Annual Report

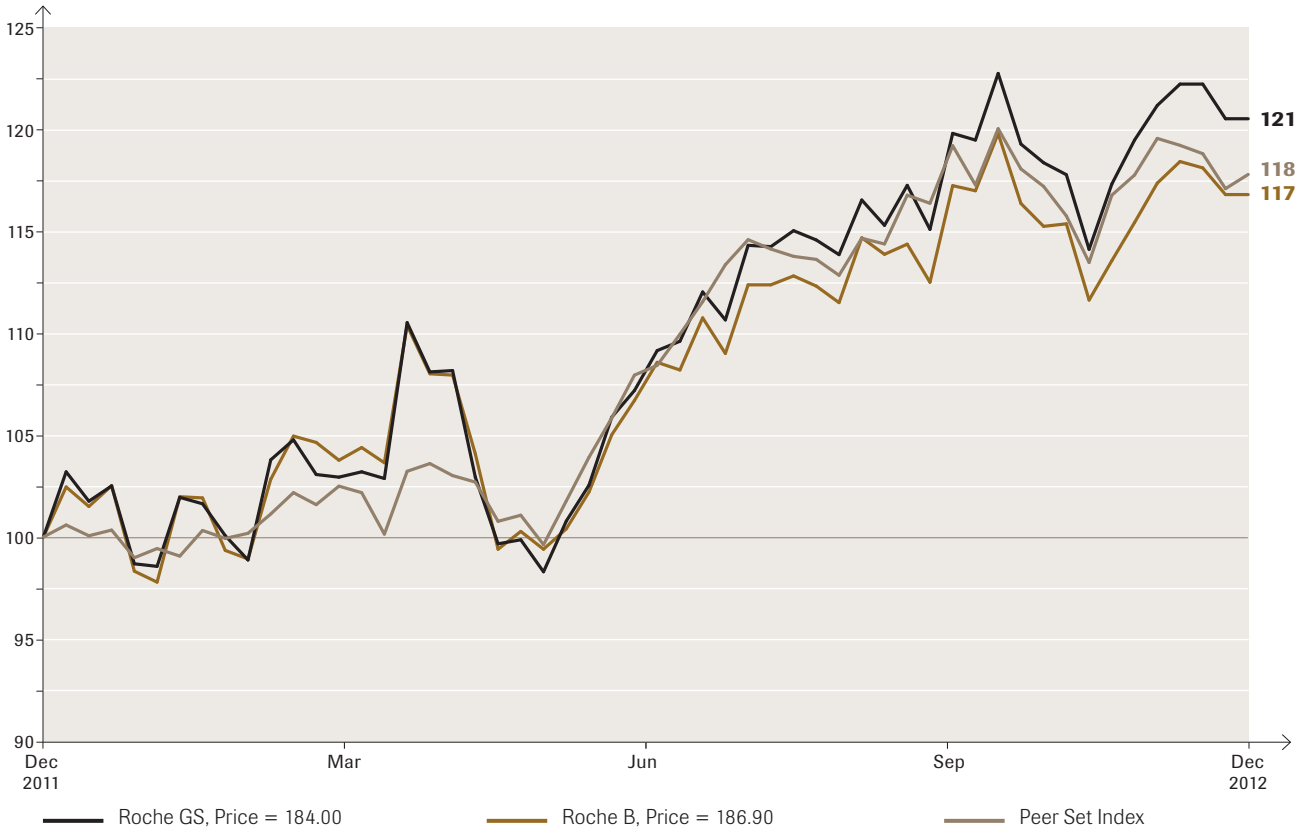
2012

Key Figures 2012

Group sales	45,499 millions of CHF	+4% (CER)[1]
Core operating profit	17,160 millions of CHF	+11% (CER)
Core earnings per share	13.62 CHF	+10% (CER)
Operating free cash flow	15,389 millions of CHF	+10% (CER)
R&D investment	8,475 millions of CHF	+2% (CER)
Dividend[2]	7.35 CHF	+8% (CER)

Total Shareholder Return 2012

The value of CHF 100[3] invested 1/1/2012, for the period ending 31/12/2012

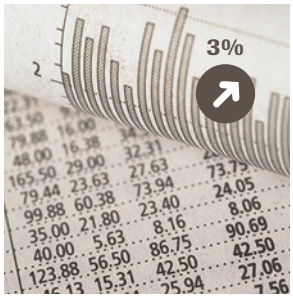


Patients on clinical trials	326,642 patients	+10.4%
Number of employees[4]	82,089 employees	+2.4%

1 CER: Constant exchange rates (average full-year 2011).
2 Proposed by the Board of Directors.
3 Prices translated at constant CHF exchange rates: USD=0.90; EUR=1.20; 100 JPY=1.10; GBP=1.40.
4 Full-time equivalents.

Key Events 2012

Roche Group



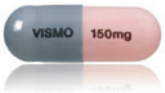
At the Roche Annual General Meeting in 2012, shareholders authorised a **3% dividend increase** to CHF 6.80 per share and non-voting equity. It was the company's 25th dividend increase in as many years.

Management changes: Daniel O'Day, former Head of Roche Diagnostics, was appointed the new Head of Roche Pharma. Roland Diggelmann has assumed the position of Head of Roche Diagnostics.

Roche continued to streamline its **research and development** activities, taking the decision to close its site in Nutley, New Jersey, USA. The respective R&D activities are being consolidated in Switzerland and Germany.

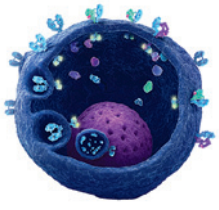
Our **late-stage pipeline** made considerable progress in 2012, with 11 out of 14 clinical trials delivering positive results, underpinning the strength of our innovation strategy.

Pharmaceuticals



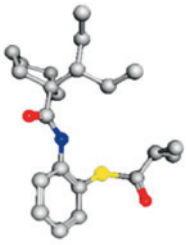
The **FDA approved Erivedge** (vismodegib), a first-in-class Hedgehog Pathway Inhibitor for adults with advanced basal cell carcinoma.

The **FDA approved Perjeta** (pertuzumab) for patients with HER2-positive metastatic breast cancer. This new personalised medicine gives patients more time without their disease worsening.



New data from the Phase III EMILIA study showed that Roche's **trastuzumab emtansine (T–DM1)** significantly improved survival of people with HER2-positive metastatic breast cancer. Roche has filed for approval at the FDA and the EMA.

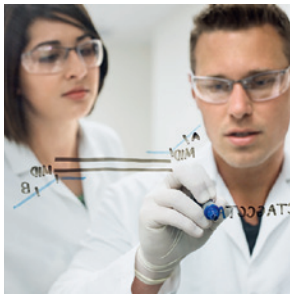
After the second interim data analysis of the dal-OUTCOMES trial, Roche decided to discontinue the development of **dalcetrapib**, a medicine to lower cardiovascular risks.



Corporate Sustainability

In 2012 we reduced our **water consumption** by 8.6% and our **greenhouse gas emissions** by 2.6%. With this, we are well on track to reach our five-year goal of a 10% improvement in efficiency by 2014.

The second **Transnet-Phelophepa Healthcare Train** was inaugurated in South Africa. Roche doubled its support, now reaching over 550,000 people a year in rural South Africa through the train's various services.



Roche has been recognised as a **great place to work,** achieving top rankings in prestigious award listings worldwide in 2012.

Roche has been named **Healthcare Supersector Leader** in the Dow Jones Sustainability Indexes (DJSI) for the fourth consecutive year. The ranking is a confirmation of Roche's commitment to long-term sustainable value creation.

sam 2012 sector leader

Diagnostics

New US guidelines recognise the benefit of genotyping the **human papillomavirus (HPV)** 16 and 18, the principal causes of cervical cancer in women.

The **FDA cleared** the **Accu-Chek Combo system,** Roche's new interactive insulin pump system for people with diabetes, and the Accu-Chek Nano SmartView system.

Roche **Applied Science** and **Diabetes Care** initiated **restructuring** measures to sustain long-term profitability.

Roche launched **GUIDE-IT,** a clinical trial involving the cardiac marker NT-proBNP to guide therapy in heart failure patients.

The value of innovation

ROCHE AT A GLANCE

Who we are

At Roche, we focus on fitting treatments to patients through innovative medicines and diagnostic tests.

A global leader in innovation
Roche is a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics.

A sustainable company
We are committed to sustainability and to running our business in a way that is ethical, responsible and creates long-term value.

A great workplace
We are driven by a shared set of standards of integrity, the courage to reach beyond boundaries and a passion for what we do.

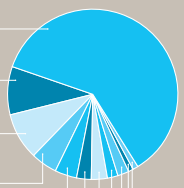
150+ **countries**	18,000,000 **patients treated**[1]	82,089 **employees**[2]
18 **research centres**	326,642 **patients in clinical trials**	26 **manufacturing sites**

#1 **in biotech** #1 **in oncology** #1 **in *in vitro* diagnostics** #1 **in hospital market**

What we do

Pharmaceuticals
We are the world's largest biotech company with a product portfolio of truly differentiated therapies and a robust pipeline of investigational new medicines.

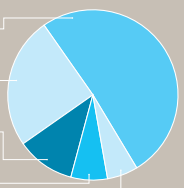
Sales by therapeutic area 2012 (CER)[3]



61%	Oncology (+9%)
9%	Virology (+14%)
9%	Inflammation/Autoimmune/ Transplantation (+5%)
5%	Metabolism/Bone (–23%)
4%	Ophthalmology (–8%)
3%	Respiratory diseases (+9%)
3%	Cardiovascular diseases (+6%)
2%	Renal anemia (–16%)
2%	Central nervous system (+1%)
1%	Infectious diseases (–1%)
1%	Other therapeutic areas (–14%)

Diagnostics
We are the global leader in *in vitro* diagnostic testing for early detection, evaluation and monitoring of disease. We are also a frontrunner in the management of diabetes.

Sales by business area 2012 (CER)[3]



51%	Professional Diagnostics (+8%)
25%	Diabetes Care (–4%)
11%	Molecular Diagnostics (+4%)
7%	Applied Science (–3%)
6%	Tissue Diagnostics (+12%)

Pharmaceuticals Sales 35.2 billion CHF **Diagnostics Sales** 10.3 billion CHF

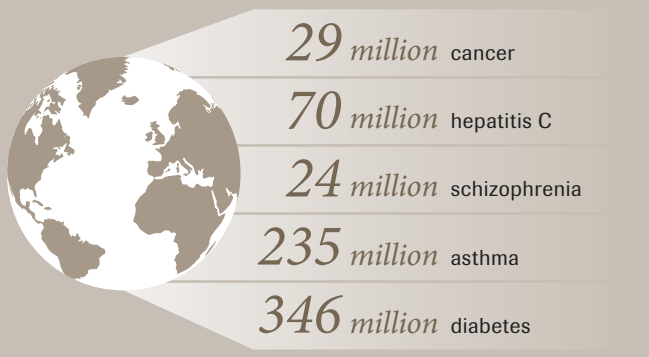
Roche Group Sales 45.5 billion CHF

1 With one of Roche's 25 top-selling products. 2 Full-time equivalents (FTE). 3 CER: Constant Exchange Rates (average full-year 2011).

Our strategic priorities

Patients in need

We strive to help patients in need with truly differentiated diagnostics and medicines. Our focus lies in five disease areas with unmet medical need, oncology, inflammation, infectious disease, metabolism and the central nervous system.

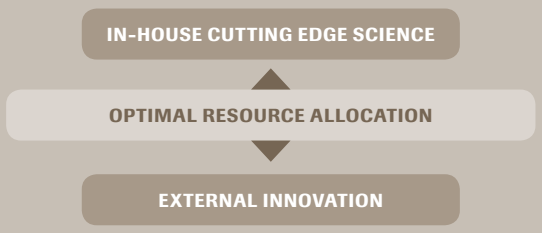


Personalised Healthcare

Personalised Healthcare at Roche is about providing the right therapy for the right group of patients at the right time. We provide medicines and diagnostics that optimise patient care, enabling tangible improvements in health, quality of life and survival.

