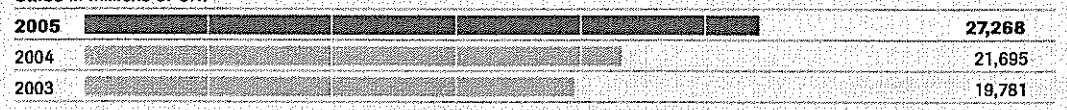
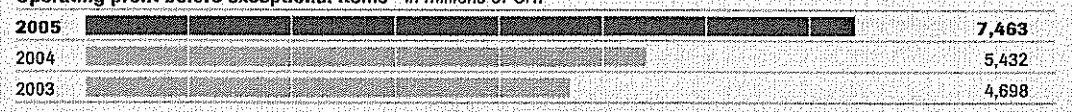
EXHIBIT E

Pharmaceuticals Division in brief

Sales *in millions of CHF*

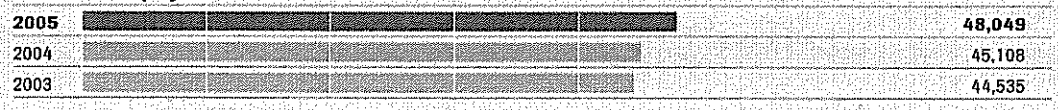


Operating profit before exceptional items[1] *in millions of CHF*



1) From 2004 including charges for all equity compensation plans.

Number of employees



Key figures

	In millions of CHF	% change in CHF	% change in local currencies	As % of sales
Sales	27,268	26	25	100
– Roche Pharmaceuticals	16,955	21	20	62
– Genentech	6,614	46	46	24
– Chugai	3,699	15	17	14
EBITDA	8,997	30	29	33.0
Operating profit[1]	7,463	37	37	27.4
Research and development	4,986	12	12	18.3

1) Before exceptional items.

Pharma Executive Committee *1 January 2006*

William M. Burns	CEO Division Roche Pharmaceuticals
George C. Abercrombie	North America
Jennifer Allerton	Informatics
Eduard Holdener	Development
Peter Hug	Partnering
Jonathan K.C. Knowles	Research
Dominic Moorhead	Finance and Controlling
Paul Newton-Syms	Human Resources
Charles Sabbah[1]	Strategic Marketing
Pascal Soriot[2]	
Claude Schreiner	Western Europe
Jan van Koeveringe	Technical Operations

1) To 28 February 2006.
2) From 1 March 2006.

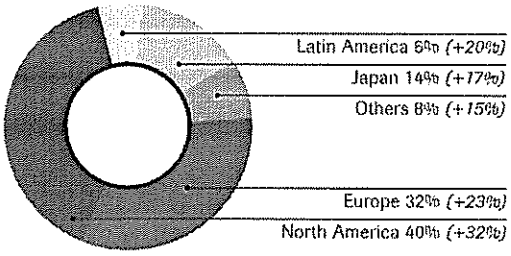
Pharmaceuticals

Results

In 2005 the Pharmaceuticals Division recorded its best result ever, exceeding the high, above-market growth of the previous year. Sales for the full year rose 25% in local currencies (26% in Swiss francs and 25% in US dollars) to 27.3 billion Swiss francs, four times as fast as the global market. The gains also more than offset the decline of the Group's former top-selling medicine Rocephin following the expiry of its US patent in July. As in 2004, growth was driven primarily by strong demand for the division's flagship oncology portfolio, now boosted by the innovative cancer treatments Avastin and Tarceva, and by strong sales of CellCept (transplantation) and Pegasys (hepatitis B and C). The anti-influenza drug Tamiflu, which many governments are stockpiling as part of pandemic readiness programmes, also contributed to growth. The division's oncology, transplantation and virology franchises significantly outpaced their respective markets.

Operating profit before exceptional items increased again, by 37% to 7.5 billion Swiss francs. The operating profit margin before exceptional items gained 2.4 percentage points, rising from 25.0% in 2004 to 27.4% in 2005. This improvement was achieved despite higher investments in R&D, continued product launch activities and, by comparison with 2004, much lower gains from product divestments. EBITDA totalled 9 billion Swiss francs or 33.0% of sales, compared with 32.0% the previous year.

Sales by region



Italic = growth rates.

Therapeutic areas

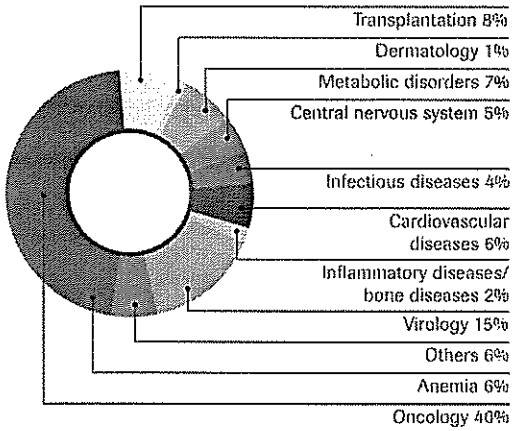
Oncology

Cancer is one of the main causes of death in industrialised countries, and the Roche Group is at the forefront of the search for better solutions for patients and physicians in this important area of unmet medical need. Roche is pioneering a number of advances in cancer treatment, including targeted therapy. MabThera/Rituxan, Herceptin, Avastin, Tarceva and Xeloda are all examples of the Roche Group's innovative cancer treatments.

Two thousand and five was an outstanding year for the Roche Group's oncology portfolio[1]. Sales of oncology products grew 42%[2] and now account

1) Oncology portfolio: MabThera/Rituxan, Herceptin, Avastin, Xeloda, Tarceva, Bondronat, Kytril, Furtulon, Neupogen, NeoRecormon (36%), Roferon-A (70%), Neutrogin, Picibanil, Vesanoid.
2) Unless otherwise stated, all growth rates are in local currencies.

Sales by therapeutic area



for 40% of divisional sales. All major brands contributed to this result, which has substantially reinforced the Group's position as the world's leading provider of cancer medications.

Non-Hodgkin's lymphoma (NHL), a group of malignancies of the lymphatic system, affects approximately 1.5 million people worldwide and claims an estimated 300,000 lives each year. Sales of MabThera/Rituxan (rituximab), for the treatment of indolent and aggressive forms of NHL, were strong throughout the year, driven by a steady rise in prescriptions for both forms of NHL in Europe. In August Genentech and Biogen Idec filed a supplemental application with the US Food and Drug Administration (FDA) for approval of the product for use in untreated patients with intermediate grade or aggressive NHL. A pivotal international phase III clinical trial has shown that two years of maintenance therapy with MabThera/Rituxan dramatically improves the chances of survival of patients suffering from indolent non-Hodgkin's lymphoma, regardless of their initial therapy. Based on these results, Roche filed an application with EU regulators in December to expand the product's indications to include maintenance treatment in patients with indolent NHL. (See *Major development activities*, pp. 26–29, for information about ongoing clinical development programmes with MabThera/Rituxan and other products.)

