.)
	Asthma	2004 (U.S.)
<i>Campto</i>	Gastric cancer	2003 (EU)
	Colorectal cancer adjuvant	2004 (EU)
<i>Ketek</i>	Pediatric use	2004 (U.S./EU)
<i>Lovenox</i>	Deep vein thrombosis prophylaxis	2003 (Japan)
	ST-elevated heart attack	2004 (U.S./EU)
<i>Taxotere</i>	Gastric cancer	2003 (U.S./EU)
	Adjuvant breast cancer	2003 (U.S./EU)
	Prostate cancer	2003 (U.S./EU)
	Neoadjuvant head & neck cancer	2004 (U.S./EU)

Regulatory achievements in 2002/3

Product	Indication	Achievements
<i>Actonel</i> (NCE)	Osteoporosis	Approved in Japan (January)
<i>Actonel</i> (LE)	Once-a week dosing	Approved in the U.S. (May); EU (December)
<i>Allegra</i> (LE)	Skin disease	Approved in Japan (April)
	Pediatric tablets	Submitted in the UK (EU-RMS) (March)
	Pediatric exclusivity	Approved in the U.S. (January 2003)
<i>Daptacel</i>	Diphtheria, tetanus and pertussis vaccine	Approved in the U.S. (May)
<i>Fluzone</i> Preservative-free	Pediatric dose influenza vaccine	Approved in the U.S. (September)
<i>Ketek</i> (NCE)	Respiratory tract infections	Submitted in Japan (January); FDA approvable letter (January 2003)
<i>Lantus</i> (NCE)	Diabetes	Submitted in Japan (April)
<i>Lantus</i> (LE)	Flexible dosing	Submitted in the EU/U.S. (June); approved in the EU (December)
<i>Lantus</i> (LE)	Pediatrics	Submitted in the EU (June)
<i>Taxotere</i> (LE)	1 st line NSCLC	Submitted in the EU/U.S. (February)
		Approved in the U.S. (November) and the EU (January 2003)
	Esophageal cancer	Submitted in Japan (August)
<i>Repevax</i>	Diphtheria, tetanus, pertussis, polio vaccine	Approved in the EU (June)
<i>Viatim</i>	Typhoid fever and hepatitis A vaccine	Approved in the EU (July)

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

NCE = New Chemical Entity

LE = Line Extension

NSCLC = Non-small-cell lung cancer

Geographic Markets

We generate the majority of our sales in the world's four largest pharmaceutical markets – the United States, France, Germany and Japan. In 2002, these countries accounted for 63.5% of core business sales compared to 61.9% in 2001.

The United States, which is the world's largest pharmaceutical market, accounted for 39% of our core business sales in 2002 versus 36% in 2001. In 2002, Aventis was the largest research-based pharmaceutical company in both France and Germany. In Japan, we are aiming to establish Aventis as one of the leading non-domestic pharmaceutical companies.

With a presence in more than 100 countries, Aventis is well-positioned in other important areas of the world to meet the growing needs of patients for innovative therapeutic and preventive healthcare solutions.

- In Europe, which accounts for a 23% share of the global pharmaceutical market, Aventis is the third-largest pharmaceutical company. We have a very strong commercial, manufacturing and research presence in the region, particularly in France, Germany, the United Kingdom and Italy.
- Aventis has sales and production operations throughout Asia-Pacific. In Japan, which is the world's second-largest national pharmaceutical market, we are aiming to expand by pursuing key regulatory filings, new indications and line extension approvals for our strategic brands. In 2002, we submitted New Drug Applications for *Ketek* and *Lantus*. In addition, *Taxotere* was submitted for approval in esophageal cancer. *Actonel* was approved and launched in Japan in 2002 and *Allegra* was approved and launched for itching associated with certain skin diseases. In early 2003, *Lovenox* will be submitted in Japan for the prevention of deep-vein thrombosis.
- In Latin America, Aventis is structured into four geographic areas: Brazil, Mexico, Southern Cone and CANAM, which encompasses the Andean region, Central America, and Caribbean countries. The regional headquarters of Aventis in Latin America are in São Paulo, Brazil. Business is supported by industrial sites located in Mexico, Brazil, Argentina, Venezuela and Guatemala. In terms of sales, Mexico ranks seventh and Brazil tenth in the top ten Aventis countries.