Excellence in science

Roche is a highly innovative healthcare company, with a robust R&D foundation. We have three autonomous research units, as well as 150 partnerships all over the world, to foster diversity of research and translate science into medicines.

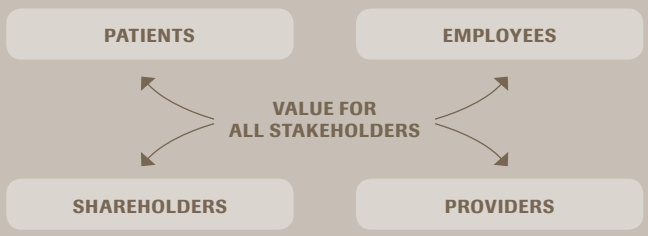


Innovative pricing models

Roche aims to bring its medicines and diagnostic tests to as many patients in need as possible. To do this, we explore innovative pricing models and patient access schemes targeted to individual markets.

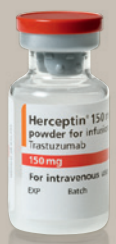
Stakeholder value

By discovering and developing innovative products, we aim to provide value to all our stakeholders, be they patients, doctors, employees, investors or society as a whole.



TOP-SELLING PHARMACEUTICALS

in millions of CHF



6,707	5,889	5,764	1,649	1,523
Product **MabThera/ Rituxan**	**Herceptin**	**Avastin**	**Pegasys**	**Xeloda**
Sales growth (CER)[1] +9%	+11%	+6%	+12%	+9%
Active substance rituximab	trastuzumab	bevacizumab	peginterferon alfa-2a	capecitabine
Indications non-Hodgkin's lymphoma, chronic lymphocytic leukemia, rheumatoid arthritis, ANCA-associated vasculitis	HER2-positive breast cancer, advanced HER2-positive stomach cancer	colorectal cancer, breast cancer, non-small cell lung cancer, kidney cancer, ovarian cancer, glioblastoma	hepatitis B and C	colorectal cancer, colon cancer, breast cancer

1 CER: Constant exchange rates (average full-year 2011).

TOP-SELLING DIAGNOSTICS

in millions of CHF

Accu-Chek Nano SmartView

cobas e 602

cobas c 502

cobas TaqMan 48

Ventana IHC reagents

2,346	*2,321*	*1,514*	*562*	*518*
Product **Accu-Chek monitoring systems**	**cobas e modules, Modular Analytics, Elecsys**	**cobas c modules, Modular Analytics, Cobas Integra**	**Cobas AmpliPrep/ Cobas TaqMan**	**immunohistochemistry and *in situ* hybridisation**
Sales growth (CER)[1] –5%	+15%	+5%	+2%	+13%
Market segment Blood glucose monitoring	Immunoassays	Clinical chemistry	Virology (hepatitis B, hepatitis C, HIV)	Advanced tissue staining
Business area Diabetes Care	Professional Diagnostics	Professional Diagnostics	Molecular Diagnostics	Tissue Diagnostics

The Value of Innovation

Roche is a global leader in innovation for medicines and diagnostic testing. This annual report highlights how innovation brings value to patients, prescribers, healthcare reimbursement and society as a whole.

A possible new medicine for HER2-positive metastatic breast cancer
A new generation of cancer treatment

Actemra/Roactemra
Relief for the agony of childhood arthritis

High-sensitivity cardiac test
Precise testing for life or death decisions

Accurate diagnosis and personalised healthcare
Focusing healthcare budgets on targeted treatments

Working with the insurance industry in China
Improving health insurance coverage for cancer patients

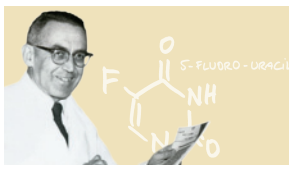
cobas HPV and CINtec tests
Better screening for cervical cancer

From mining to biotech – Roche Penzberg
Innovation creating value for the local economy

Innovation in the pharmaceutical industry
A lasting contribution to world health

50 years of cancer research at Roche

The fight against cancer goes on



Contents

Letter to Shareholders from Franz B. Humer

Dear Shareholders

High levels of public debt, especially in Europe and the United States, and the continued strength of the emerging economies were the two dominant influences on the healthcare sector in 2012, bringing both challenges and opportunities. Overall, it was a demanding year for the industry and one where cost pressure in many markets continued to increase. Notwithstanding these challenges, Roche again posted very good results for the year, with a firm strategy of developing medically differentiated medicines and diagnostic products for diseases in areas of high unmet medical need.

Group sales increased 4%, at constant exchange rates, to 45.5 billion Swiss francs (+7% in Swiss francs), with both the Pharmaceuticals and Diagnostics Divisions growing faster than their respective markets. Roche delivered strong growth in the United States and the emerging markets, whilst in Europe we continued to feel pricing pressure from healthcare budget cuts. Our focus on high-value medicines and diagnostic tests, however, meant that, relative to the rest of the industry, our sales in Europe held up well.

In general, what we are seeing is an increasing shift from the established markets, especially in Europe, to the faster growing emerging market nations in Asia and Latin America, where Roche already records a fifth of its sales. Cancer and cardiovascular disease are now among the leading causes of death in emerging economies and demand for our medicines is rising as a result. We are actively expanding our position in Asia and Latin America, thereby improving global access to our medicines and diagnostics products.

We have optimised our organisational structure over the past year, adapting our processes to this changing market environment. A notable move was the closure of the Roche site in Nutley, New Jersey in the United States as part of the conso-

lidation of research and early-stage development activities. Closing the site was not an easy decision. Nutley has played a pivotal role in the company's success over the past 80 years.

Core operating profit for 2012 again improved significantly, while net income was slightly higher at 9.8 billion Swiss francs, as the good operating performance was offset by costs associated with a number of major restructuring programmes and a higher tax rate. On a comparable basis, core net income was up 10% over the previous-year period at constant exchange rates (+11% in Swiss francs).

Another highlight for the year was the Dow Jones Sustainability Indexes naming Roche Supersector Leader for the fourth consecutive year, ranking us as the world's most sustainable healthcare company.

Leading the way in personalised healthcare

As a leader in personalised healthcare, Roche is uniquely positioned to develop treatments that raise current standards of care and extend and improve the lives of patients. Some 60% of the projects in our pharmaceuticals pipeline are being developed in conjunction with companion diagnostic tests. In 2012 we further strengthened Personalised Healthcare, launching the cancer medicines Perjeta, for breast cancer and Zelboraf, for melanoma, alongside their companion diagnostics.

Medical innovation not only benefits patients, but also our partners in the healthcare market, payers, the economy and society in general. Regrettably, in Europe in particular, there continues to be too much focus on costs and short-term thinking, which harbours the risk of missing longer-term opportunities for our economy and society. This longer-term perspective tends to be neglected in the discussions about rising healthcare costs, as does the contribution that pharmaceuticals and diagnostics make to medical progress.

Sustainable success — and this applies not only to Roche but to business generally — requires long-term thinking and forward-looking investments. Innovation is, and will continue to be, the motor driving our long-term success. This success story must be continued through open dialogue between politicians and industry.

Board to propose 7.35 Swiss francs dividend for 2012

In view of these good results, the Board of Directors is proposing an 8% dividend increase, to 7.35 Swiss francs per share and non-voting equity security (2011: 6.80 Swiss francs). More than half of net income will be distributed to shareholders as dividends. Subject to your approval, this will be our 26th dividend increase in as many years.

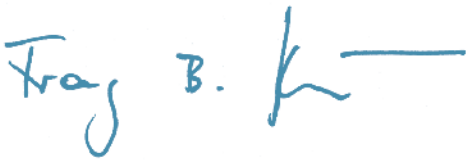
As previously announced, Prof. Bruno Gehrig and Lodewijk J.R. de Vink (both members of the Board of Directors since 2004) have decided not to stand for re-election to the Board of Directors at our next Annual General Meeting. During their many years of service, both have made exceptionally valuable contributions to the growth of our company. We owe them a debt of gratitude.

The Board of Directors proposes the election of Dr Severin Schwan, CEO of the Roche Group, as a new member of the Board of Directors of Roche Holding Ltd. This will enable the Board of Directors and Corporate Executive Committee to work together even more closely, which will help promote the growth of the company in today's challenging market environment.

The two new Corporate Executive Committee members announced in the second half of 2012 were recruited from within the company: Daniel O'Day, former Chief Operating Officer (COO) of the Diagnostics Division, was appointed COO of the Pharmaceuticals Division effective 1 September 2012. Roland Diggelmann, former Head of the Asia–Pacific region within Roche Diagnostics, was appointed as a new member of the Corporate Executive Committee and Daniel O'Day's successor as COO of the Diagnostics Division.

In its newly constituted form, the Corporate Executive Committee will continue to progress the Group's current strategic course and sustainably drive Roche's success as a global leader in healthcare. Clinical differentiation is the key to serving patients' medical needs in a better, safer and more cost-effective way, which is even more crucial in this increasingly cost-sensitive environment.

Roche will continue to advance its successful strategy of focus and innovation — for the benefit of patients, physicians, employees and you, our shareholders.



Franz B. Humer
Chairman of the Board

Letter to Shareholders from Severin Schwan

Dear Shareholders

In a difficult market environment, your company delivered a strong performance in 2012, continuing the positive growth trend of recent years. We met all our sales and earnings targets, and importantly, made significant strides in product development. Three new Roche cancer medicines have been approved in the last 18 months and a new cancer drug has also been filed for approval.

Before I expand on our advances in research and development, I would first like to summarise our key financial results.

Sales in the Pharmaceuticals Division rose 5% at constant exchange rates to 35.2 billion Swiss francs (+7% in Swiss francs), with growth driven by cancer medicines Herceptin, MabThera/Rituxan, Avastin and Zelboraf; as well as our rheumatoid arthritis drug Actemra/RoActemra, Pegasys, our hepatitis C medicine, and Tamiflu.

The Diagnostics Division consolidated its global market leadership with sales up 4% to 10.3 billion Swiss francs (+5% in Swiss francs), driven by strong demand from clinical laboratories. Immunoassays, sophisticated blood tests to diagnose a range of diseases, also performed very well, continuing a more than decade-long trajectory of double-digit growth.

Core operating profit increased 11% (at constant exchange rates) to 17.2 billion Swiss francs, outpacing sales growth significantly. The Group core operating profit margin rose 2.1 percentage points to 37.7%, driven mainly by productivity gains and cost savings.

Core earnings per share – a key metric of underlying business performance, which excludes items such as global restructuring charges, amortisation and impairment of intangible assets – increased 10% at constant exchange rates, above original expectations.

In achieving these results, I would like to thank our employees for their hard work, commitment and professionalism. Their efforts continue to make Roche one of the world's most successful healthcare companies.

Bringing innovation to patients

Our development pipeline, a key foundation for Roche's future, also showed healthy growth in 2012 and now has 72 new molecular entities in clinical development. Overall, we had positive data from 11 trials for drugs in late-stage clinical testing, strengthening our business with innovative products and securing our future for years to come. The Diagnostics pipeline remains solid, with 55 new products launched in key markets in 2012.

A significant highlight of 2012 was the extension of Roche's product portfolio for treating the highly aggressive HER2-positive form of breast cancer. Backed by decades of research, Roche is currently leading a wave of innovative developments to combat these severe tumours. Our new breast cancer drug Perjeta was approved by the US Food and Drug Administration in June 2012 after priority review. Therapy combinations designed to overcome treatment resistance whilst targeting multiple pathways in cancer are becoming more and more important. Clinical trials show that patients treated with Perjeta, Herceptin and chemotherapy live significantly longer than those receiving standard therapy and with our companion diagnostic tests, patients who are likely to respond to these targeted medicines can be quickly identified.