Breast cancer is the most common cancer among women worldwide, with over 1 million women newly diagnosed and almost 400,000 dying from the disease each year. There are different types of breast cancer, and knowledge of tumour characteristics is essential for determining appropriate treatment. Herceptin (trastuzumab) is designed specifically for a particularly aggressive type of tumour (HER2-positive) that accounts for approximately 20–30% of all breast cancers. Sales of Herceptin, the only targeted treatment approved for HER2-positive breast cancer, showed impressive gains in all key markets in 2005. Strong growth in the US and Europe was driven by extensions in treatment duration and increased first-line penetration. Herceptin is also supported by a considerable, and growing, body of clinical data showing that the product offers significant survival benefits in the advanced and early disease settings. As a result of very strong data reported in 2005, Herceptin is already being used and reimbursed in some countries in the adjuvant (early disease) setting in advance of approval. (See also *Major development activities, Oncology*, p. 27, *Setting new standards in cancer treatment*, p. 30, and patient story, p. 71.)

Skeletal complications, including hypercalcemia, bone lesions and fractures, are often associated with cancer. Following the rollout of Bondronat (ibandronic acid) in major European markets for the prevention of skeletal events in patients with breast cancer and bone metastases, sales increased strongly, by 108% to 79 million Swiss francs.

Colorectal cancer – cancer of the large intestine or rectum – accounts for over 1 million new cases (around 10% of all newly diagnosed cancers) worldwide each year. It is the second most common cause of cancer deaths in Europe. The main treatment is surgery, which may also be combined with radiotherapy and chemotherapy.

Avastin (bevacizumab), the first anti-angiogenic drug for the treatment of cancer, generated an impressive 1.7 billion Swiss francs in sales in its first full year on the market. Already approved in the US for the treatment of advanced colorectal cancer, Avastin received EU approval for the same indication in January 2005 and has now been launched in

Oncology professionals moved at ASCO

More than 20,000 oncology specialists and other professionals attended the 41st American Society of Clinical Oncology (ASCO) Meeting in Orlando, Florida, last May. Also present was Jonas Marques, oncology/hematology sales manager at Roche Brazil, who was particularly interested in the special session on Avastin and Herceptin.

Both products were featured in a packed session that clearly moved the attendees, who considered the studies presented extremely important because of their impact and consistent findings. During the Herceptin presentation, one of the world's leading oncologists remarked, 'Biology has spoken, and we must listen,' and added, 'Herceptin has ushered in a new era of breast cancer treatment.'

The presentation's impact was evident. 'After the session,' says Jonas 'one Brazilian specialist called his clinic to prescribe Herceptin as adjuvant therapy for patients he had already treated for breast cancer in the last six months.'

Oncologists were also very impressed with the data on Avastin, which appears to have potential for treatment of cancers other than colorectal. It is currently awaiting approval in Brazil.

The 7,000 attendees responded with a standing ovation. 'This is the first time I have seen this at any type of data presentation,' says Jonas. 'I think it says a lot about the impact of these products on the cancer world.'

Jonas joined the Roche Brazil oncology team in 2002 and has always been aware of the importance of his work to patient care. 'The Herceptin presentation at the 2005 ASCO Meeting has given my job new meaning. Women with HER2-positive breast cancer may now have a real chance for long-term survival.'

key European markets. Sales in the US continue to show rapid growth, while uptake in Europe has also been very strong. (See patient story, p. 85.)

Sales of Xeloda (capecitabine) continued their strong upward trend in 2005, with impressive gains in all major markets. Growth has been fuelled by recent US and EU approvals for the use of the product for adjuvant treatment (after surgery) of colon cancer.

With an estimated 1.2 million new cases annually, lung cancer is the most common cancer worldwide. It is the leading cause of cancer deaths in the world and in Europe. Pancreatic cancer, one of the most aggressive malignancies, kills a higher proportion of patients in the first year after diagnosis than any other cancer. It is often resistant to chemotherapy and radiotherapy and tends to spread quickly to other parts of the body. Pancreatic cancer is the fifth leading cause of cancer deaths in the developed world and the tenth most frequent cancer in Europe, where it kills some 78,000 people per year.

In its first full year on the market, Tarceva (erlotinib), a novel targeted cancer drug with proven survival benefit in advanced non-small cell lung cancer and pancreatic cancer, generated robust

sales. Market response to the product has been very positive. Following US approval late in 2004 for second- or third-line treatment of non-small cell lung cancer, the product received EU approval for the same indication in September 2005. It has already been launched in several European countries, with rollouts in further markets scheduled throughout 2006. In November the FDA approved Tarceva for the treatment of advanced pancreatic cancer; a filing for this indication was submitted to EU regulators in October.

Anemia

Anemia occurs when the number of red blood cells falls below normal, starving organs and tissues of oxygen. It is seen in over 80% of patients with impaired renal function due to chronic kidney disease and in up to 60% of patients with cancer. The potential long-term effects of anemia include cardiovascular disease in renal patients and reduced survival in patients with cancer. Anemia can be fatal if left untreated.

Sales of Roche's NeoRecormon and Chugai's Epogin (epoetin beta), for the treatment of anemia, showed healthy growth in 2005. NeoRecormon retained its leadership position in its markets despite sustained pricing pressure, with both indications (cancer-related anemia and renal anemia) contributing to an 11% increase in sales. In the oncology setting NeoRecormon continued its strong market penetration, posting growth of 21%, well ahead of the market (9%), thanks primarily to continued adoption of the convenient once-weekly prefilled syringe formulation. NeoRecormon is now indicated for the treatment of anemia in patients with all solid and lymphoid cancers receiving any form of chemotherapy.

Transplantation

Some 70,000 people worldwide receive life-saving organ transplants each year. Thanks to advances in surgical procedures and immunosuppressive therapy to prevent organ rejection, transplant recipients can now survive for many years with their new organs. This means increased demand for effective, low-toxicity immunosuppressant drugs like CellCept (mycophenolate mofetil), which has proven long-term organ and patient survival benefits. Zenapax (daclizumab), which prevents the acute rejection of newly transplanted organs, and Valcyte (valganciclovir), for the prevention of cytomegalovirus (CMV), a dangerous infection associated with transplantation, complete the Roche transplantation portfolio. Roche supports basic transplantation research through its funding of the independent Roche Organ Transplantation Research Foundation.

The Roche Group maintained its global leadership in the transplantation market in 2005. The Group's transplantation portfolio generated total sales of 2.2 billion Swiss francs, a rise of 19% over the previous year. The immunosuppressant CellCept posted solid double-digit gains globally and in its key regions, maintaining its leadership of the mycophenolic acid market (with a market share of over 95%) despite the entry of a new competitor.