Aventis Core Businesses – Sales by Country(1)

	YTD 2002	YTD 2001	Activity variance(2)	Structure variance
	(in € million)			
United States	6,859	5,964	21.4%	
France	2,295	2,245	4.7%	– 2.3%
Germany	1,086	1,058	2.9%	– 0.3%
Japan	923	987	2.7%	– 1.5%
Italy	628	586	7.2%	
United Kingdom	448	373	21.4%	
Mexico	396	416	3.6%	
Canada	387	371	11.4%	
Spain	328	312	5.5%	– 0.4%
Brazil	287	349	4.3%	
Subtotal	13,639	12,663	13.1%	– 0.6%
in % of total	77.5	76.4		
Other countries	3,952	3,912	6.9%	1.8%
Total Net Sales	17,591	16,576	11.6%	

(1) Unaudited.

(2) On a comparable basis.

For a comprehensive breakdown of our group sales by geographic region, we refer you to Note 26 to the Aventis Consolidated Financial Statements included at Item 18 of this report.

Marketing and Distribution

Aventis has a global sales force of nearly 20,000, including approximately 4,400 representatives in the United States. These representatives present the therapeutic and economic benefits of our products to physicians, pharmacists, hospitals, insurance groups, managed care organizations and other customers.

During 2002, we successfully implemented initiatives to maximize the commercial value of our global strategic brands by fundamentally changing the way we manage their launch and life cycle. Cross-functional teams of business leaders from key countries jointly develop ambitious, locally driven global brand plan strategies aimed at achieving higher peak sales for our key strategic brands. By deploying more rigorous forecasting models based on data from systematic market research, we aim to proactively shape the market and our products.

In order to enhance interactions between Aventis representatives and physicians, we are making use of virtual detailing and Web-enabled videoconferencing, for example via iPhysician.Net. Virtual detailing technologies are being deployed to increase the quality and efficacy of communications with physicians.

In the United States, certain products such as the seasonal allergy drug *Allegra* and the flu vaccine *Fluzone* are also marketed directly to consumers by way of television, newspaper and magazine advertising.

Aventis operates the e-commerce site VaccineShoppe (www.vaccineshoppe.com) in the U.S., which offers healthcare professionals the opportunity to go online for secure, automated product ordering. The site features immediate pricing confirmation and order-tracking functions as well as complete prescribing information for all Aventis vaccines and products.

While seasonality does not impact the core pharmaceutical business significantly, sales of individual products such as the allergy drug *Allegra/Telfast* and flu vaccines may reflect seasonal fluctuations in demand. In the northern hemisphere, for example, approximately 80% to 85% of flu vaccine sales are generated between August and November.

Although specific distribution patterns vary by country, Aventis generally sells its prescription drugs primarily to wholesale drug distributors, independent and chain retail drug outlets, physicians, hospitals, clinics, managed care organizations and government institutions.

Aventis also pursues co-promotion/co-marketing opportunities with other companies when economically attractive. Major arrangements currently include an agreement with Procter & Gamble for the osteoporosis drug *Actonel*, with Teva Pharmaceuticals for the multiple sclerosis drug *Copaxone*, with Yakult for *Campto*, and with Daiichi for *Tavanic*.

Competition

Aventis operates in a global environment in which our pharmaceutical products compete primarily against other branded, patented drugs from large national and international competitors. However, we may also face competition, sometimes significant, from generic prescription products, which typically enter the market as patent protection and regulatory exclusivity expire, but they may also gain entry to the market through successfully challenging patents of the innovator company. Aventis also can be subject to competition from over-the-counter and behind-the-counter products, i.e. drugs available without a prescription but only dispensable by a trained pharmacist. This is often the case when, for example, a significant competing prescription drug switches to over-the-counter status, or a competing U.S. prescription product might be sold behind-the-counter in another country while our product is sold by prescription there.

Another competitive issue facing pharmaceutical manufacturers is the increasing prevalence of parallel trade, which takes place when drugs sold abroad under the same trade name as in the domestic market are then imported into the home market by parallel traders, who repackage and resize the original branded product. The rationale for parallel imports lies in economic advantages arising from different prices for the drugs due to different sales costs, market conditions (e.g. intermediate trading stages) and tax rates or because of national price fixing arrangements. Although for the past few years parallel trade had been traditionally confined to some markets within the European Union, there are signs that it is now taking a foothold in several other regions including South Africa, the Philippines, India, Russia and Israel, and is expanding into eastern Europe under the EU Enlargement program.