Adding to this group of medicines, we have filed for regulatory approval of a new drug, an antibody–drug conjugate known as trastuzumab emtansine (T–DM1). Roche is at the forefront of developing antibody–drug conjugates (ADCs), nine of which are currently in clinical development. ADCs combine the specificity of antibodies with the power of chemotherapy, targeting the cancer cells directly and significantly reducing the side effects of systemic chemotherapy. The risk of death for breast cancer patients receiving T–DM1 was shown in trials to be 32% lower than for those receiving standard treatment.

Promising drugs are also currently being studied in global programmes in chronic lymphocytic leukemia and non-Hodgkin's lymphoma. They have the potential to improve on MabThera/Rituxan, the current standard of care in fighting hematological tumours.

In addition to oncology, Roche is also focusing on other disease areas of high unmet medical need, in the field of neuroscience for Alzheimer's disease and schizophrenia, as well as on metabolic, inflammatory and autoimmune diseases. Despite the recent decision to terminate the dalcetrapib clinical programme, Roche remains committed to developing medicines for patients with cardiovascular disease and diabetes. Discovering and developing new drugs means taking calculated risks – there is no other road to real innovation.

Maximising R&D productivity

Operationally, we are restructuring our pharmaceutical research and development activities in order to better allocate resources and further improve our efficiency. This has resulted in the difficult decision to close the Roche site in Nutley, New Jersey. The resulting savings from the site consolidation and related infrastructure costs will allow us to reallocate resources to our growing number of clinical programmes, whilst maintaining stable R&D expenditure overall. I am aware of the impact this has had on all the employees affected by the closure, and on their families. We are providing the affected employees with financial support and professional advice to help prepare them for new job opportunities.

We will establish a Translational Clinical Research Center in New York, keeping our presence on the East Coast of the United States. The Center will accommodate over 200 employees and support clinical trials and early development programmes, as well as continue collaborations with academic institutions and biotech companies.

Going forward, I am convinced that we have taken the right measures and we will continue to see the benefits coming through. Overall, for 2013, we are expecting to achieve sales growth at constant exchange rates in line with the Roche Group's results for the previous year. We target core earnings per share to grow ahead of sales. Based on this outlook, we anticipate being able to raise our dividend again in 2013.

Severin Schwan
Chief Executive Officer

Board of Directors

Dr Franz B. Humer

Prof. Bruno Gehrig

André Hoffmann

Dr Andreas Oeri

Prof. Pius Baschera

Prof. Sir John Irving Bell

Paul Bulcke

William M. Burns

Lodewijk J.R. de Vink

Dr Christoph Franz

Dame DeAnne Julius

Dr Arthur D. Levinson

Peter R. Voser

Prof. Beatrice Weder di Mauro

Board of Directors
per 31 December 2012

Board of Directors

	Name (year of birth)			Term ends	First elected
Board of Directors	Dr Franz B. Humer (1946)	D*, E	Chairman	2014	1995
	Prof. Bruno Gehrig (1946)	C*, D, E	Vice-Chairman	2013	2004
	André Hoffmann (1958)	A, C, D, E	Vice-Chairman	2014	1996
	Prof. Pius Baschera (1950)	A, E		2013	2007
	Prof. Sir John Irving Bell (1952)	B, E		2014	2001
	Paul Bulcke (1954)	B, E		2013	2011
	William M. Burns (1947)	A, E		2013	2010
	Lodewijk J.R. de Vink (1945)	B, E		2013	2004
	Dr Christoph Franz (1960)	C, E		2013	2011
	Dame DeAnne Julius (1949)	B*, E		2013	2002
	Dr Arthur D. Levinson (1950)	C, E		2013	2010
	Dr Andreas Oeri (1949)	A*, E		2013	1996
	Peter R. Voser (1958)	C, E		2013	2011
	Prof. Beatrice Weder di Mauro (1965)	B, E		2013	2006
Secretary to the Board of Directors	Dr Gottlieb A. Keller (1954)				
Honorary Chairman of the Board of Directors	Dr Fritz Gerber (1929)				

A Corporate Governance and Sustainability Committee.
B Audit Committee.
C Remuneration Committee.
D Presidium/Nomination Committee.
E Non-executive director.

* Committee chairperson.

Board of Directors

At the 94th Annual General Meeting (AGM) of Roche Holding Ltd, on 6 March 2012, shareholders re-elected John I. Bell, André Hoffmann and Franz B. Humer as members of the Board of Directors for the term of two years as provided by the Articles of Incorporation.

Corporate Executive Committee

Dr Severin Schwan

Daniel O'Day

Roland Diggelmann

Dr Alan Hippe

Silvia Ayyoubi

Dr Gottlieb A. Keller

Dr Richard Scheller

Dr Mike Burgess[1]

Dr Sophie Kornowski-Bonnet

Osamu Nagayama

Dr Stephan Feldhaus

Corporate Executive Committee
per 31 December 2012

Corporate Executive Committee

	Name (year of birth)	Position
Corporate Executive Committee	Dr Severin Schwan (1967)	CEO of the Roche Group
	Dr Alan Hippe (1967)	Chief Financial and IT Officer
	Daniel O'Day (1964)	COO Division Roche Pharmaceuticals
	Roland Diggelmann (1967)	COO Division Roche Diagnostics
	Dr Gottlieb A. Keller (1954)	General Counsel
	Silvia Ayyoubi (1953)	Head Group Human Resources
Enlarged Corporate Executive Committee	Osamu Nagayama (1947)	Chairman and CEO Chugai
	Dr Richard Scheller (1953)	Head Genentech Research and Early Development (gRED)
	Dr Mike Burgess[1] (1962)	Head Roche Pharma Research and Early Development (pRED) *(ad interim)*
	Dr Stephan Feldhaus (1962)	Head Group Communications
	Dr Sophie Kornowski-Bonnet (1963)	Head Roche Partnering
Secretary to the Corporate Executive Committee	Per-Olof Attinger (1960)	
Statutory Auditors of Roche Holding Ltd	KPMG Klynveld Peat Marwick Goerdeler SA (reporting years 2004–2008) KPMG AG (since 2009) Auditor in charge: John A. Morris (2004–2010) Ian Starkey (since 2011)	
Chief Compliance Officer	Dr Urs Jaisli (1956)	

1 John C. Reed will assume the position of Head of Pharma Research and Early Development (pRED) on 2 April 2013 and will become a member of the Enlarged Corporate Executive Committee.

Corporate Executive Committee

Sophie Kornowski-Bonnet was appointed Head of Roche Partnering and joined the Enlarged Corporate Executive Committee on 1 February 2012.

Mike Burgess assumed the ad-interim position of Head of Pharma Research and Early Development (pRED) on 1 July 2012 and became a member of the Enlarged Corporate Executive Committee.

Daniel O'Day was appointed COO of the Roche Pharmaceuticals Division and Roland Diggelmann, COO of the Roche Diagnostics Division. Both appointments were effective from 1 September 2012.

A possible new medicine for HER2-positive metastatic breast cancer

A new generation of cancer treatment

When treating cancer, oncologists are looking for medicines that will deliver the best results with the fewest side effects. An advance in this area could mean that physicians may soon be able to prescribe a treatment that is even more effective and better tolerated than existing therapies. Our late-stage drug candidate, trastuzumab emtansine (T–DM1), is able to deliver a potent dose of chemotherapy to the cancer cells because the chemotherapy is linked to an active antibody. This could potentially reduce the side effects of traditional therapy. Developing a drug that can limit the impact of chemotherapy provides true value for both prescribers and patients.

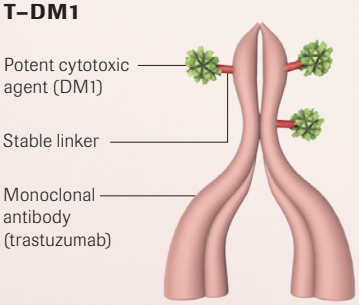
Prof. Paul Ellis, Guy's Hospital, was an investigator in the EMILIA trial:

'I very much hope that our patients will actually need less of the traditional systemic cytotoxic chemotherapy and as such be exposed to less in the way of the debilitating side effects normally associated with those agents. I think apart from the effectiveness that is one of the real legacies of these new types of treatments, such as T–DM1.'

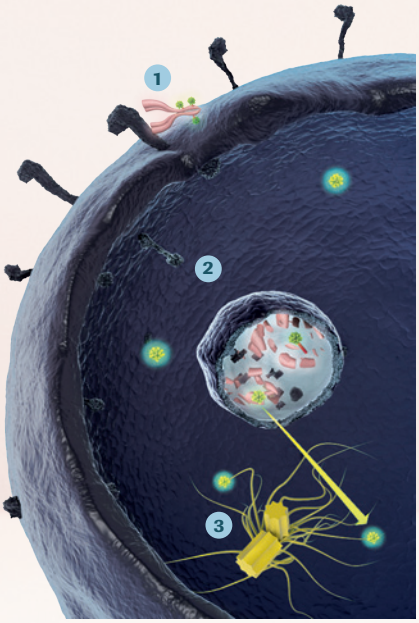
How the T–DM1 antibody–drug conjugate works:

The drug is made up of trastuzumab[1], a chemotherapy called DM1, and a linker. The linker connects trastuzumab and DM1. T–DM1 binds to the HER2-positive cancer cells, and is thought to block out-of-control signals that make the cancer grow while also calling on the body's immune system to attack the cancer cells. Once T–DM1 is absorbed into those cancer cells, it is designed to destroy them by releasing the DM1.

T–DM1



T–DM1 (1) binds to the HER2 receptor on the tumour cell surface, initiating several antitumour activities before being absorbed into the cell. Once inside the cell, T–DM1 breaks down and releases the active form of DM1 (2). DM1 then binds to a protein structure that plays a key role in cell division (3). This prevents the cell from dividing and ultimately results in cancer cell death.



↗ **More on the web:**
http://www.roche.com/valueofinnovation

1 Trastuzumab is the active ingredient in Herceptin.


Evolution of therapy for HER2-positive metastatic breast cancer
Chemotherapy
Targeted therapy and chemotherapy
Highly targeted antibody-drug conjugates

13.6

Swiss francs
core earnings per share

2

BUSINESS REVIEW

Reached financial targets for 2012.

Delivered strong growth in the US and emerging markets.

Strengthened operating free cash flow, lowered net debt.

Improved R&D efficiency.

Key figures

Group sales	45,499 millions of CHF	+4% (CER)[1]
Core operating profit	17,160 millions of CHF	+11% (CER)
Net income	9,773 millions of CHF	+1% (CER)

	In millions of CHF		% changes			As % of sales	
	2012	2011	CER	CHF	USD	2012	2011
Group sales	45,499	42,531	4	7	1	100	100
– Pharmaceuticals Division	35,232	32,794	5	7	2	77	77
– Diagnostics Division	10,267	9,737	4	5	0	23	23
Core operating profit	17,160	15,149	11	13		37.7	35.6
– Pharmaceuticals Division	15,488	13,406	13	16		44.0	40.9
– Diagnostics Division	2,187	2,178	-2	0		21.3	22.4
Operating free cash flow	15,389	13,733	10	12		33.8	32.3
Core earnings per share (CHF)	13.62	12.30	10	11			

Group results and outlook

Roche delivered a strong performance in 2012, reaching its financial targets for the year. Group sales increased 4%[1] to 45.5 billion Swiss francs (+7% in Swiss francs). This reflected strong demand for oncology products, as well as for clinical laboratories diagnostic products. The US and emerging markets, especially China and Brazil, were the main regional growth drivers. In Western Europe, however, despite some resilience to pricing pressure, sales were slightly lower and there was additional pressure from generic competition.

Group core operating profit rose 11% to 17.2 billion Swiss francs due to a solid sales performance combined with productivity improvements that lowered the cost of sales ratio. R&D costs were stable, and savings from the closure of the Nutley site in New Jersey, USA were reinvested into our strong, emerging clinical product pipeline. The Group's core operating margin further improved by 2.1 percentage points to 37.7%.

The Group's core earnings per share (EPS), which excludes non-core items such as global restructuring charges and amortisation and impairment of goodwill and intangible assets, rose 10%.