Valcyte, the market leader for prevention of CMV disease, showed consistent growth throughout the year. A solid double-digit gain was recorded for combined sales of Valcyte and Cymevene (ganciclovir).

Virology

The liver is one of the body's most important organs, performing over 500 vital functions. The hepatitis B and C viruses (HBV, HCV) both cause acute and chronic liver disease, potentially leading to liver failure, cirrhosis and cancer. Worldwide, 350 million people are thought to be chronically infected with HBV, a highly infectious pathogen that is responsible for an estimated 1 million deaths annually. More than 170 million people around the world are infected with HCV, and 3 to 4 million new cases occur each year. Hepatitis C is the main reason for liver transplantation.

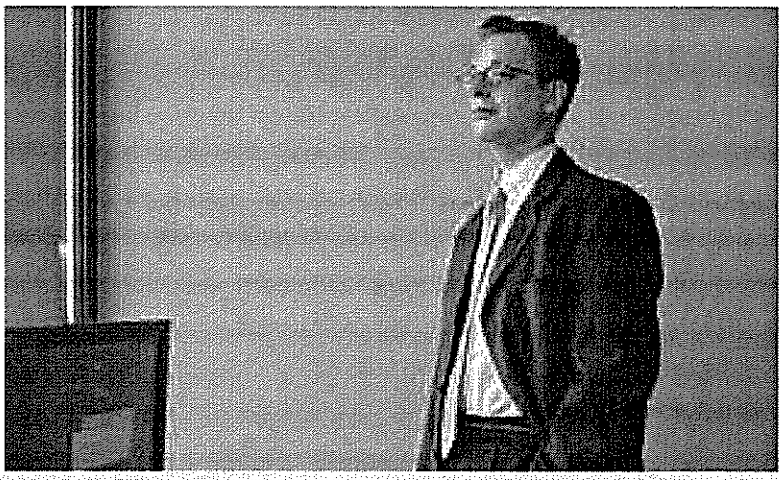
Combined sales of Pegasys (peginterferon alfa-2a) and Copegus (ribavirin) showed strong growth in 2005. In particular, higher sales volumes in Europe were driven by market share increases and market expansion as a result of new indications. Significant approvals towards the end of 2004 and early in 2005 have given the Pegasys plus Copegus combination the broadest range of hepatitis C indications

Meeting world demand for Tamiflu

The World Health Organization (WHO) recommends that governments stockpile antivirals in preparation for a possible influenza pandemic as part of their overall pandemic plans. Roche is assisting governments by dramatically expanding Tamiflu production capacity to respond to this critical need.

Armin Knoblich, global supply chain leader for Tamiflu, is proud to be part of an international task force of Roche specialists who have been working around the clock to ramp up supply quickly. 'To be able to produce over 300 million treatments annually by 2007,' he says, 'we are expanding our network of suppliers, third-party manufacturers, and licensees and selectively investing in our own facilities. That way, we can meet the demand for Tamiflu while keeping our manufacturing network flexible enough to respond to the situation in future.'

New production processes will also play a role. For example, shikimic acid, the starting material for Tamiflu,



is extracted from star anise, a plant native to four provinces in China. But shikimic acid can also be produced in large quantities by a special fermentation method that does not rely on star anise. By expanding production of shikimic acid by fermentation, Roche is helping to ensure that Tamiflu production is not held back by a crop failure or other disruption of supply.

of any product or combination, including use in patients co-infected with HIV and in those with normal liver enzyme levels. An application for approval of combined Pegasys and Copegus in hepatitis C by Chugai has been designated for priority review by the Japanese authorities. Pegasys is also approved for the treatment of hepatitis B in over 50 countries worldwide.

Worldwide sales of Tamiflu (oseltamivir) rose to 1.6 billion Swiss francs, driven by a severe influenza season in Japan early in the year and increased orders for pandemic readiness supplies. Over 60 countries have now placed orders for pandemic stocks of Tamiflu, with some purchasing enough to cover 25–40% of their populations. Roche has agreed to donate over five million packs of Tamiflu to the World Health Organization (WHO): two million packs to be kept in regional stockpiles for use in the event of outbreaks of avian influenza and another three million packs in central storage, reserved for use as a rapid response stockpile to contain an influenza pandemic outbreak. Roche continues to substantially expand its Tamiflu production capacity and will be able to produce over 300 million treatments annually by 2007, using a collaborative network of its own facilities and those of a significant number of independent companies. In October Roche announced its willingness to enter discussions with governments and other manufacturers on the production of Tamiflu for emergency pandemic use. Roche has since signed sublicensing agreements with Shanghai Pharmaceuticals for China and Hetero Drugs in India and is in discussion with twelve additional partners to enhance the Tamiflu production network. At the end of the year the FDA approved and the EMEA and the Swiss authorities recommended approval of the product for prevention of influenza in children aged 1–12 years. (See *Meeting world demand for Tamiflu*, above, and *Access to medicines*, p. 31.)

Major product approvals and launches in 2005[1)]

Product	Generic name	Indication	Country
Avastin	bevacizumab	first-line treatment in combination with chemotherapy of metastatic colorectal cancer	EU
Bonviva/Boniva	ibandronic acid	osteoporosis, oral once-monthly formulation	EU, USA, Switzerland
		osteoporosis, intravenous formulation	USA
Invirase	saquinavir	HIV disease, 500 mg formulation	EU, Switzerland
Pegasys	peginterferon alfa-2a	chronic hepatitis B	EU, USA
		HCV-HIV co-infection	EU, USA, Switzerland
Tarceva	erlotinib	second- or third-line treatment of advanced non-small cell lung cancer	EU, Switzerland
		advanced pancreatic cancer, in combination with gemcitabine	USA
Xeloda	capecitabine	adjuvant colon cancer monotherapy	EU, USA Switzerland

1) Includes supplemental indications; updated to 6 January 2005.

HIV is a worldwide pandemic, and the number of people living with HIV continues to rise. The World Health Organization estimates that 40.3 million people, including more than 2.3 million children, were living with HIV/AIDS at the end of 2005. For almost 20 years Roche's innovative drugs and diagnostic tests have placed it at the forefront of efforts to combat HIV infection and AIDS, and we will continue working to improve the standard of HIV care worldwide. For information on Roche's HIV/AIDS initiatives, see *Access to medicines* (p. 30), *Ensuring access to healthcare worldwide* (p. 79), and visit www.roche.com.

Sales of Fuzeon (enfuvirtide) increased 53% to 259 million Swiss francs in 2005, helped by data from major studies showing the added value of Fuzeon when prescribed together with the latest anti-HIV agents. Recent updates to key treatment guidelines also support Fuzeon use in treatment-experienced patients and are expected to drive further uptake of the drug.