The global pharmaceutical industry, which is highly fragmented, is undergoing a process of consolidation worldwide, driven by rising research and development costs for new therapies, healthcare cost-containment efforts and the desire to achieve synergies and economies of scale. The ten leading

producers account for about 46% of the market, with no single company estimated to account for more than 8% of total global pharmaceutical sales in 2002. Individual companies may have much higher market shares in specific countries or within a targeted therapeutic area. Our principal competitors are other international research-based pharmaceutical companies, particularly AstraZeneca, Bristol Myers Squibb, Eli Lilly, GlaxoSmithKline, Merck & Co., Novartis, Pfizer, Pharmacia, Roche, Sanofi-Synthelabo and Wyeth. In the human vaccines business, four main players control approximately 85% of the vaccine market: Wyeth, GlaxoSmithKline, Merck & Co. and Aventis Pasteur, each of which holds a roughly equivalent market share.

Regulation

The pharmaceutical industry is highly regulated. Government laws and regulations control testing, approval, manufacturing, labeling and marketing. Significant clinical trials must be conducted to establish for the satisfaction of regulatory authorities that proposed new products are safe and effective. Monitoring of adverse reaction reports continues after approval to assess a drug's continued safety. Regulatory authorities in many countries establish prices for many products. These requirements – which vary according to product and the jurisdiction concerned – are significant factors in determining whether a compound can be developed into a marketable product and in which markets it can be sold.

Product Regulation

Prescription pharmaceuticals must receive regulatory approval before they can be marketed in individual countries. The regulatory requirements follow stringent standards that vary among different countries. In general, before a drug can qualify for marketing approval, a registration dossier must be submitted to a regulatory authority for review and evaluation. The registration dossier principally contains detailed information about the safety and efficacy of a new medication. It also provides details about the manufacturing process, the proposed production facility and information to be provided to patients. The registration process can last from a few months to several years and depends, among other things, on the jurisdiction in which the review takes place, the nature of the medication under review, the quality of the submitted data and the efficiency of the review procedure.

If a drug meets the approval requirements, a regulatory authority may grant a product license for marketing. After the product launch and during marketing, the manufacturer monitors for potential adverse reactions and reports information as appropriate to the relevant regulatory authorities.

The process of developing a pharmaceutical product from discovery through testing, registration and initial product launch typically takes 10 to 15 years and, according to recent research by the Tufts Center for Drug Development, exceeds US\$ 800 million. There are three phases to clinical testing of unapproved new compounds in humans:

- Phase I involves the first trial of a new compound in humans. The focus at this phase is an assessment of clinical safety, tolerability, and metabolic and pharmacologic properties. Testing generally is performed in a small number of human volunteers.
- Phase II trials are controlled clinical studies that test the safety and efficacy of the compound in several hundred patients with the targeted disease. The goals of this phase include determining the appropriate dose(s) for further testing and evaluating potential study endpoints, as well as identifying common side effects and risks that may be associated with the drug.
- Phase III trials establish safety and effectiveness for regulatory approval for indicated uses and to evaluate overall benefit-risk relationship. These studies usually include from several hundred to several thousand people.

The results of these clinical trials are then submitted to appropriate regulatory authorities with the objective of obtaining approval to sell the drug. After approval and commercial launch, additional clinical trials may be conducted to further evaluate the safety and efficacy of the products in large patient groups and to investigate potential new applications.

The principal regulatory authority in the United States is the Food and Drug Administration (FDA), which administers and executes requirements covering the testing, approval, safety, effectiveness,

manufacturing, labeling and marketing of prescription pharmaceuticals. Pharmaceutical companies and the FDA follow careful scientific procedures to evaluate drug safety at four distinct stages:

1. Preclinical safety assessment
2. Pre-approval safety assessment in humans (clinical trials)
3. Safety assessment during FDA regulatory review (usually completed in 10 to 12 months)
4. Postmarketing safety surveillance

In the European Union, there are two procedures for granting marketing authorization:

- The centralized procedure is compulsory for medicinal products derived from biotechnology and is also available at the request of companies for other innovative products including all new active ingredients. In the centralized procedure the license application is submitted directly to the European Agency for the Evaluation of Medicinal Products (EMA), in London. After assessing the application, as a rule within the stipulated 210 days the Committee for Proprietary Medicinal Products (CPMP) votes on its acceptance or rejection. Within a further 90 days the European Commission takes a final binding decision. During the decision-making process a Member State can oppose the decision. Approval via the centralized procedure is valid through the European Union without further action and the drug may be marketed within all EU member states.
- The Mutual Recognition Procedure operates by having one country carry out the primary evaluation of a new compound. The other EU member states then have 90 days to decide if they accept or reject the decision made by the reference member state. If the countries do not follow the decision of the reference country, then the process can be referred to the CPMP and will be reviewed there as in the centralized procedure. The European Commission makes the formal decision based on this evaluation. Taking into account the Commission's decision, each member state will individually make a decision with respect to the application, which may or may not be consistent with the Commission's decision.