In 2012 Roche took the decision to restructure Pharma Research and Early Development, and to make more resources available for the growing number of products in late-stage development by closing the Nutley site. This process is well underway. Restructuring measures were also taken in the Diabetes Care and Applied Science businesses to enable these units to better adapt to increasingly challenging market conditions.

The cost of these restructuring activities, together with a number of other one-time items, resulted in a slightly higher net

1 Unless otherwise stated all growth rates are calculated using constant exchange rates (CER).

income on an IFRS basis of 9.8 billion Swiss francs (+2% at Swiss francs).

Pharmaceuticals – strong growth from oncology

Sales for the Pharmaceuticals Division rose 5% in 2012 to 35.2 billion Swiss francs with robust demand for the three top-selling products MabThera/Rituxan, Herceptin and Avastin. Avastin is also now back into growth, supported by its launch in ovarian cancer in Europe.

The division additionally benefited from strong demand for rheumatoid arthritis medicine Actemra/RoActemra, which showed superiority in monotherapy against adalimumab in the ADACTA trial, as well as for hepatitis C drug Pegasys. Newly-launched skin cancer medicine Zelboraf also performed well during the year.

Herceptin, MabThera/Rituxan, Avastin, Actemra/RoActemra, Zelboraf and Pegasys, which together represent 60% of the portfolio, generated 2.4 billion Swiss francs in additional sales for the year.

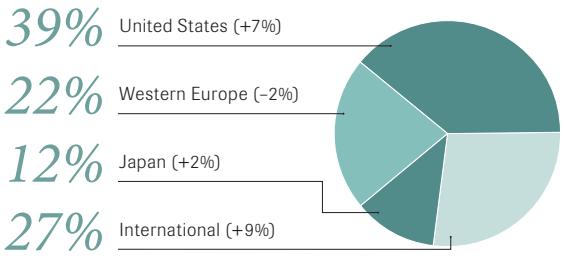
Two new cancer drugs were also launched in 2012: Perjeta for breast cancer and Erivedge for advanced basal cell carcinoma, a type of skin cancer. Initial uptake for both products was positive.

Sales of eye medication Lucentis for wet age-related macular degeneration (wAMD) fell in 2012, as competitive pressure intensified, however the uptake of Lucentis to treat another indication, diabetic macular edema, has been strong. Bonviva/Boniva and CellCept sales were also lower due to ongoing generic erosion, particularly in Western Europe.

Regionally, US sales (+7%), along with the key seven emerging markets (+14%)[2] were the main growth drivers with strong demand for oncology products, as well as increased health-care spending in a number of markets. Sales in Western Europe (–2%) were impacted by generic competition and continued price pressure. However, the major products, including Herceptin, MabThera/Rituxan and Avastin continued to grow, and Zelboraf emerged as a key growth driver. Japan posted sales growth of 2% for the year, with Mircera, Avastin and MabThera performing strongly.

2 Roche's key seven emerging markets, also referred to as the E7 key emerging markets, are Brazil, China, India, Mexico, Russia, South Korea and Turkey.

Pharmaceuticals Division – sales by region

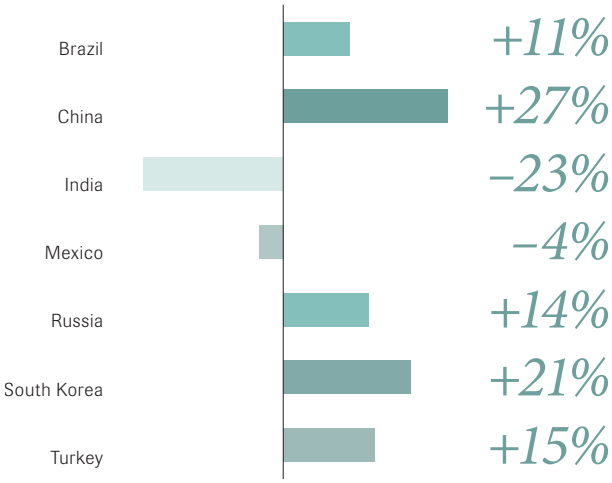


At constant exchange rates (average full-year 2011).

The HER2 product group was further strengthened by the launch of Perjeta and the filing of trastuzumab emtansine (T–DM1), a new generation of cancer treatment, for approval in Europe and the US. Perjeta and T–DM1 will allow Roche to build on the long-term success of Herceptin as the standard of care for women with HER2-positive metastatic breast cancer, a particularly aggressive form of the disease.

The pipeline remained robust, delivering 11 positive results out of 14 late-stage studies in 2012, including strong results for Avastin in platinum-resistant recurrent ovarian cancer in the AURELIA trial.

Pharmaceuticals Division – sales growth in E7 leading emerging markets



At constant exchange rates (average full-year 2011).

The Pharmaceuticals Division core operating profit increased 13% to 15.5 billion Swiss francs, as a result of strong sales and efficiency gains. Core operating profit margin increased 3.1% to 44.0%.

Diagnostics – strong clinical labs sales

Diagnostics sales increased 4% to 10.3 billion Swiss francs, continuing to grow faster than the global IVD market which showed a slowdown in 2012.[3] With 20% market share, Roche solidly maintained its market leadership. Divisional sales were driven by the business with clinical laboratories, particularly Professional Diagnostics (+8%), which grew twice as fast as the global market, as well as Tissue Diagnostics (+12%) and Molecular Diagnostics (+4%).

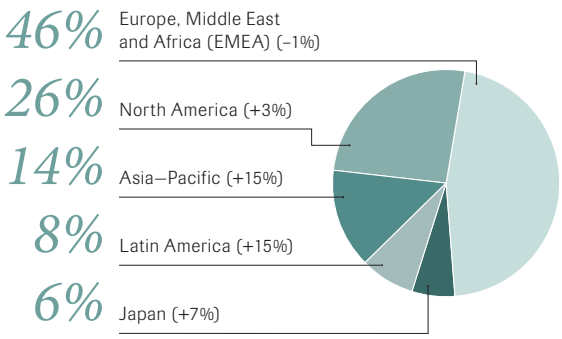
The largest overall product contributor to growth was the immunoassay business (+15%), which helps diagnose various diseases through highly automated immunochemical blood testing.

The Diabetes Care and Applied Science businesses faced a challenging year. Reimbursement cuts for blood glucose monitoring products in Europe, along with intensified price pressure impacted sales in the Diabetes Care business (–4%). The decline in sales in the Applied Science business (–3%) was a result of lower public research funding and competition in gene sequencing. Both businesses undertook restructuring during the year to sustain long-term profitability and to refocus their portfolios for future growth.

The division consolidated or expanded its leading market position in all regions. In Asia–Pacific and Latin America, Professional Diagnostics remained the main growth driver, with strong contributions from Diabetes Care in Latin America. The clinical laboratories business was the key growth driver in North America, and the launch of over 40 major products in the US in 2012 started to create further growth momentum. In the EMEA region (Europe, Middle East and Africa) austerity measures and pricing pressure had an impact on sales, particularly in Diabetes Care. In Japan, sales grew at three times the rate of the market, driven by Professional Diagnostics.

The division launched 55 major products in key markets over the year, representing important advances in lab automation, near patient testing and diabetes management, as well as further expanding test menus. The division also made further progress with its Personalised Healthcare strategy, with over 200 ongoing biomarker and companion diagnostics projects with Roche Pharmaceuticals and 12 new agreements concluded with external pharmaceutical companies.

Diagnostics Division – sales by region



At constant exchange rates (average full-year 2011).

Core operating profit in the Diagnostics Division fell 2% to 2.2 billion Swiss francs, reflecting increased price pressure in Diabetes Care. The margin was 21.3%, above that achieved in the first six months of the year, however 1.1 percentage points lower than in 2011.

Strong Group operating free cash flow and improved net debt position

Operating free cash flow remained strong in 2012, rising 10% to 15.4 billion Swiss francs and contributing to the lower net debt position of 10.6 billion Swiss francs at the end of 2012, down from 15.6 billion francs at the start of the year. As a result of the strong cash flow, bonds totalling a nominal value of 1.6 billion euros were bought back early in 2012.

Outlook 2013

Roche expects Group sales in 2013 to increase in line with the sales growth recorded in 2012 at constant exchange rates. Core EPS is targeted to grow ahead of sales. Roche expects to further increase its dividend for 2013.

3 Estimated IVD market growth is 3% (source: company and independent reports, to end of September 2012).

Market Environment and Group Strategy

The healthcare market continues to be driven by the competing pressures of supply of financial resources and an ever increasing demand for better healthcare outcomes. Cost-effective, targeted medicines and diagnostics like those produced by Roche have a key role to play in tackling these challenges.

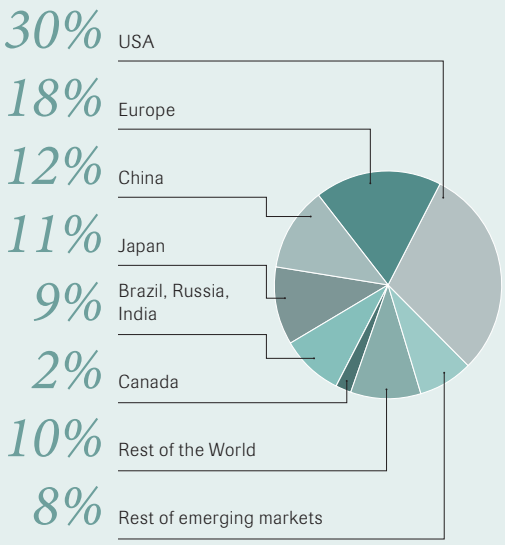
Challenges in 2012

Rising life expectancy and higher incidences of chronic diseases have significantly increased the need for rapid scientific and technological advances for better health outcomes.

Market Trends

Despite advances in modern medicine the need for improved healthcare and treatments remains enormous. Over 3,000 of all known diseases – about two-thirds – remain untreatable or lack satisfactory treatment. A growing and ageing world population, meanwhile, is accelerating demand: the 65-and-older population is forecast to triple to 1.5 billion by 2050, giving rise to more age-related, chronic diseases such as cancer, diabetes and Alzheimer's disease. Ageing and lifestyle-related diseases are no longer just a problem in the affluent west: they constitute the fastest growing public health problems in developing countries.

Regional market share of global pharma sales 2016*



* IMS Health Market Prognosis, April 2012

Pharmaceutical market

Pharmaceutical markets are continuing to expand worldwide, although the pace of growth is slowing, with more and more medicines going off patent. Global sales are forecast to reach more than a trillion Swiss francs in 2013.

Emerging markets are showing the most robust growth, creating new opportunities for the pharmaceutical industry, as governments invest in public healthcare systems. China is expected to be the main contributor to global growth by 2015.

Growth in developed markets, however, is expected to stay modest at best. The US is the largest healthcare market, but growth rates there are forecast to slow, with lower GDP growth and increasing generic competition.

Speciality pharmaceutical markets are the largest and among the fastest growing healthcare segments, with a total market share of 22% [2011 data; source: IMS], with the largest share of growth in the US. Key growth areas are oncology and autoimmune disease, and in general the hospital and biologics segments – where Roche is the global leader.

Diagnostics market

The global *in vitro* diagnostics market, estimated at approximately 50 billion Swiss francs, has grown at a slower pace in 2012, but is expected to grow on average by about 5% annually over the longer term [source: independent IVD consultancy]. The highest growth rates are forecast for emerging markets and for molecular and tissue diagnostics.

As the global need for new and better treatment options increases, so too does the pressure to control healthcare costs. In the US and Europe in particular, economic conditions are driving cost efficiency measures and putting pressure on the healthcare industry to deliver innovative solutions at lower costs.