Primary care

Osteoporosis causes a gradual loss of bone density, making bones brittle and prone to break. It affects millions of people worldwide, especially women after the menopause.

Bonviva/Boniva (ibandronic acid), the first and only once-monthly oral bisphosphonate approved for the treatment of postmenopausal osteoporosis, was launched by Roche and its copromotion partner GlaxoSmithKline in the US in April and in Europe in September. Sales totalled 86 million Swiss francs and are expected to gain further momentum as physicians and patients recognise and prefer the simplicity and convenience of a once-monthly tablet. In January 2006 Boniva Injection became the first intravenous medication to be approved in the US for the treatment of postmenopausal osteoporosis, providing the proven bone-strengthening benefits of bisphosphonate therapy to more women. Given once every three months, Boniva Injection is designed to meet the needs of patients who are unable to take or tolerate oral bisphosphonates. The EU authorities are currently reviewing a marketing application for the same innovative formulation of Bonviva. (See patient story, p. 43.)

Top-selling pharmaceutical products – Roche Group

Product	Generic name	Indication	Sales in millions of CHF	% change in local currencies
MabThera/Rituxan	rituximab	non-Hodgkin's lymphoma	4,154	22
NeoRecormon, Epogin	epoetin beta	anemia	2,252	8
Herceptin	trastuzumab	metastatic breast cancer	2,146	48
CellCept	mycophenolate mofetil	transplantation	1,705	20
Avastin	bevacizumab	metastatic colorectal cancer	1,665	141
Tamiflu	oseltamivir	treatment and prevention of influenza A and B	1,558	370
Pegasys	peginterferon alfa-2a	hepatitis B and C	1,403	17
Rocephin	ceftriaxone	bacterial infections	927	–29
Xeloda	capecitabine	colorectal or breast cancer	796	47
Xenical	orlistat	weight loss, weight control	635	5
Kytril	granisetron	nausea and vomiting induced by chemotherapy or radiation therapy or following surgery	500	9
Nutropin, Protropin	somatropin, somatrem	growth hormone deficiency	476	6
Xolair	omalizumab	asthma	408	74
Copegus	ribavirin	hepatitis C	407	6
Cymevene, Valcyte	ganciclovir, valganciclovir	cytomegalovirus infection	394	19
Pulmozyme	dornase alfa/DNase	cystic fibrosis	393	15
Tarceva	erlotinib	non-small cell lung cancer, pancreatic cancer	387	2,224
Neutrogin	lenograstim	neutropenia associated with chemotherapy	364	15
Dilatrend	carvedilol	chronic heart failure, hypertension, coronary artery disease	326	–11
Activase, TNKase	alteplase, tenecteplase	myocardial infarction	310	11

Global sales of Xenical (orlistat) were up 5% in a flat market. In 2005 the product's EU labeling was expanded to include data on the use of the product in obese adolescents. Xenical is thus the first and only weight-loss medication in the United States and Europe with such information in the label. In February the existing agreement with GlaxoSmithKline was expanded to include promotion of prescription Xenical in the US by one of GSK's sales forces. In January 2006 an FDA advisory committee recommended approval of an application filed by GSK last June to market low-dose orlistat as an over-the-counter medicine for weight loss.

Other major products

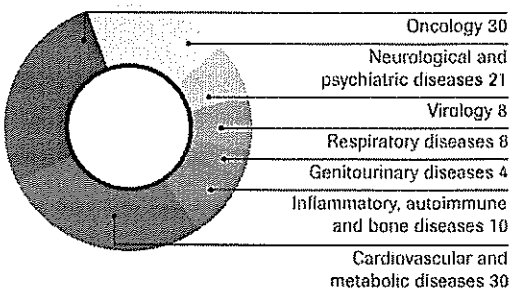
As expected, sales of Rocephin (ceftriaxone) declined markedly following the expiry of the product's US patent in July and the emergence of generic competitors in the second half of the year.

Research and development

Roche is committed to discovering and developing clinically differentiated medicines in key therapeutic areas, including oncology, inflammatory, autoimmune and bone diseases, virology and transplantation. The broad interdisciplinary approach made possible by the combined expertise of the Group's Pharmaceuticals and Diagnostics Divisions is helping to expand our understanding of diseases and biological processes and translate scientific advances into innovative medicines. Innovation in science and technology is the core of the Roche Group's focused R&D strategy.

The success of this strategy is reflected in the richness of the Group's pharmaceuticals pipeline. Its strength is expressed not only in the number of new molecular entities (NMEs) in the R&D portfolio. The success rate of the Group's late-stage clinical

111 research projects in major therapeutic areas
(31 December 2005)



trials – in 2005 fifteen out of fifteen phase III trials met their clinical endpoints – also makes Roche an industry leader. This is due in part to selection decisions based on aggressive screening and thorough profiling of compounds at the discovery, preclinical and early clinical stages.

Another cornerstone of our R&D strategy emphasises the value of leveraging key product assets by expanding their use into new indications. MabThera/Rituxan is a case in point: already established as a cancer medicine, it has now been tested in another important area of unmet medical need, rheumatoid arthritis (*see Rheumatoid arthritis and autoimmune diseases*, p. 29).

Roche is continuing to implement initiatives that aim to achieve better patient selection in clinical development programmes by developing predictive biomarkers. This is a key area of collaboration between the Pharmaceuticals and Diagnostics Divisions. Tests that enable predictions of how different patients might respond to particular drugs will allow identification of the most effective drug combinations for patient subpopulations while also limiting undesirable effects.

The acquisition of GlycArt Biotechnology, completed in July 2005, represents a significant addition of expertise in therapeutic antibody research and adds new, cutting-edge technologies and products to the Roche R&D organisation and pipeline. GlycArt's unique protein technology complements efforts to develop biological compounds that offer patients superior efficacy and safety.

R&D pipeline

At the end of 2005 the Pharmaceuticals Division's R&D pipeline comprised 108 projects, including 59 new molecular entities (NMEs) and 49 additional indications. Fourteen NMEs are currently in phase 0, 21 in phase I, 19 in phase II and five in phase III or filed for regulatory review. In 2005 13 projects entered phase I development, 12 entered phase II and 13 entered phase III. Seven projects moved out of the R&D portfolio following regulatory approvals.

Roche Pharmaceuticals currently has 111 projects in preclinical research across seven therapeutic areas and 78 development projects in nine therapeutic areas.

In 2005 four Roche-managed R&D projects were discontinued in phase 0 (one of which reverted to the R&D partner); eight were discontinued in phase I (with two reverting to R&D partners and two outlicensed); three were discontinued in phase II (of which one reverted to the partner). There were no discontinuations in phase III.