In Japan, although the Japanese regulatory authorities now recognize foreign clinical data developed outside of Japan, we still face two particular challenges that make the approval process sometimes difficult for drugs developed outside of Japan. First, the Japanese regulatory authorities request so-called "bridging studies" to verify that foreign clinical data is applicable to Japanese patients. Second, the Japanese authorities require the tests to determine appropriate dosages for Japanese patients be conducted on Japanese patient volunteers. Due to these requests, delays of two or three years in introducing a drug developed outside Japan to the Japanese market are possible.

In recent years, efforts have been made between the European Union, the United States and Japan to achieve shorter development and registration times for medicinal products by harmonizing the individual requirements of the three regions. The process is called the International Conference on Harmonization. For the foreseeable future, however, approval must be obtained in each market.

Price Controls

In most markets in which Aventis operates, governments exercise some degree of control over pharmaceutical prices. The nature of these controls and their effect on the pharmaceutical industry vary greatly from country to country. In recent years, national healthcare reimbursement policies have become more stringent in a number of countries in which we do business as part of an overall effort to reduce the cost of healthcare. Different methods are applied to both the demand and supply side to control pharmaceutical costs, such as reference pricing, patient co-payment requirements, reimbursement limitations and volume containment measures.

We believe that the governments in markets important to our businesses will continue to enact measures in the future aimed at reducing the cost of pharmaceutical products to the public. It cannot be predicted with certainty what future effects the various pharmaceutical price control efforts will have on our pharmaceutical business. These efforts could have significant adverse consequences for the pharmaceutical industry as a whole and consequently, also for Aventis. Increasing budgeting and price controls, the inclusion of patent-protected drugs in fixed price systems and approved drug lists and other similar measures may continue to occur in the future.

United States. In the United States, Medicaid, Medicare and other healthcare programs govern provider reimbursement levels in many cases. The Medicaid program requires that pharmaceutical manufacturers pay

rebates to individual states on Medicaid reimbursed pharmaceutical products so that the Medicaid program receives the manufacturer's "Best price." U.S. federal and state governments are actively seeking ways to reduce the costs of pharmaceutical products paid for with federal and state funds. Further attempts to reform Medicaid/Medicare can be expected to shift public sector beneficiaries from traditional fee-for-service coverage into managed care plans.

France. In France, the government regulates prices on new prescription pharmaceutical products and price increases on existing drugs. In 2002, the French government introduced another new set of healthcare reforms known as the "Mattei Plan." This plan is aimed at redefining reimbursement conditions and criteria for the pricing of pharmaceutical products through the Drug Pricing Committee, and encouraging generic drug development. In June 2002, French doctors and health insurers reached an agreement under which doctors were given an incentive to prescribe by international non-proprietary names (INN). A new reference pricing system is to be introduced in France in July 2003 under which the government will reimburse off-patent products only up to a certain level with patients paying the remainder. In addition, the French health ministry has proposed to delist several hundreds products of "insufficient" medical benefit. In return, the government introduced the principle of a "fast-track" procedure to set prices and provide reimbursement for new innovative drugs. This measure could extend by many months the commercialization duration under patent.

Japan. The Ministry for Health, Labor and Welfare ("MHLW") controls the pricing of pharmaceutical products in Japan. The MHLW determines the drug reimbursement price paid by the National Health Institute ("NHI") to medical institutions. The NHI drug reimbursement price is determined for each prescription drug by the MHLW. The price of a new drug is based on the daily price of comparable drugs, with certain premiums added as necessary. Since the price at which medical institutions purchase drugs can be set at a price lower than the reimbursement price through negotiation with wholesalers, a gap may exist between the selling price and the NHI drug price. Periodically, the MHLW carries out a revision of drug reimbursement prices aimed at bringing NHI prices closer to the market prices.