In the US, additional conditions were introduced to the regulatory process for approval of new medicines. New legislation now encourages the comparison of medical treatments, not only on the basis of safety and efficacy, but additionally on cost. The increasing influence of non-prescribing decision makers is evident in other markets such as the UK and Germany, where state-run organisations are reviewing the clinical and wider economic benefit of new medicines in comparison with established products on the market. Health technology assessments are becoming more common in Europe and the US, to evaluate reimbursement decisions on medical evidence. This comes frequently with value-based pricing systems, where payment is structured around treatment outcome. Health systems around the globe generally are increasing their focus on clinical outcome and real world evidence data that enable the real value of new medicines to be assessed after product launch. The pharmaceutical industry is also active in working with health authorities to structure clinical trials to provide evidence of medical value more quickly, so that innovative medicines can reach the patients more quickly.

Focusing on innovation

As a research-based healthcare company, Roche focuses on innovation, investing significantly in R&D to develop highly differentiated and effective treatments to help people live longer and healthier lives. Personalised Healthcare at Roche is one example of this strategy – pinpointing exactly which patients will respond to a particular therapy, ensures that patients receive the right treatment at the right time and without wastage of healthcare budgets. This targeted approach delivers value to all healthcare stakeholders – patients, providers, regulators and payers. Effective diagnostic testing also plays an important role in increasing the overall efficiency of healthcare delivery. Although spending on *in vitro* diagnostics only represents around 2% of healthcare expenditure, 70% of all medical decisions depend on accurate and fast diagnosis, which in turn, can reduce healthcare costs considerably.

Demonstrating this value is a strategic priority for Roche. We collaborate extensively with healthcare providers, insurers and other payers, in particular, on the value of timely and accurate diagnosis, which is not always fully recognised.

The Diagnostics Division is working to support the development of reimbursement programmes that accurately assess the validity of advanced diagnostic testing.

Our Business Model: Changing the practice of medicine

For over a decade, Roche has maintained its strategic focus on innovative diagnostics and therapeutics. Today, we are intensifying our commitment to develop personalised healthcare and other medically differentiated products – medicines and diagnostics that create superior value for our patients, customers and society. To advance this goal, we focus exclusively on prescription pharmaceuticals and *in vitro* diagnostics, following a business model that drives medical innovation along three dimensions:

- Fitting treatments to patients
- Pursuing excellence in science
- Delivering value to all stakeholders

Fitting treatments to patients

Eighteen million patients were treated with Roche medicines last year, and over 500,000 patients participated in clinical trials of new drugs we are developing. The patient frames our strategy for discovering and developing new medicines and diagnostics – from deciding what molecules we research to how we design our clinical trials.

New diagnostic techniques have enabled us to develop therapies that can increasingly be targeted at particular patient populations. Two patients can have the same diagnosis yet respond in different ways to the same medicine. One patient may be helped by treatment, while the other experiences unwanted side effects without the desired clinical benefit. Mostly, this variability is due to genetic and other biological differences between patients.

Drawing on insights into these differences at the molecular level, we can now develop treatments and tests tailored to the needs of specific patient populations. This personalised approach has enormous potential to make healthcare better, safer and more cost-effective. Additionally, these medically differentiated products are more likely to obtain regulatory approval and be accepted by patients, physicians and payers.

Owing to their significant clinical benefits, Roche's new cancer medicines Erivedge, Zelboraf and Perjeta received accelerated approval in their first markets, the latter two approved with a companion diagnostic. Today, roughly half the new molecular entities in our late-stage portfolio are tailored to subsets of

patients who can be identified using the diagnostic tests that are central to Personalised Healthcare.

Pursuing excellence in science

Excellence in science through discovery and innovation is our answer to the medical challenges the world faces. By continuously investing in research and development, we seek to gain a better understanding of disease and harness the potential of modern biological sciences in treating those diseases. That is why Roche has invested more than 75 billion Swiss francs in R&D over the past ten years — more than most other companies in the world.

Science's rapidly expanding knowledge of disease biology and the causes of disease hold particular promise for transforming the practice of medicine. While this knowledge is leading to dramatic improvements in identifying biological targets to fight many diseases, the complexity in research is rising significantly. This is resulting in lengthy and costly R&D cycles for new products of up to 12 years and approximately 1.5 billion Swiss francs, on average, to obtain approval for a new drug. At the same time, increasingly stringent regulation is slowing the approval of new molecular entities for the industry as a whole.

Only by excelling in science can we achieve the breakthroughs in science and technology needed to speed the discovery, development and approval of new medicines. Interweaving the knowledge of our Pharmaceuticals and Diagnostics Divisions throughout the value chain increases the efficiency and productivity of research and development. Over the last two years, Roche has achieved 26 out of 32 positive late-stage trials — a success rate clearly above industry-average.

We combine our strong in-house research capabilities with the latest advances in science at other biotech companies through about 150 partnerships. Today, about one-third of our pipeline and our marketed products originated from this external network. We also foster innovation by interacting with academic institutions and universities worldwide.

Delivering value to all stakeholders

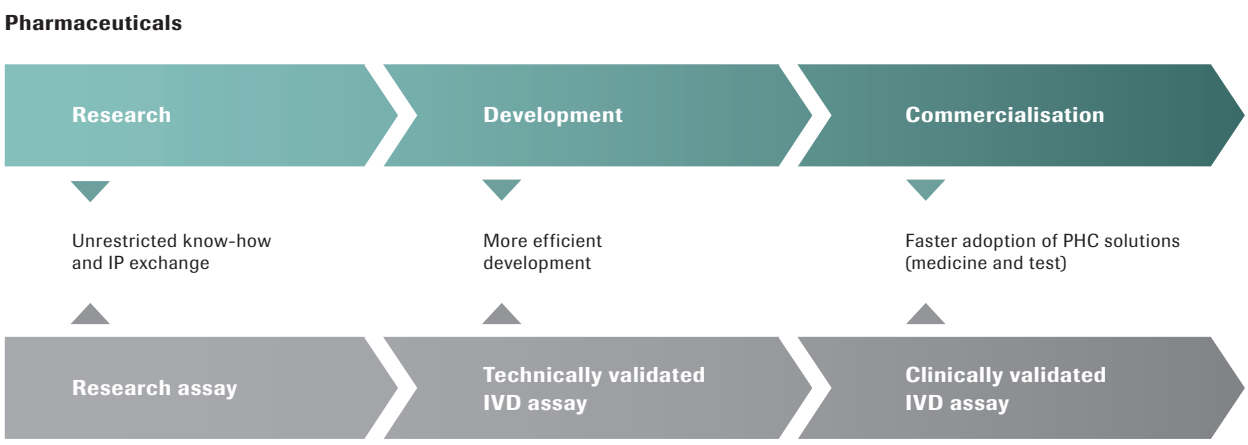
Since its formation in 1896, Roche's most valuable contribution to society has been the discovery and development of novel therapies that improve health and help patients live longer, better lives.

Our continued success hinges largely on our ability to combine social and environmental responsibility with a focus on sustainable economic growth. Roche is convinced that sustainable corporate policies and practices promote innovation and create long-term value among all stakeholders:

- Patients and doctors, by ensuring product quality and safety, improving access to medication, enabling medical laboratories to work more efficiently and helping to contain healthcare costs.
- Employees, by giving our people opportunities to make their mark and improve lives, by creating great places to work and by embracing diversity across the organisation.

Roche strategy: Leveraging Pharmaceuticals and Diagnostics

Throughout discovery market



- Investors, by ensuring transparency and achieving superior valuations to our industry peers, aiming to provide them with a Total Shareholder Return in the top quartile of our industry peer set.
- Communities, by stimulating engagement in science, promoting cultural activities and tackling social causes that make a lasting impact.
- Society at large, by conducting businesses responsibly with a view to having a positive influence on society and minimising our impact on the environment. Roche was recognised as the Supersector Leader in Healthcare for the fourth time in a row in 2012 in the Dow Jones Sustainability Indexes.

Our Management Model: Enabling an innovation-driven culture

Our management model is aimed at enabling a culture of innovation by embracing a diversity of approaches. Like our business model, it has three dimensions:

- Inspiring integrity, courage and passion among our people
- Encouraging accountable and transparent decision making
- Structuring our business to capitalise on innovation

Our People: Integrity. Courage. Passion.

Our ability to leverage our combined expertise in pharmaceuticals and diagnostics ultimately depends on our people. Representing virtually every country on the globe, our more than 82,000 employees bring to their work a diversity of perspectives and experiences that stimulates creativity and innovation. We respect, embrace and value diversity as actively as we foster high standards of integrity, the courage to reach beyond boundaries and a passion to improve patients' lives. Integrity, passion and courage are the values that we seek as a company and that bind us together as a team to constantly grow further.

Our Decision Making: Accountable and transparent

We believe that good leadership is not a question of hierarchy, but a function of effective decision making. Given our highly networked organisation and the complex nature of our business, decisions must be informed by a dialogue that is systematic, fact-based, open and transparent. Every decision requires a single, accountable decision maker who collects and critically reviews information and competing views. Empowerment is essential, which is why we delegate decision making, as much as possible, to the lowest qualified level in the organisation.

Our Structure: Built for innovation

Mastering the complex biology of the various diseases and pathways is our biggest challenge in developing new diagnostic tests and medicines. To overcome this challenge, we not only encourage our people to consider different perspectives and approaches in drug research and early development, but we also structure our business to foster creativity and excellence in science.

Our two complementary in-house research and early development arms, pRED and gRED, as well as Roche Diagnostics and Chugai, each operate independently within the Group. We believe that this decentralised approach combines the critical mass of the Roche Group with the flexibility, creativity and entrepreneurial spirit that are common among smaller businesses. At the same time we consolidate and coordinate Group-wide activities in clinical development, manufacturing, marketing and commercial operations to make the best use of our global scale and reach.

The fight against cancer goes on

50 years of cancer research at Roche

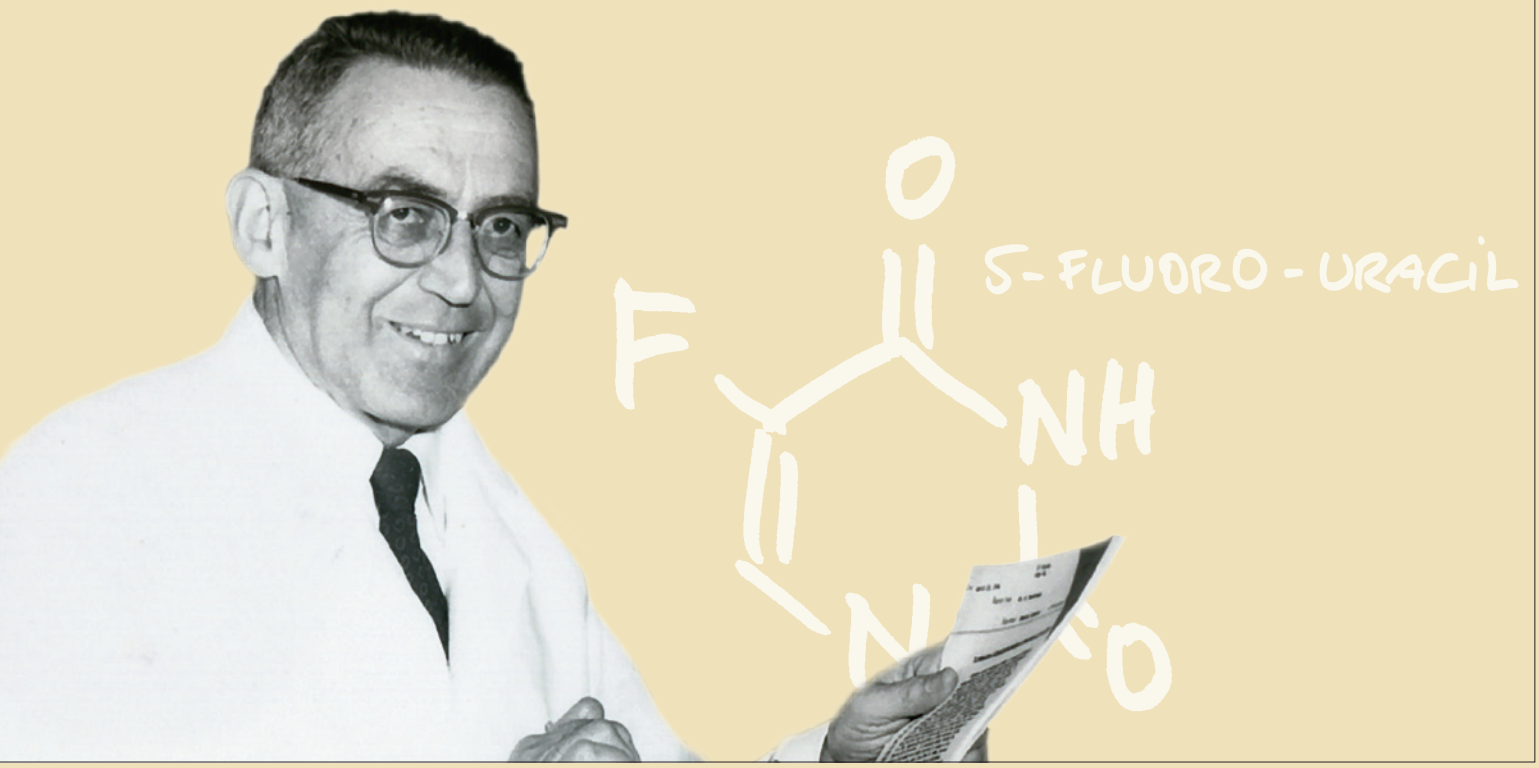
One in three people will develop cancer during their lifetime. And yet the challenge to find a cure remains elusive. One of the reasons it is so difficult to treat is that cancer is, strictly speaking, not just one disease but a group of different diseases. So far, over 250 different types have been identified. What cancers have in common though, is that they are all caused by the uncontrolled proliferation of human cells.