Partnering for success

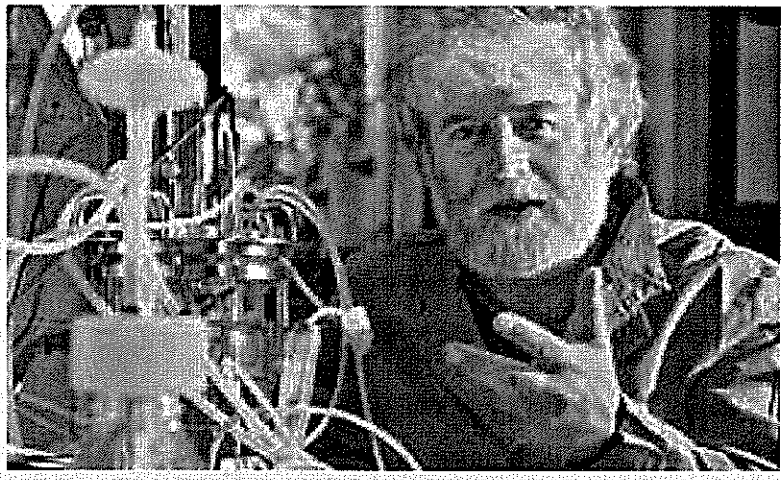
By pursuing innovative strategic alliances to complement the Group's strong internal research, the Roche Pharma Partnering unit continued helping to build a dynamic and robust pharmaceuticals portfolio (see *Partnering for innovation*, p. 28). In 2005 Roche Pharmaceuticals signed 31 new licensing agreements, including six product-related and 17 research and technology partnerships, and extended relationships with long-term partners such as GlaxoSmithKline, Protein Design Labs and Evotec.

Therapeutic proteins – building a stronger portfolio

Biopharmaceuticals are promising candidates for innovative therapies in a number of disease areas. However, creating protein-based drugs is a complex process that poses challenges very different to the manufacturing of small molecules. Roche Pharmaceuticals established the Therapeutic Protein Initiative (TPI) to build and expand its expertise in this area.

TPI is a global initiative, uniting contributions from many divisional functions, with protein discovery and development activities in Penzberg and protein formulation in Basel as its cornerstones. By acquiring and developing external and internal knowledge and skills, Roche has established novel technologies in cell-line development, automated product isolation and advanced analytical technologies.

Since its inception in 2001 TPI has helped increase Roche Pharmaceuticals' R&D productivity, with the number of protein-based projects rising from four to now more than 25. Most of these are in the key areas of oncology, inflammatory and autoimmune disorders and transplantation.



'Recombinant proteins, especially monoclonal antibodies, have demonstrated their value as novel therapeutic agents due to their high target specificity. They already provide safe and effective therapies for many patients,' says Stephan Fischer, Global Head of Biologics Research and Development at Roche. 'Our expertise and competence in all functions involved in protein research, development and manufacturing put the Roche Group in a unique position to keep delivering breakthrough medicines.'

Major development activities

Oncology

Major clinical development programmes are exploring the benefits of MabThera/Rituxan, Herceptin, Avastin, Tarceva and Xeloda in additional important indications.

Recent phase III data have shown that Avastin has significant survival benefit in metastatic non-small cell lung cancer and metastatic breast cancer, increasing the drug's potential to become a mainstay of cancer treatment (see *Setting new standards in cancer treatment*, p. 30). Regulatory filings for these new indications are planned for 2006. In addition, Avastin is being studied in phase III trials in the treatment of adjuvant colon cancer, advanced renal cell carcinoma, and pancreatic, prostate and ovarian cancer. It is also being tested in combination with Tarceva in non-small cell lung cancer (NSCLC).

Roche is evaluating MabThera/Rituxan in chronic lymphocytic leukemia (CLL) in two phase III programmes exploring its use as first-line treatment and in the therapy of relapsing CLL.

Phase III and IV trials with Herceptin are ongoing in the metastatic and adjuvant settings in breast cancer. Herceptin is also being evaluated in the treatment of gastric cancer. Data from four large clinical trials in patients with early-stage breast