Germany. Since the late 1980s the German government has imposed a wide range of supply- and demand-side restrictions intended to curb the level of overall spending on pharmaceuticals. A reference pricing system that requires patients to pay the difference between the actual price of the prescribed drug and the reference price has been in existence since 1989. In practice, patients are not generally willing to pay the difference. As a result, pharmaceutical companies face the decision either to adopt the reimbursement price or risk a substantial drop in prescriptions. Since 1993, all prescription drugs have been subject to patient co-payments that depend on the pack size. In order to restrict the prescribing practices of physicians, prescription drug budgets for physicians were in effect from 1993 through the end of 2001. Physicians were penalized if they exceeded their budgets. New legislation replacing these budgets requires the negotiation of pharmaceutical expenditures between the Institutes of Statutory Health Insurance (SHI) and the National Association of SHI-accredited Physicians, and individual prescription limits for physicians. The objectives of the legislation include an increase in the prescribing of generic and imported drugs. In addition, sickness funds and pharmacists have agreed on a quota for sales of imported pharmaceuticals (parallel imports) of 5.5% of the German market for 2002, which will increase to 7% in 2003. To encourage greater use of generics, generic substitution by pharmacists, commonly referred to as the aut-idem law, was introduced in February 2002. Under healthcare legislation that came into effect on January 1, 2003, pharmaceutical companies are required to provide a 6% rebate on innovative medicines which are not covered by pharmacy substitution or reference pricing but are reimbursed by the statutory health insurance.

Italy. A series of cost-cutting initiatives were introduced in Italy in 2002, including the introduction of a reference pricing system and a 5% pharmaceutical price cut. A new reimbursement system, which will set maximum reimbursement limits by therapeutic class, is expected to take effect in January 2003. Under the new system, government reimbursements will be set at a level determined by the Health Ministry's Pharmaceutical Committee (CUF) based on sales by defined daily dose for all active ingredients. Products priced at levels above the reference prices will no longer be reimbursed unless their prices are cut. The maximum price reduction per product has been set at 13%.

United Kingdom. The Department of Health has power, now contained in the Health Act 1999, to limit prices of pharmaceuticals and control the profits of pharmaceutical companies. Against this background, a voluntary agreement called the Pharmaceutical Price Regulation Scheme (PPRS) has been concluded between the industry association and the Department of Health. Within a framework relating to profit (as defined), manufacturers are free to set initial prices but restricted in making subsequent price changes. The current form of the PPRS runs from 1999 to 2004. The National Institute for Clinical Excellence (NICE) is empowered

to issue guidelines in relation to therapeutic areas and guidance on the clinical effectiveness and cost effectiveness of particular treatments. Guidance by NICE influences the extent to which supply of the product is financed within the National Health Service.

Intellectual Property

Aventis invested € 3.14 billion in core business R&D activities in 2002, and we are committed to rigorously protecting the value of the intellectual property associated with these activities.

Intellectual property includes patents, trademarks, registered designs and copyrights as well as all of the inventions and innovations of significant commercial value which arise from our drug discovery, development, manufacturing, marketing and other business activities.

Aventis has obtained patents covering our important pharmaceutical products in major markets and we intend to secure patent protection for products currently under development. We routinely monitor the activities of our competitors relating to our intellectual property, and we intend to enforce our intellectual property rights as necessary.

In the United States, the Hatch-Waxman Act of 1984 significantly influences the effectiveness of regulatory protection for prescription drugs (other than biological products). This Act assures that a newly approved drug or indication benefits from a statutory period of exclusivity (five years for a new drug and three years for a new indication for an existing drug) during which the U.S. Food and Drug Administration (FDA) will not grant marketing approval to generic competitors, even in the absence of patent protection on the original product. However, the expiration of the five-year exclusivity period does not reduce any patent protection that may otherwise apply. The same Act, however, has greatly accelerated the approval process for generic competitors using the same active ingredients once the statutory exclusivity (also referred to as “data exclusivity”) has expired. The Act may actually encourage more aggressive legal challenges to the patent protection of the original products.

Our portfolio of strategic brands sold in the United States is subject to the overlapping provisions of patent protection and Hatch-Waxman “data exclusivity.” These products may be subject to increased risk of competition from generics approved by the FDA. In particular, “data exclusivity” has expired with respect to a number of our products, including some strategic brands, and applications for approval of generic versions have been, or at any time can be, filed by third parties. The following is a description of U.S. patent and “data exclusivity” coverage of our strategic brands sold in the United States:

Actonel (risedronate sodium)

Procter & Gamble holds the New Drug Application (NDA) for *Actonel* that was filed with the FDA. The U.S. patent claiming the active ingredient, risedronate sodium, as a compound expires in December 2013, and patents covering different formulations expire in 2017 and 2018. This drug has non-patent “data exclusivity” as a new chemical entity until March 2003 and non-patent “data exclusivity” covering various indications that expires in April 2003.