Roche has been at the forefront of cancer research for decades and is today the leading pharmaceutical and diagnostic company in the field. Well over 50 years ago, Robert Duschinsky (see picture) from Nutley, in collaboration with Charles Heidelberger from the University of Wisconsin, synthesized 5-Fluoro-uracil (5 FU), Roche's first anticancer drug. Although this was considered a breakthrough at the time, it caused severe side effects because it attacks both healthy cells and cancer cells.

From the start, our aim was to advance the treatment of cancer. As a result, Roche later developed several successor drugs with the aim of preferentially generating the cytotoxin 5-FU in the tumour itself, and consequently of achieving greater efficacy with fewer side effects.

Since those early beginnings, cancer research conducted by Roche and others has provided doctors and patients with better and better medicines and diagnostic agents.

Cancer cells, unfortunately, are inventive – they discover ways of escaping treatment, often reproliferating at a later stage. Despite tremendous progress in the treatment of cancer, much remains to be done to combat this insidious disease.



The long-running battle against cancer
and our contributions

≤ 1960s and 1970s

- **Diagnostic tumour markers in the blood**
- **Radiotherapy and chemotherapy**
- **CAT scan**
- **Viruses can cause cancer (HPV)**
- **Breast-conserving surgery**

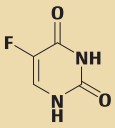
1980s

- **Global guidelines for pain management**
- **Treatment of early-stage colon cancer**
- **Medicines for increasing red blood cell production in patients with anemia**
- **First cancer medicines produced by biotechnology**
- **Foundations of molecular diagnostics**

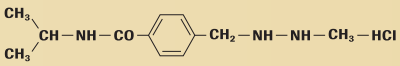
1990s

- **Cancer mortality starts to decline**
- **Intensive exposure to sunlight recognised as a cause of skin cancer**
- **Natural cytostatics used for cancer treatment**
- **First targeted biopharmaceuticals**
- **Relationship demonstrated between obesity and cancer**
- **Molecular diagnostic tests advance cancer detection**

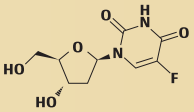
1962: 5-Fluoro-uracil (5-FU), a synthetic substance that inhibits cell growth and is administered intravenously. Causes tumours to shrink, but attacks all dividing cells, including healthy ones.



1965: Procarbazine (Natulan®) for the treatment of lymph tissue tumours. The active substance interferes with the genetic material (DNA) and in so doing disrupts cell division.



1970: 5-Fluorodeoxyuridine (Floxuridine®), a 5-FU derivative.



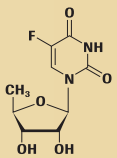
1971: Efudix, a cream containing 5-FU for the local treatment of skin tumours.

1973/74: The world's first immunodiagnostic test for a tumour marker (CEA: carcinoembryonic antigen).

1983: First enzyme immunoassay from Roche for the detection of tumour antigens.

1986: Alpha-interferon (Roferon®-A), Roche's first biotechnological product approved for the treatment of a previously fatal form of blood cancer, with a positive response rate of about 90% of all cases.

1987: Doxifluridine (Furtulon®), a further development of 5-FU, designed to generate active 5-FU preferentially in tumours, resulting in fewer side effects.



1990: Epoetin beta (NeoRecormon®), for treatment of chemotherapy-induced anemia.

1991: Filgrastrim (Neupogen®), prevents white blood cell depletion and the risk of infection after chemotherapy.

1995: Retinoic acid (Vesanoid®), for the treatment of acute promyelocytic leukemia.

1997: Rituximab (MabThera®), first targeted, biotechnologically produced drug, used for treatment of non-Hodgkin's lymphoma (blood cancer) and other indications.

1998: Capecitabine (Xeloda®), orally administered, inactive precursor of 5-FU; designed to generate doxifluridine after it is absorbed from the gut, thereby reducing the risk of intestinal damage.

1998: Trastuzumab (Herceptin®), biotechnological drug for the treatment of a particularly aggressive (HER2-positive) form of breast cancer, accounting for 15–20% of all breast cancers. High HER2 protein levels must first be detected by a companion diagnostic test before treatment; **first example of a medicine geared to the needs of a specific patient group (personalised healthcare).**

2000s

- **Decoding of the human genome**
- **Cancer cells become resistant to first-line drugs**
- **Combination treatments with targeted drugs**
- **First medicine to inhibit tumour blood supply**
- **Cervical cancer vaccine**
- **Genetic and tissue cancer tests**

≥ 2010

- **Record number of cancer survivors**
- **Breakthrough medicines against skin cancer**
- **New drug class of antibody–drug conjugates**
- **Personalised cancer therapies with companion diagnostic tests**
- **Combination treatments against resistance**

2004: Bevacizumab (Avastin®), first biotechnological cancer drug to block angiogenesis, in other words, the formation of blood vessels that supply cancer tissue with nutrients and oxygen. It specifically blocks the naturally occurring protein VEGF (vascular endothelial growth factor), an important mediator of angiogenesis. Avastin possesses a novel mechanism of action and is used in several types of tumours.

2005: Erlotinib (Tarceva®), an oral lung cancer drug that inhibits tumour development by attacking the HER1/EGFR protein which is important for cell growth.

2011: Vemurafenib (Zelboraf®) and its companion **BRAF-V600E mutation detection test.** A mutated form of the BRAF protein occurs in about half of all melanoma patients. After the companion test identifies patients with this specific mutation, Zelboraf launches a targeted attack against the tumour, making it the first treatment for this aggressive skin cancer to considerably improve quality of life and prolong survival.

2011: Eight important new oncology tests, including cobas HPVin the US to detect women at increased risk of cervical cancer.

2012: Vismodegib (Erivedge®), an oral, targeted drug for the treatment of advanced (inoperable and metastatic) basal cell carcinoma. Erivedge specifically blocks a mediator of a hyperactive signal pathway in these cancer cells.

2012: Pertuzumab (Perjeta®), a biotechnological drug for the treatment of a particularly aggressive form of breast cancer (HER2 positive) in combination with chemotherapy and Herceptin. The dimerisation inhibitor is designed specifically to prevent the HER2 receptor from pairing with other HER receptors.

Cancer: a growing global challenge

Cancer remains unconquered – only cardiovascular disease claims more victims. Each year, almost 12 million people worldwide are diagnosed with cancer. Around eight million people die annually from some form of cancer. In developing countries, which account for about half of all cases, cancer kills more people each year than AIDS, malaria and tuberculosis combined.

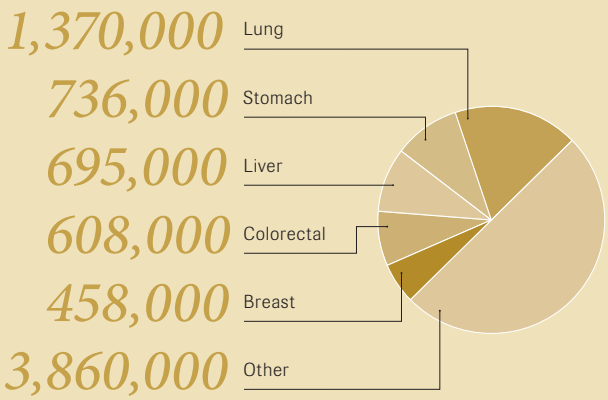
Cancers are on the increase chiefly because of a growing and ageing world population. Breast, lung and prostate cancers are those most frequently diagnosed in industrialised countries.

Unhealthy lifestyle choices are also contributing to an increase in cancers. It is estimated that 30% of all cancers could be prevented by avoiding behaviours such as smoking or alcohol abuse and conditions like being overweight.

Recent progress in the diagnosis and treatment of cancer has contributed to encouraging overall improvement in survival rates, even in advanced cases. Survival for breast cancer patients, for example, has almost tripled.

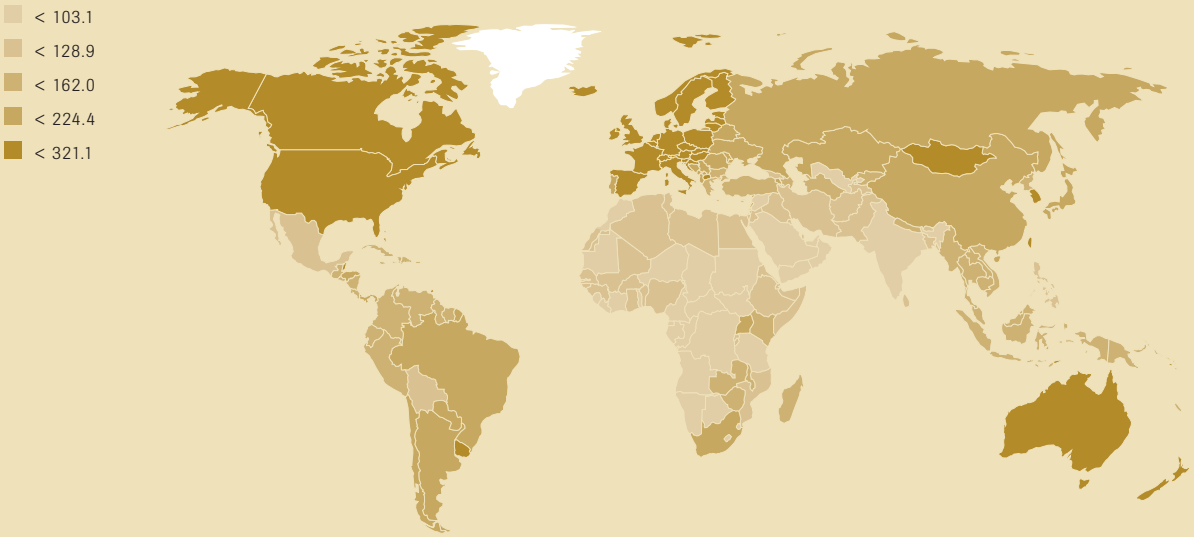
Cancer-related deaths

(worldwide, 2008)



Medically promising approaches include better early detection and the combination of treatment regimens with different effects to attack the tumour from new angles. Today targeted medicines with effects adapted to the genetic changes in tumours are ushering in a new era of cancer therapy.

Currently every year over 12 million people are diagnosed with cancer



Estimated Age Standardised incidence rate per 100,000. All cancers (excluding non-melanoma skin cancer) both sexes, all ages.
Reference: WHO International Agency for Research on Cancer Globocan Cancer Fact Sheet, 2008. Accessed online at http://globocan.iarc.fr (04/05/2011).