R&D pipeline: all major development projects successfully brought forward

Therapeutic area	Project ID	Project/product (generic name)	Pharmacological class	Indication	Phase	Partner
Cardiovascular and metabolic diseases	R1439		enzyme inhibitor	type 2 diabetes	II	
	R1439			type 2 diabetes	I	
	R1440		enzyme modulator	type 2 diabetes	II	
	R1511			type 2 diabetes	0	
	R1579			type 2 diabetes	0	
	R1593			dyslipidemia	I	Nippon Shinyaku (NS-220)
	R1659		CETP inhibitor	dyslipidemia	II	Japan Tobacco (JTT-705)
	R1664			dyslipidemia	0	
	R483	insulin sensitiser	insulin sensitiser	type 2 diabetes	II	
Genitourinary disease	R1648			overactive bladder	0	
	R873		GPCR agonist	male erectile dysfunction	II	
Hematology and nephrology	R744	CERA	continous erythropoietin receptor activator	cancer-related anemia	II	
	R744	CERA	continous erythropoietin receptor activator	renal anemia	III	
Inflammatory, autoimmune and bone diseases	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	rheumatoid arthritis, DMARD inadequate responders	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	rheumatoid arthritis, anti-TNF inadequate responders	filed	Genentech and Biogen Idec
	R127	Valcyte (valganciclovir)	inhibitor of CMV replication	ulcerative colitis	I	
	R1285			rheumatoid arthritis	I	
	R1503		kinase inhibitor	rheumatoid arthritis	II	
	R1581			inflammatory bowel disease	I	
	R1569	Actemra (tocilizumab)	humanised anti-IL-6 receptor monoclonal antibody	rheumatoid arthritis	III	Chugai
	R1569	Actemra (tocilizumab)	humanised anti-IL-6 receptor monoclonal antibody	systemic onset juvenile idiopathic arthritis	III	Chugai
	R1594		humanised anti-CD20 monoclonal antibody	rheumatoid arthritis	II	Genentech (PRO70769)
	R1599			osteoarthritis	0	
	R3421			autoimmune diseases, transplantation	I	BioCryst
	R99	CellCept (mycophenolate mofetil)	IMPDH inhibitor	lupus nephritis	III	Aspreva
	R99	CellCept (mycophenolate mofetil)	IMPDH inhibitor	myasthenia gravis	III	Aspreva
Neurological and psychiatric diseases	R1459			Alzheimer's disease	0	
	R1647			depression	0	
	R1678			schizophrenia	I	
	R841			Alzheimer's disease	0	
	R7080			anxiety	I	
	R7119			schizophrenia	0	
Oncology	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	chronic lymphocytic leukemia, relapsed	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	chronic lymphocytic leukemia (1st line)	III	
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	indolent non-Hodgkin's lymphoma – maintenance	filed	Genentech and Biogen Idec
	R1273	Omnitarg (pertuzumab)	anti-HER2 monoclonal antibody	ovarian cancer	II	Genentech
	R1273	Omnitarg (pertuzumab)	anti-HER2 monoclonal antibody	metastatic breast cancer	II	Genentech
	R1415	Tarceva (erlotinib)	EGFR inhibitor	glioblastoma multiforme	II	Genentech and OSI Pharmaceuticals
	R1415 + R435	Tarceva+Avastin (erlotinib + bevacizumab)	EGFR inhibitor + anti-VEGF monoclonal antibody	NSCLC (1st line) – maintenance	III	Genentech and OSI Pharmaceuticals
	R1415	Tarceva (erlotinib)	EGFR inhibitor	NSCLC (1st line) – combo with chemotherapy	III	Genentech and OSI Pharmaceuticals
	R1415 + R435	Tarceva+Avastin (erlotinib + bevacizumab)	EGFR inhibitor + anti-VEGF monoclonal antibody	NSCLC (2nd line)	III	Genentech and OSI Pharmaceuticals
	R1415	Tarceva (erlotinib)	EGFR inhibitor	pancreatic cancer	filed	Genentech and OSI Pharmaceuticals
	R1454			solid tumours	I	
	R1492		epothilone D	solid tumours	II	Kosan Biosciences (KOS862)
	R1507			solid tumours	0	
	R1530			solid tumours	I	
	R1550		monoclonal antibody	metastatic breast cancer	I	Antisoma
	R1594		humanised anti-CD20 monoclonal antibody	hematologic malignancies	I	Genentech (PRO70769)
	R1640		epothilone D	solid tumours	I	Kosan Biosciences (KOS1584)
	R340	Xeloda (capecitabine)	fluoropyrimidine	adjuvant breast cancer	III	
	R340	Xeloda (capecitabine)	fluoropyrimidine	adjuvant colon cancer – combo	III	
	R340	Xeloda (capecitabine)	fluoropyrimidine	metastatic colorectal cancer (1st line) – combo	III	
	R340	Xeloda (capecitabine)	fluoropyrimidine	metastatic colorectal cancer (2nd line) – combo	III	
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	NSCLC, squamous	II	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	adjuvant colon cancer	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	metastatic breast cancer (1st line)	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	metastatic breast cancer (1st line) – extension	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	metastatic colorectal cancer (1st line) – combo extension	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	renal cell carcinoma	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	NSCLC (1st line)	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	pancreatic cancer	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	ovarian cancer	III	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	prostate cancer	III	Genentech
	R547			solid tumours	I	
	R597	Herceptin (trastuzumab)	anti-HER2 monoclonal antibody	metastatic breast cancer – combo with hormonal therapy	III	Genentech
	R597	Herceptin (trastuzumab)	anti-HER2 monoclonal antibody	adjuvant breast cancer	III	Genentech
	R597	Herceptin (trastuzumab)	anti-HER2 monoclonal antibody	gastric cancer	III	
	R925	Bondronat (ibandronic acid)	bisphosphonate	metastatic bone pain	III	
Respiratory diseases	R35	(daclizumab)	anti-CD25 monoclonal antibody	asthma	II	PDL BioPharma
	R411		dual integrin antagonist	asthma	II	
	R667		nuclear receptor agonist	emphysema	II	
Transplantation	R35	(daclizumab)	anti-CD25 monoclonal antibody	transplant maintenance	I	PDL BioPharma
Viral and other infectious diseases	R1200			HIV	0	
	R1558		antibiotic	bacterial infections	II	Sankyo (CS023)
	R1626			HCV	I	
	R1656			HCV	I	Pharmasset
	R7025			HCV	0	Maxygen
	R7128			HCV	0	Pharmasset
Participation through Chugai	SG-75	Sigmart (nicorandil)		acute heart failure	filed	
	EPOCH	Epogin (epoetin beta)		chemotherapy-induced anemia	III	
	CHS13340		recombinant parathyroid hormone	osteoporosis	II	Daiichi Asubio Pharma
	ED-71		activated vitamin D derivate	osteoporosis	III	
	AVS	Anteves (nicaraven)	hydroxyl radical scavenger	subarachnoid hemorrhage	filed	
	CAL		humanised anti-PTHrP monoclonal antibody	bone metastases	II	
	CHC12103			solid tumours	I	Cell Therapeutics
	CGS20267	Femara (letrozole)	aromatase inhibitor	breast cancer	filed	Novartis
	GM-611	(motrenicinal fumarate)	motilin agonist	gastroparesis, irritable bowel syndrome	II	
	VAL	(valilnu)		post-hepatectomy	II	
Participation through Genentech		Raptiva (efalizumab)	anti-CD11a antibody	adult atopic dermatitis	I	
		Lucentis (ranibizumab)	antibody fragment to VEGF	age-related macular degeneration	filed	Novartis Ophthalmics
		Xolair (omalizumab)	anti-IgE antibody	pediatric asthma, peanut allergy	II, III	Novartis and Tanox
Opt-in opportunities	PRO128115	VEGF	topical VEGF	diabetic foot ulcer	I	Genentech
	BR3-Fc		BAFF inhibitor	rheumatoid arthritis	I	Genentech
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	primary progressive multiple sclerosis	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	relapsed remitting multiple sclerosis	II	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	lupus nephritis	II	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	ANCA-associated vasculitis	III	Genentech and Biogen Idec
	R105	MabThera/Rituxan (rituximab)	anti-CD20 monoclonal antibody	systemic lupus erythematosus	III	Genentech and Biogen Idec
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	glioblastoma multiforme	II	Genentech
	R435	Avastin (bevacizumab)	anti-VEGF monoclonal antibody	adjuvant breast cancer	II	Genentech
	G-024858		topical hedgehog antagonist	basal cell carcinoma	I	Genentech and Curis
	PRO1762	Apo2L/TRAIL		cancer	I	Genentech
	R1564		vascular targeting agent	solid tumours	II	Antisoma (DMXAA)
	R1648		E2F modulator	solid tumours	I	ArQule (ARQ501)
	R1583	GLP-1	GLP-1	type 2 diabetes	II	Ipsen (BIM51077)
	R1624		calcineurin inhibitor	renal transplant	II	Isotechnika (ISA247)
	R1485		non-nucleoside reverse transcriptase inhibitor	HIV	0	Medivir
	R1589			Alzheimer's disease	I	Memory Pharmaceuticals

At the end of 2005 the Pharmaceuticals Division's R&D pipeline comprised 108 projects, including 59 new molecular entities (NMEs) and 49 additional indications. Fourteen NMEs are currently in phase 0, 21 in phase I, 19 in phase II and five in phase III or filed for regulatory review. In 2005 13 projects entered phase I development, 12 entered phase II and 13 entered phase III.

Blue type signifies first indication, **black** type additional indications.
Current as of 31 December 2005.