Allegra/Telfast (fexofenadine)

Aventis Pharmaceuticals Inc., the U.S. pharmaceutical business of Aventis, filed patent infringement lawsuits against Barr Laboratories, Inc., in August and September of 2001 and in January 2002 after Barr filed Abbreviated New Drug Applications (ANDAs) seeking authorization to produce and market a generic version of fexofenadine HCl 60 mg capsules, 30, 60 and 180 mg tablets of fexofenadine HCl, and *Allegra-D*. In addition, Aventis Pharmaceuticals Inc. filed a patent infringement lawsuit against Impax Laboratories in March 2002 after Impax filed an ANDA for a generic version of *Allegra-D*. In the U.S., Aventis holds multiple method of use, formulation, process and composition patents with respect to *Allegra*. Under applicable federal law, marketing of FDA-approved generic fexofenadine HCl capsules or tablets or *Allegra-D* may not commence unless and until a decision favorable to a generic challenger is rendered in the patent litigation or until 30 months have elapsed, whichever comes first. Regulatory exclusivity for tablet formulations of *Allegra* expires in the third quarter of 2003. In late 2002 and early 2003, three other generic companies filed ANDAs for *Allegra* products. API has either brought a patent infringement lawsuit or is evaluating its legal options with respect to these additional filings.

Amaryl (glimepiride)

Non-patent “data exclusivity” for *Amaryl* expired in November 2000, but the U.S. patent claiming the active ingredient, glimepiride, as a compound does not expire until April 2005.

Arava (leflunomide)

Arava has non-patent “data exclusivity” as a new chemical entity until September 2003.

Lantus (insulin glargine)

Lantus has non-patent “data exclusivity” until October 2005 (extended from April 2005 due to pediatric exclusivity). The patent claiming the active ingredient, insulin glargine, as a compound does not expire until March 2015.

Lovenox/Clexane (enoxaparin sodium)

Non-patent “data exclusivity” for *Lovenox/Clexane* as a new chemical entity expired in March 1998. This product currently has non-patent “data exclusivity” covering one indication that expires in late 2003. Aventis holds two U.S. patents relating to *Lovenox/Clexane* that expire in 2004 and 2012, respectively.

Nasacort (triamcinolone acetonide)

Nasacort currently has a method of treatment patent expiring in 2007 and *Nasacort AQ* currently has two formulation patents expiring in 2016. At the present time, this product no longer benefits from non-patent “data exclusivity.”

Taxotere (docetaxel)

Non-patent “data exclusivity” for *Taxotere* as a new chemical entity expired in May 2001. The U.S. patent claiming the active ingredient, docetaxel, as a compound expires in May 2010, and a number of other U.S. patents covering this drug do not expire until between 2012 and 2013. In addition, non-patent “data exclusivity” covering one indication expired in December 2002.

Delix/Tritace (ramipril)

Aventis does not market *Delix/Tritace* in the United States. In the largest markets for this drug, patents claiming the active ingredient, ramipril, as a compound expire in Germany and Great Britain in 2004, in France in 2006 and in Italy in 2010. Aventis holds other patents in certain of these countries that expire between 2005 and 2008. In Canada, the patent claiming the active ingredient as a compound expires in 2018. However, an application for a generic version of *Delix/Tritace*, which challenges this patent, has been submitted to Canadian regulatory authorities. In addition, an ANDA for a generic has been filed in the U.S., where Aventis manufactures ramipril for the U.S. marketer. If this or any other ANDA for a generic ramipril is approved in the U.S., it could negatively affect Aventis’ revenues from manufacturing the product for U.S. distribution.

Property, Plant & Equipment

Our principal production plants and manufacturing facilities are located in France, Germany, the United States, the UK, Italy and Singapore.

The global Industrial Operations function of Aventis, which supplies approximately 450 brands in 29,000 presentation forms, consists of a network of roughly 55 sites in about 30 countries.

In 2002, Industrial Operations introduced several new initiatives to support the product leadership strategy of Aventis, to align its processes with those of DI&A and Commercial Operations and to differentiate and focus the plant network on strategic and non-strategic brands. As a result, a new product organization and site network structure have been established; the implementation of this site network concept began in 2002.