Gaining a better understanding of this insidious disease

Why is cancer so difficult to control? An important finding of research at the molecular level, is that cancer is a collective term for more than 250 tumours. These can affect all of the body's tissues and can occasion a multitude of signs, symptoms and late effects.

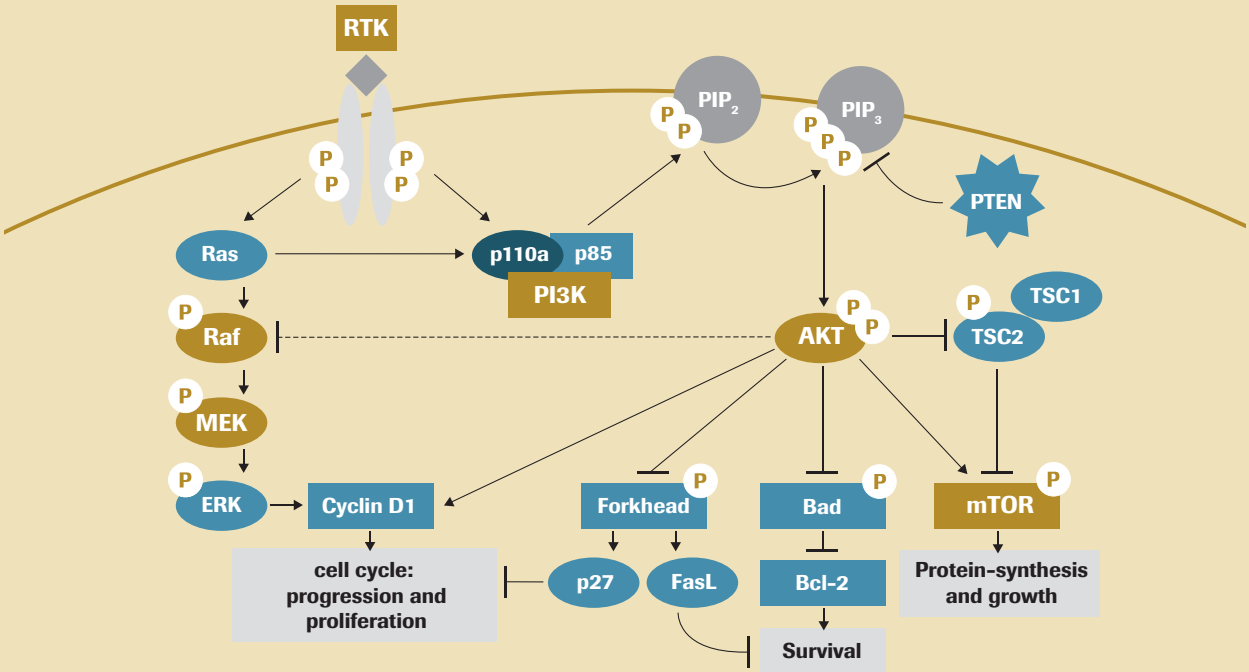
Ultimately, all types of cancer are due to damage to the DNA and hence to changes in genes. The genetic defects that cause tumours are to some extent inherited. Often, however, they are acquired over the course of life from cancer-engendering substances, such as tobacco, viruses or radioactive rays, that damage genes and hence cells' blueprints.

Tumours develop mainly from a few cells displaying gene changes or mutations. These changes affect important cellular mechanisms that normally control cell proliferation.

Those signal chains whose function is disrupted by mutations of the corresponding genes are often those involving antennas in the cell membrane. These cell surface receptors, which are partly responsible for controlling the signal pathways triggering cell division and multiplication, become hyperactive, leading to uncontrolled cell division. The proliferating cells then displace and damage healthy tissue.

Researchers at Roche are working on identifying characteristic changes in the genome and in the signalling pathways for each particular tumour. The aim is to combat cancer more effectively by blocking those overactive mechanisms.

Signal pathways triggering cell division and proliferation; in cancer these pathways are often disrupted

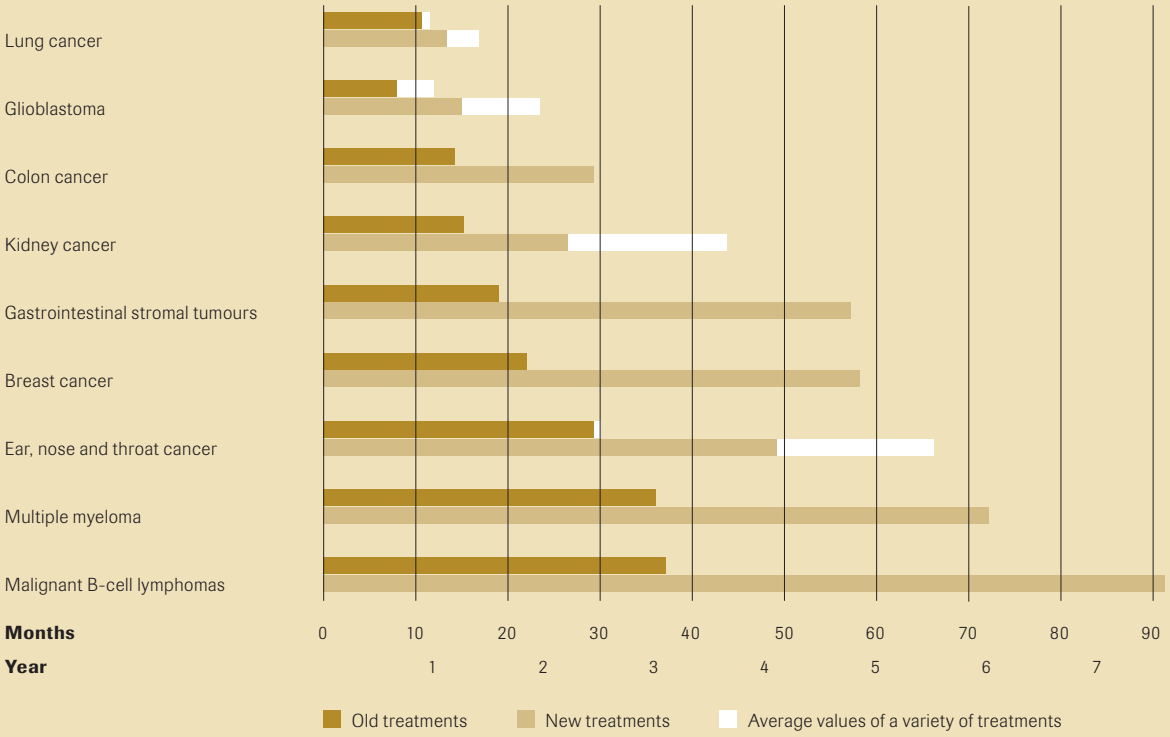


Improving survival benefits for cancer patients

Advances in cancer medicine in the last ten years have prolonged life and improved quality of life considerably for cancer patients. Ten years ago, patients with advanced breast cancer lived 22 months from diagnosis, on average. Today they live almost three times as long.

The survival benefits of new cancer medicines may be better than indicated, however. New treatments are initially used only in advanced stages of the disease. Unfortunately, patients in this situation have often already experienced a series of treatment failures, which can lead to an understatement of the survival benefits of some new medicines.

Progression of overall survival (average in months) in advanced cancers in the last decade



1 Source: Prof Christoph Zielinski, University of Vienna, March 2010. 'Optimising outcome in the treatment of malignant disease using modern treatment strategies: Impact on cancer patient survival', http://www.onkologie-wien.at/forschung-und-lehre/positionspapier

Promising research into cancer treatments of the future

At Roche, we direct more than four billion Swiss francs annually to oncology research — 50% of our entire expenditure in R&D.

By pursuing a variety of strategies, we are gaining an increasingly better molecular understanding of cancer that is leading to improved detection and new and broader treatments. Our recent advances include:

- drug combinations that block an array of signal pathways that spiral out of control in cancer, thereby preventing the development of resistance in tumour cells
- a new type of targeted and selective cancer therapy, antibody–drug conjugates, that kills cancer cells and exerts only minor negative effects on normal tissue
- gearing the human immune system to attack tumour cells more effectively with our PD-L1 antibody, which blocks the PD-L1 protein found in many tumours that prevents immune system cells from destroying malignant cells
- our glyco-engineered antibody GA101 that first binds to tumour cells, then attracts immune system cells, such as T-lymphocytes and natural killer cells, which then destroy the flagged tumour cells

Most of our targeted therapeutic agents are combined with a companion diagnostic test that predicts the probability of a patient responding to treatment. This personalised approach to cancer treatment is not only better for the patients, but also enables an efficient use of financial and human resources of national health systems.

Roche's oncology portfolio: Broad set of technologies for targeted therapies

Tumour types	HER2-positive breast	Gastric	HER2-negative breast	Colorectal	Lung	Skin	Glioblastoma	Hematological
Antibody–drug conjugates	T-DM1	T-DM1						Anti-CD 22 Anti-CD 79b
Antibody combinations	Perjeta + Herceptin	Perjeta + Herceptin	MetMab + Avastin	MetMab + Avastin EGFL7 + Avastin	MetMab + Avastin EGFL7 + Avastin		MetMab + Avastin	
Glyco-engineered antibodies				GA201	GA201			GA101 (obinutuzumab)
Immuno-therapies						e.g. Zelboraf + PDL1		
Small molecules		PI3K			PI3K	Zelboraf + MEKi		Bcl-2 PI3K

The Experts' View

Susanne Arbogast
Pathologist, Oncology franchise

'All Roche projects designed to produce a new cancer drug are now combined with a biomarker programme. Probing analyses begin at the preclinical stage and lead to licensed diagnostic tests that are then put to pioneering use primarily in phase III projects. In fact, the number of biomarker studies we conduct in collaboration with external partners, but also in-house, considerably exceeds the number of Pharma projects, because we are exploring several avenues simultaneously for classifying markers that give insights into the response to a particular therapy. Thus we are screening patients and tumour samples for differences at the level of the genes (DNA), the molecules that transfer genetic information (RNA) and the gene products (proteins).

Cancer diagnostics appear set to evolve from the single test approach to the simultaneous testing of several parameters in order to identify the best possible treatment for a particular patient.'

Hal Barron
Chief Medical Officer

'Our progress in oncology and other therapeutic areas during the last two years has been incredibly robust. In addition to receiving regulatory approval of three new molecular entities for cancer in less than 18 months, we had results from 32 key clinical trials of our oncology and non-oncology medicines, 26 of which had positive results. This success rate means that basically about every three weeks we had news from results that will have a meaningful impact for patients.

It is likely that many factors contributed to these successful studies including rigourous early research, efficient study execution, smart risks and a focus on personalised healthcare to identify which patients are more likely to benefit from certain medicines. Combined, these measures by our talented people increase our probability of technical success and allow us to deliver transforming medicines to patients.'

200

collaborations between Pharmaceuticals and Diagnostics

RESEARCH AND DEVELOPMENT

Received approvals for three new cancer medicines.

Delivered positive results in 11 out of 14 late-stage clinical trials.

Continued clinical development of 72 promising new molecular entities.

Launched 55 diagnostic products in key markets.

Key figures

Core Research and Development (R&D) expenditure in 2012

Roche Group	8,475 millions of CHF	+2% (CER)[1]	18.6% of sales
Pharmaceuticals	7,529 millions of CHF	+2% (CER)	21.4% of sales
Diagnostics	946 millions of CHF	+4% (CER)	9.2% of sales
Employees in R&D	18,279 Roche Group	15,145 Pharmaceuticals	3,134 Diagnostics

1 Constant exchange rates (average full-year 2011).

Highlights of 2012

Pharmaceuticals

Milestone	Compound	Indication
Approvals – US	Erivedge	Advanced basal cell carcinoma
	Perjeta	Metastatic HER2+ breast cancer
Approvals – EU	Zelboraf	BRAF V600 mutation-positive metastatic melanoma
	Avastin	Recurrent, platinum-sensitive ovarian cancer
Filings – US	T-DM1	Metastatic HER2+ breast cancer
Filings – EU	Perjeta	Metastatic HER2+ breast cancer
	T-DM1	Metastatic HER2+ breast cancer
Key phase III trial results	EMILIA – T-DM1 adds nearly six months on average to the lives of women with HER2-positive metastatic breast cancer (second line). CLEOPATRA – Perjeta significantly extends the lives of HER2-positive metastatic breast cancer patients who are given this new drug alongside Herceptin and chemotherapy (first line). ADACTA – Actemra/RoActemra is shown to be more effective than adalimumab as monotherapy in rheumatoid arthritis.	