■ Therapeutic protein
■ Small molecule

Phase 0: Transition from preclinical to clinical development
Phase I: Initial studies in healthy volunteers and possibly in patients
Phase II: Efficacy, tolerability and dose-finding studies in patients
Phase III: Large-scale studies in patients for statistical confirmation of safety and efficacy

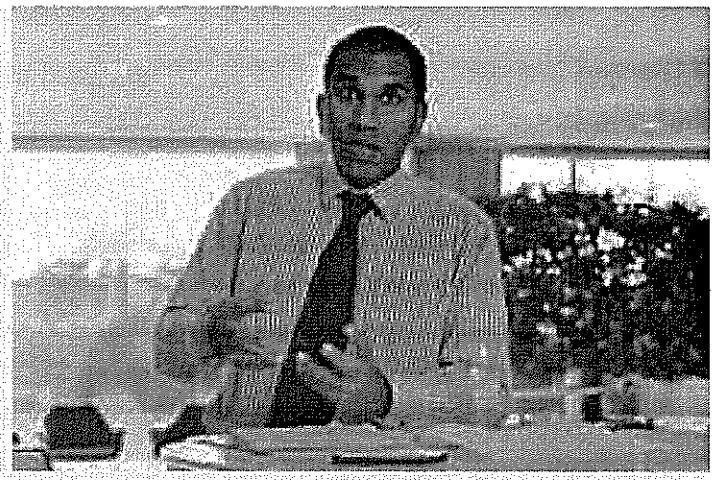
Partnering for innovation

Partnering is a key element in Roche's strategy to develop innovative, differentiated medicines for patients. Pharma Partnering (PP), the company's business development and licensing department, analyses over 1,500 external opportunities each year to find cutting-edge science to complement Roche's own R&D.

How does Roche find external innovation? 'We focus on emerging, innovative science,' says immunologist and marketing veteran Hari Kumar, one of PP's 'finders'. 'Strategy teams tell us what they need, be it a drug for a condition with no effective treatment or a technology, and we go out and look for it.'

Finders are specialists who combine scientific expertise with business acumen. Their job is to identify opportunities that could lead to new treatments, including new uses for existing Roche products.

Once a finder identifies an opportunity, a larger PP team assesses it based on three key questions: Is the science viable and differentiated? Will the opportunity complement Roche's overall strategy? What is its commercial potential? Senior management then make a decision based on the answers.



PP's alliance directors take over once a deal is approved. While the contract is being negotiated, they prepare Roche for the project's integration and ensure that communication with partners is open and clear.

Throughout the process Roche relies on its core partnering values: flexibility, respect for partners' culture and autonomy, and commitment that both sides will benefit from the collaboration. An organisation-wide partnering culture helps ensure our continued access to a broad range of external innovation and expertise.

cancer (adjuvant setting) have shown that adding Herceptin to chemotherapy significantly reduces the risk of cancer recurrence in this population. US and EU filings for this indication are planned for the first quarter of 2006.

Tarceva, a human epidermal growth factor receptor (HER1/EGFR) inhibitor, is designed to interfere with a molecular signal that plays a significant role in tumour cell growth in numerous types of cancer. It is currently being tested in the first-line and adjuvant NSCLC settings and in combination with Avastin in second-line NSCLC. Tarceva is also being evaluated in the treatment of glioblastoma multiforme, one of the most aggressive types of primary brain tumour.

Extensive late-stage programmes studying Xeloda in adjuvant breast cancer, in combination with chemotherapy in the adjuvant colon cancer setting, and in first- and second-line therapy of metastatic colorectal cancer are continuing. Recent interim analysis of a large collaborative group study of the drug as first-line treatment for advanced pancreatic cancer showed that adding Xeloda to standard chemotherapy (gemcitabine) significantly extends patient survival and improves quality of life.

A head-to-head phase III study comparing Bondronat and zoledronic acid in the treatment of metastatic bone pain has commenced, with results expected in 2007. Filings for this indication are planned in the US and Europe.

Hematology and nephrology (anemia)
Clinical development of CERA, the first continuous erythropoietin receptor activator for the treatment of anemia, is progressing on track. The phase III renal programme for this product includes six trials involving over 2,400 patients with chronic kidney disease (both on dialysis and not on dialysis). The first four phase III trials in dialysis patients were successfully completed at the end of 2005. CERA is the only anti-anemia drug ever studied using long dosing intervals (once every four weeks) in all patients for its initial filing. Roche plans to file marketing applications worldwide for CERA in renal anemia in 2006. Roche does not view the patent infringement litigation initiated by Amgen in the US as an impediment to the development and launch of CERA in the United States.

Rheumatoid arthritis and autoimmune diseases
Rheumatoid arthritis (RA) is an autoimmune disorder characterised by joint inflammation that, even when treated, can result in progressive joint destruction and, ultimately, loss of function. Its exact cause is unknown, and as yet there is no cure. Within two years of developing RA, up to 70% of patients have X-ray evidence of joint destruction, and within ten years 80% are unable to work or perform everyday tasks. RA is one of the most common autoimmune disorders and is now thought to affect over 21 million people worldwide. Current treatments include disease-modifying antirheumatic drugs (DMARDs) and biologic therapy such as the anti-TNF drugs.

In 2005 Roche significantly advanced the development of two medicines with the potential to substantially improve the treatment of RA.

MabThera/Rituxan is the first selectively targeted B cell therapy to be studied in this disease. The US and EU filings in August and September for the product's first rheumatoid arthritis indication represent a significant milestone. The filings, based on data from the pivotal REFLEX trial, cover the use of MabThera/Rituxan in patients who have failed to respond adequately to current biologic therapies, the subgroup of RA patients considered to be the most difficult to treat. Positive outcomes have also been seen in a phase IIb clinical trial (DANCER) with patients who had previously failed treatment with one or more DMARDs.

Development of Actemra (tocilizumab, formerly MRA) in RA is progressing well. Phase III data from Japan were presented at the American College of Rheumatology meeting in November. They show that treatment with Actemra significantly reduces the progression of joint damage and improves RA signs and symptoms. Based on these data, Chugai plans to file a marketing application for Actemra for RA in Japan in the first half of 2006. Patient recruitment for international phase III trials is proceeding as planned. Regulatory filings in the US and EU are expected in 2007. In 2005 Chugai launched Actemra in Japan in its first indication, Castleman's disease, a rare condition that causes severe enlargement of the lymph nodes.

CellCept is being developed in collaboration with Aspreva Pharmaceuticals for autoimmune applications, including the treatment of lupus nephritis (kidney complications associated with the autoimmune disease lupus erythematosus) and myasthenia gravis (a chronic autoimmune disease characterised by episodes of muscle weakness). Phase III clinical trials of the drug in both indications are under way. CellCept is the first potential new treatment for either of these debilitating and sometimes fatal conditions in many years. In January 2006 CellCept was designated an orphan drug in the treatment of myasthenia gravis by the FDA.