Headquartered in Frankfurt, Germany, Industrial Operations comprises:

- Active Pharmaceutical Ingredient (API) Operations, which is responsible for global production, process development and bulk sales of active pharmaceutical ingredients. API employs around 6,500 people in nine countries. The products of API cover 80% of our global demand for active ingredients. API produces more than 300 different active ingredients. Currently, there are 13 Production sites and five Process Development sites.
- Drug Product (DP) Operations, which is responsible for global manufacturing of drug products. DP Operations is divided in the regions North America, France, Germany, North and South Europe, International, Japan and Latin America.
- Global Quality and EHS looks after quality issues at Industrial Operations as well as all environment safety and health issues of Aventis.
- Global Purchasing provides purchasing services for Aventis.

Our major Active Pharmaceutical Ingredient (API) sites are located in:

France

Vitry

The Vitry site is dedicated to the production of pharmaceutical active ingredients for several therapeutic areas, such as oncology, cardiovascular diseases, anti-infectives, anti-inflammatories and neuroleptics. The area of the site is 210,000 m² and is FDA-approved.

Vertolaye

Production at this site, which covers an area of 200,000 m², is dedicated to pharmaceutical active ingredients, most of them for human use, and a few for veterinary use. The site has been approved by the FDA since 1974. The site is well-equipped and experienced in final processing of active ingredients, including micronization.

Neuville

The site area is about 300,000 m² and includes all necessary resources for production, as well as process development. It is FDA approved since 1981.

Smaller API sites are located in Elbeuf, Le Mans, Ploërmel, Romainville and Villeneuve.

Germany

Frankfurt-Höchst

The site covers an area of around 4 km² and is located in the suburb of Höchst, 10 km outside Frankfurt. Within API, seven production plants belong to the chemistry and another five to the biotechnology departments. The site is FDA approved.

Italy

Brindisi

The Aventis site is dedicated to fermentation (one plant) and the corresponding chemical down-stream processing steps (two plants), covers 150,000 m². The site is FDA approved.

Garessio

The Aventis site is exclusively dedicated to the chemical production of active ingredients and intermediates. It covers 280,000 m² and is FDA approved.

Jurong, Singapore

The Aventis site covers an area of 40,000 m² and employs 100 people in two chemical plants. Aventis has reserved the right to lease an adjacent second plot of land (4,000 m²) which would allow for future expansion. The site mainly produces enoxaparin, the active ingredient of *Lovenox*. The site is FDA approved.

Ankleshwar, India

API operates two multi-purpose chemical plants producing active ingredients for the region as well as intermediates for the global API network. The entire site, which is shared with Bayer CropScience, covers an area of 180,000 m².

Drug Product Operations (DPO) has eight sites with a strategic brand focus:

Location	Strategic brand
United Kingdom	
Dagenham	<i>Taxotere, Campto</i>
Holmes Chapel	<i>Nasacort AQ</i>
France	
Le Trait	<i>Lovenox</i>
Maisons-Alfort	<i>Lovenox</i>
Germany	
Frankfurt-Höchst	<i>Lantus, Insuman, insulin glulisine (1964)</i>
United States	
Kansas City	<i>Allegra, Amaryl, Tritace, Ketek</i>
Italy	
Agnani	<i>Targocid, Synercid</i>
Scoppito	<i>Allegra, Amaryl, Tritace, Ketek</i>

Drug Product Operation sites with a non-strategic brand focus are also located in Compiègne, France; Kawagoe, Japan; Laval (Quebec), Canada; Suzano, Brazil; and Ocoyoacac, Mexico.

The policy of Aventis is generally to acquire our own facilities or lease them under long-term leases. The net book value of our property, plant and equipment was € 4,455 million as of December 31, 2002. Our pharmaceutical production plants and manufacturing facilities are in full compliance and generally adequate to meet our needs for the foreseeable future. However, we conduct annual reviews of our production plants with regard to environment, health and safety issues, quality compliance and capacity utilization. Based on this review, we record, if necessary, impairment losses for the modernization, divestment or closing of specific production plants. We are not aware of any environmental issues that we believe could have a significant effect on the utilization of our industrial assets.

The locations and size of our manufacturing facilities for human vaccines are as follows:

- Marcy l'Etoile; 340,000 m²
- Val de Reuil, France: 290,000 m²
- Swiftwater, Pennsylvania U.S.A. 1,100,000 m²
- Toronto, Canada: 210,000 m²

For more information on our Property, Plant and Equipment, see "Item 5. Other Material Financial Elements" and Note 3 of the Aventis Consolidated Financial Statements included at Item 18 of this Annual Report.

For a discussion of environmental factors related to our principal production plants and manufacturing facilities, we refer you to Exhibit 99.1, the "Aventis Sustainability Report for 2002," the portion of which under the caption "Environmental Performance" is incorporated herein by reference.

Non-Core Businesses

Aventis CropScience

In October 2001, Aventis and partner Schering AG of Germany announced the intention to divest Aventis CropScience to Bayer AG in a sale assigning this business an enterprise value of approximately € 7.25 billion, including € 1.9 billion in debt. The transaction closed on June 3, 2002. Bayer is currently seeking a substantial post-closing price adjustment as permitted under Section 6 of the stock purchase agreement between us and Bayer. Bayer also has requested compensation for damages it claims to have suffered as a result of alleged inaccuracies in contractual representations and warranties. Aventis has recorded provisions that it believes will be sufficient to cover potential liability to Bayer. Up until its disposal in June 2002, Aventis CropScience generated consolidated sales for Aventis of € 1,831 million compared to € 4,303 million for all of 2001.

Aventis Animal Nutrition

In April 2002, we completed the sale of the animal nutrition business to CVC Capital Partners Ltd., a Europe-based financial private equity company. Up until its disposal in April 2002, the animal nutrition business generated consolidated sales for Aventis of € 143 million compared to € 572 million for all of 2001.

Aventis Behring

The therapeutic proteins business, Aventis Behring, is a global leader in the therapeutic protein and recombinant products industry, providing a wide range of innovative, high quality therapies and unique support services to patients worldwide. Sales in 2002 totaled € 1,068 million, which compares with € 1,129 million in 2001.

Rhodia

As of December 31, 2002, Aventis held a 25.2% equity stake in the specialty chemicals group Rhodia, which was formerly a unit of Rhône-Poulenc and was listed on the Paris stock exchange as well as the New York Stock Exchange in 1998. After the listing, Rhône-Poulenc continued to divest its interest in Rhodia through a secondary placement of Rhodia shares and an issuance of notes exchangeable into the remaining Rhodia shares held by Aventis. The notes had a principal amount of € 23.22 each and were exchangeable at the option of the holder into one share of Rhodia until October 2003 (subject to early redemption rights of Aventis). On November 29, Aventis launched a cash tender offer with respect to all of its 45,211,662 outstanding 3.25% exchangeable bonds due October 22, 2003, nominal value € 23.22 each. Following the five-day offer period that closed on December 5, 2002, almost all the bonds had been tendered, and Aventis acquired 98.6% of the bonds initially issued. This level was well above the 80% minimum acceptance threshold and Aventis has exercised its early redemption option on all the outstanding bonds. The early redemption was completed on January 17, 2003. This tender offer and redemption will provide Aventis with increased flexibility regarding the disposal of its stake in Rhodia. In connection with our 1999 business combination, we have committed to the European Commission that we will complete this disposal by April 2004.

Wacker

In December 2000, we agreed to sell our 50% stake in Wacker-Chemie GmbH, a 50-50 joint venture between Hoechst and the Wacker family trust, to the Wacker family in two stages. In the first stage carried out in January 2001, Alexander Wacker Familien GmbH, a holding company in which the remaining 50% stake in Wacker is held, acquired the majority of voting rights in Wacker via a capital increase, and gained management control over the group. Hoechst is currently in discussions with the Wacker family concerning the terms and the timing of the second stage of the transaction.

DyStar

Aventis, through its Hoechst subsidiary, holds a 35% stake in DyStar, a global leader in the textile dyes business. In October 2000, DyStar was enlarged to include the textile dyes business of BASF, a former principal competitor, from its prior status as a 50-50 joint venture between Hoechst and Bayer. Under the new structure, Hoechst and Bayer each hold a 35% stake and BASF holds 30%.

Dade Behring

Dade Behring, a leading diagnostics company, was formed in 1997 through the combination of Hoechst's diagnostics business, Behring Diagnostics, with Dade International. We have classified our stake in Dade Behring as a non-strategic holding since January 1, 2001 and wrote off its book value in full in 2001.

On August 1, 2002 Dade Behring filed for a voluntary reorganization under Chapter 11 of the U.S. bankruptcy law. On October 3, Dade Behring emerged from Chapter 11. At that point Aventis contributed its 51.8% stake and is now no longer a shareholder.