Diabetes
Roche has now completed the two-year animal carcinogenicity programme for the insulin sensitiser R483, required by the FDA for all members of this class of agents. A final decision on the commencement of phase III clinical testing of the compound in type 2 diabetes will be taken once the FDA and other agencies have completed their reviews of the carcinogenicity data.

Two other compounds being developed for the treatment of type 2 diabetes moved into phase II clinical testing in 2005, a glucokinase activator and a dipeptidyl peptidase (DPP-IV) inhibitor.

Setting new standards in cancer treatment

At the 41st meeting of the American Society of Clinical Oncology (ASCO), in Orlando, Florida, in May Roche and its partners presented data from an unprecedented eight major phase III trials that had successfully met their primary endpoints.

Product (generic name)	Indication (clinical trial)	Benefit
Avastin (bevacizumab)	Metastatic HER2-negative breast cancer, 1st line treatment (E2100)	49% improvement in overall survival
	Metastatic non-small cell lung cancer, 1st line treatment (E4599)	30% improvement in overall survival
	Metastatic colorectal cancer, 2nd line treatment (E3200)	24% reduction in risk of death
Herceptin (trastuzumab)	HER2-positive breast cancer, adjuvant treatment (NSABP B-31 and NCCTG N9831, joint analysis)	52% reduction in risk of disease recurrence
	HER2-positive breast cancer, adjuvant treatment (HERA)	46% reduction in risk of disease recurrence
MabThera/Rituxan (rituximab)	Relapsed indolent NHL, maintenance treatment (GSLG)	100% improvement in response duration at 3 years
Tarceva (erlotinib)	Pancreatic cancer, 1st line treatment (PA3)	23% improvement in overall survival

Expanding biotech production capacity

In 2005 the Roche Group continued to reconfigure its manufacturing capacities to meet the requirements of a changing product portfolio and increase the efficiency of its global manufacturing operations. In particular, a shift from chemically derived active pharmaceutical ingredients towards biologics and a corresponding trend towards sterile liquid dosage forms are driving current activities in this area. Technical development activities also reflect the impact of the Pharmaceuticals Division's dynamic R&D portfolio (including development of in-licensed products by Roche). Ongoing projects to further reduce supply chain complexity and optimise inventory levels remain on track.

Four major new facilities were dedicated last year: new biotech production facilities for epoetin and CERA in Penzberg (Germany); a state-of-the-art packaging and storage facility for injectable drugs in Mannheim (Germany); and a plant for high-potency pharmaceutical products in Shanghai. The new Penzberg and Mannheim facilities have been operational since the middle of 2005. The Shanghai facility, the first of its kind in China, is scheduled to come on stream this year; it will produce CellCept and Xeloda for the Chinese market.

The Oceanside (California) facility acquired by Genentech from Biogen Idec last June is currently being converted to produce Avastin; manufacturing of bulk drug substance is expected to commence in 2006, with FDA licensure expected in the first half of 2007. In 2005 Genentech received FDA licensure for a new Avastin manufacturing facility in Porriño, Spain.

Work on the new Basel (Switzerland) and Penzberg production facilities for therapeutic antibodies, both scheduled for technical completion in 2007, is moving ahead as planned.

Access to medicines

While the primary role of the Roche Pharmaceuticals Division is to discover, develop and commercialise innovative medicines, the adoption of policies that extend access to critically needed products to people affected by poverty throughout the world is an integral part of healthcare's mission. Therefore, in addition to supporting local initiatives to expand healthcare access, Roche has implemented patent and pricing policies and joined major international efforts aimed at addressing this problem.

Roche does not file new patents for its medicines in the 50 Least Developed Countries (as defined by the UN), nor does it enforce patents it already holds in these countries. In response to the devastating HIV/AIDS pandemic, the company has extended this policy to sub-Saharan Africa, the poorest and hardest-hit region.

The prices Roche charges for its products in low and lower-middle income countries are below the corresponding prices in Switzerland at launch. Roche supplies the HIV medicines Invirase and Viracept at no profit to Least Developed Countries and sub-Saharan Africa. As a result, reduced prices for these products apply to 93% of all people living with HIV/AIDS worldwide.

In addition, Roche is a member of the Accelerating Access Initiative, which is helping increasing numbers of HIV/AIDS patients in developing countries to receive treatment. The company also supports two other HIV treatment access programmes, the CARE programme in four African countries and the Cambodian Treatment Access Programme. In addition to providing funding, medicines and diagnostics through these programmes, Roche has also contributed to providing training in HIV/AIDS care and treatment to hundreds of healthcare professionals from more than 14 African countries and Cambodia. (See also *Ensuring access to healthcare worldwide*, p. 79, and visit www.roche-hiv.com.)

In its most recent move to extend access to vital HIV/AIDS treatments in the world's neediest areas, Roche announced in January 2006 that, as part of its new Technology Transfer Initiative, the company will provide local manufacturers within sub-Saharan Africa and Least Developed Countries with the technical expertise required to produce generic HIV medicines. This assistance will be offered free and with no conditions attached.

The threat of an avian flu pandemic represents another critical global health challenge, and Roche is closely involved in ensuring that vital medicines are available where they are most needed. Following warnings by the WHO that the next global influenza pandemic is imminent, Roche has been doing all it can to ensure worldwide availability of its influenza drug Tamiflu for pandemic use. The steps taken include implementing a tiered pricing system with significant reductions for pandemic use and licensing agreements with local companies for production of the drug for pandemic use in India and China. In addition to taking unprecedented steps to ramp up Tamiflu production capacity (see *Meeting world demand for Tamiflu*, p. 23), Roche is working with the US National Institute of Allergy and Infectious Diseases and international virology experts to expand the information base regarding the optimal use of Tamiflu against the H5N1 avian influenza strain.

Access to medicines is an issue that affects more than the developing world – it can pose significant challenges in industrialised countries, as well. In the United States, for example, Roche is committed to making sure that every patient who needs a Roche drug has access to it, whether that patient is a senior citizen being treated for cancer, or a member of a working family facing an organ transplant. The Roche Patient Assistance Program, established in the 1960s, was the first in the industry to provide prescription drugs free of charge to qualifying patients who need them but lack prescription coverage and the means to pay for them.

Roche is also a founding member of the Partnership for Prescription Assistance, a programme sponsored by the Pharmaceutical Research and Manufacturers of America, which represents the country's leading pharmaceutical research and biotechnology companies. The programme offers a single point of access to over 475 public and private patient assistance programmes.

Similarly, Genentech provides its marketed products free of charge to eligible uninsured patients treated in the United States through the Genentech Access to Care Foundation and the Genentech Endowment for Cystic Fibrosis. Genentech is also a member of the Partnership for Prescription Assistance. To further support patient access to therapies for various diseases, in 2005 Genentech donated approximately 21 million dollars to independent, third party, public charities that offer copayment assistance to eligible patients.