Diagnostics

Major product launches	55 major launches, including: – three devices for people with diabetes – three instruments for point-of-care testing – eleven systems driving efficiency in clinical and research labs – 36 assays for diagnosis of cancers, infections and metabolic diseases.
Key clinical study results	VISION – Troponin T cardiac test helps identify patients at risk after major non-cardiac surgery. ABACUS – Accu-Chek Aviva Expert's bolus advisor helps people with diabetes to improve their ability to reach glycemic targets.

Our pipeline remained solid in 2012, delivering positive results in 11 out of 14 late-stage studies. We now have a total of 72 new molecular entities in clinical development and we are confident that several of these compounds will become important therapies in coming years.

The Diagnostics Division launched 55 major products in key markets, including three diabetes care devices and a vitamin D test in the United States.

A highlight in 2012 was our ability to further improve the treatment options available to women suffering from HER2-positive breast cancer, a particularly aggressive form of the disease. Each year around 1.4 million women are diagnosed with breast cancer across the world, and over 450,000 die of the disease. HER2-positive breast cancer affects approximately 20% of women with breast cancer, and women must be tested to see whether they have this type of breast cancer.

Building on the success of Herceptin over the past 14 years, we launched the new medicine Perjeta in the United States and secured a positive recommendation from the European Union's Committee for Medicinal Products for Human Use. We also filed for approval of novel therapy trastuzumab emtansine (T–DM1) in both Europe and the United States. Data from late-stage trials have shown that both of these drugs could make a real difference to the many women diagnosed with HER2-positive breast cancer each year.

The CLEOPATRA phase III study showed that women with HER2-positive metastatic breast cancer who were treated with Perjeta, Herceptin and chemotherapy lived significantly longer than those who were given Herceptin and chemotherapy only. The study also showed that the risk of death was cut by a third.

The late-stage EMILIA trial showed that patients with HER2-positive metastatic breast cancer, who had already received treatment for their illness, survived a median of 5.8 months longer when treated with T–DM1 than those who received lapatinib and Xeloda. The risk of death was reduced by a third.

Trials are ongoing to examine the use of both Perjeta and T–DM1 in women with earlier stages of HER2-positive breast cancer. We are also examining the combination of Perjeta and T–DM1.

Herceptin, Perjeta and T–DM1 work by targeting the HER2-receptor, a protein found in abnormally high quantities on the outside of cancer cells in HER2-positive cancers. Perjeta and Herceptin are complementary to each other because they target the HER2- receptor in different places. T–DM1 is a particularly interesting compound because it is one of the first examples of an antibody–drug conjugate (ADC), a new technology that could make a significant difference to cancer treatment. See more on page 16.

A disappointment in 2012 was the second interim analysis of the dal-OUTCOMES phase III trial, which showed a lack of clinically meaningful efficacy for dalcetrapib, a drug that aimed to reduce the risk of cardiac events, such as heart attack, by raising high-density cholesterol. We decided to stop the development of dalcetrapib on the basis of this data.

Fighting HER2-positive breast cancer

Until just over a decade ago, women diagnosed with HER2-positive breast cancer faced a bleak future. Survival rates for patients with this type of cancer were among the worst, and death would likely follow within three years of diagnosis.

In the 1980s scientists discovered that overexpression of a gene known as the human epidermal growth factor receptor 2 (HER2) was to blame for this deadly form of breast cancer, and they began to develop a targeted therapeutic antibody that would block the HER2-growth factor receptors. Eventually Herceptin was approved for women with late-stage HER2-positive breast cancer in 1998.

Herceptin, which can now also be used to treat women with earlier stages of HER2-positive breast cancer, has given women with this type of breast cancer a great deal of hope. Survival rates have significantly improved, and many women who are treated with Herceptin in the early stages of their illness live disease free for several years after treatment. More than 1.3 million* people have now been treated with Herceptin.

But the story is not over, and with the approval of Perjeta and the strong data on T–DM1, the next chapter is just beginning.

* Includes patients treated with Herceptin for breast cancer and stomach cancer.

Antibody–drug conjugates (ADCs)

ADCs will allow patients to get the benefits of chemotherapy without having to suffer many of the toxic side effects. Chemotherapy works by attacking both the healthy and the cancerous cells, but we now know how to securely attach chemotherapy to antibodies. This allows a more targeted delivery of the chemotherapy to the cancer cells, which should increase efficacy and may decrease the side effects of chemotherapy, such as hair loss, nausea and infection.

T–DM1 is made up of trastuzumab, which is the active ingredient in Herceptin, potent chemotherapy agent DM1, and a linker that connects DM1 to trastuzumab.

Roche currently has eight ADCs in clinical development for ten oncology indications, and we are optimistic that we will soon be able to replicate the success of T–DM1 in various other types of cancer, such as blood cancer.

Extensive pipeline of ADCs for oncology indications

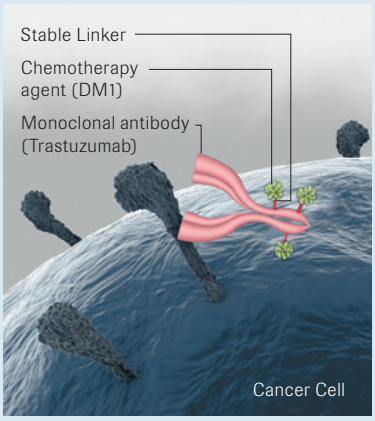
Indication	Phase I/II	Registration
Breast		T–DM1*
NHL	Anti-CD22/RG7593	
NHL	Anti-CD79b/RG7596	
Prostate	Anti-STEAP1/RG7450*	
Ovarian	RG7458*	
Multiple myeloma	RG7598*	
Lung and Ovarian	RG7599*	
Pancreatic and Ovarian	RG7600*	
Melanoma	RG7636*	

* Diagnostics.

How ADCs work:

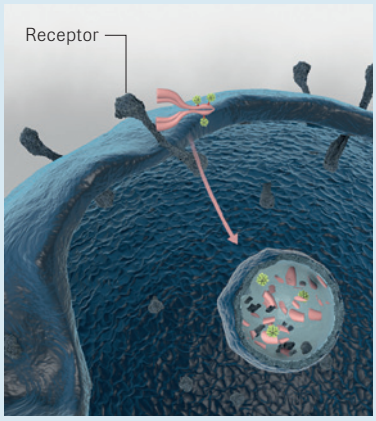
Certain proteins that are not found elsewhere in the body can sometimes be found on the surface of tumour cells. By developing an antibody that recognises these proteins and attaching the chemotherapy to the antibody it is possible to deliver a toxin directly to the cancer cell and potentially spare the rest of the body from the impact of the cytotoxic drug, or chemotherapy.

'The main challenge is ensuring that the chemotherapy is properly attached to the antibody and that it will not fall off in the blood stream and act just like chemotherapy. If this happens the patient does not get any benefit from the technology,' Richard Scheller, Head of gRED said. 'This was key to securing T–DM1's success.'



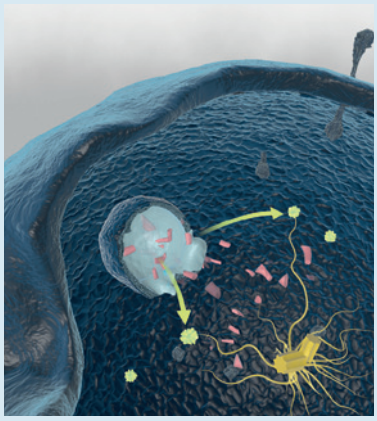
Step 1

The trastuzumab component of T–DM1 detects and binds to the HER2-positive cancer cell.



Step 2

The trastuzumab component blocks out-of-control signals that make the cancer grow, while also calling upon the body's immune system to attack the cancer cells. T–DM1 is taken up by the HER2-positive cancer cell.



Step 3 and 4

Once in the cell, T–DM1 is degraded releasing the active DM1 form. This then binds to a protein structure playing a key role in cell division. DM1 prevents the cell from dividing. The cell dies.

Hematology

We are working on the next generation of targeted therapies to treat certain blood cancers like non-Hodgkin's lymphoma (NHL) and chronic lymphocytic leukemia (CLL). MabThera, known as Rituxan in the United States, has proven to be an extremely effective medicine for such hematological cancers. Since its launch in 1997, it has been used to treat around 2.7 million patients in oncology.

There is still, however, an unmet medical need in this area. Drawing on our understanding of the biology of B-cells and their role in blood cancers, we are developing a number of compounds that could further improve the treatment of hematological cancers.

Obinutuzumab (GA101) is designed to be an even more effective drug than MabThera/Rituxan. Obinutuzumab works by targeting the CD20 protein on malignant B-cells and binding to the cell surface in a way that restores the natural process of cell death (apoptosis). At the same time it activates the body's own immune system to aid cell death through a process known as Antibody-Dependent Cell-Mediated Cytotoxicity (ADCC). Obinutuzumab's clinical development programme is designed to demonstrate superiority over MabThera/Rituxan in multiple frontline, head-to-head trials in NHL and CLL. The first phase III trial to report will be CLL11, with stage 1 results looking at its use in first-line CLL due in 2013. Recruitment for obinutuzumab's other phase III trials is going well.

RG7601 inhibits BCL-2 protein, which is highly expressed in CLL, indolent non-Hodgkin lymphoma and some aggressive lymphomas as well as other B-cell neoplasms. Data from a phase I trial presented at the 2012 American Society of Hematology (ASH) annual meeting showed it had anti-tumour activity in patients with mantle cell lymphoma (MCL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma and Waldenstroem macroglobulinemia (WM).

We are also developing ADCs that target CD79b and CD22, two additional antigens that are expressed in nearly all B-cell lymphomas. Phase I data presented on anti-CD79b ADC (RG7596) and anti-CD22 ADC (RG7593) at ASH showed these two compounds have promising anti-tumour activity and an acceptable tolerability profile in heavily pre-treated patients with relapsed or refractory B-cell NHL, including follicular lymphoma, DLBCL and MCL. A head-to-head phase II trial looking at these two agents combined with rituximab is ongoing. Both ADCs are being developed using Seattle Genetics technology.

Blood cancer: an introduction

The most common blood cancer is lymphoma. It occurs when lymphocytes, a type of white blood cell, grow abnormally. Two main types of lymphocytes can develop lymphomas: B-lymphocytes, or B-cells, and T-lymphocytes, or T-cells. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood and other organs.

A patient is tested for CD20, a protein on the surface of B-cells, to find out whether he or she has a B-cell or T-cell derived cancer. MabThera/Rituxan works by targeting the B-cells that have high levels of CD20 and that are growing abnormally.

The two main types of lymphoma are non-Hodgkin's lymphoma and Hodgkin's lymphoma. NHL is the most common cancer of the lymphatic system, which is part of the immune system. By 2015, it is expected that there will be nearly 225,000 annual deaths worldwide from non-Hodgkin's lymphoma.

RG7112 is a selective inhibitor of p53-MDM2 binding. The gene p53 plays a central role in controlling cell growth and division, and helps to suppress tumours. Scientists have tried to find ways of restoring the function of p53's gene product, known as P53, after it has been damaged. One way of doing this is through the MDM2 gene. This gene works with p53 to keep the division of cells under control by preventing excessive production of P53. Drugs that target MDM2 could therefore allow the body to produce more P53 and restore normal cell growth. Phase I results presented at ASH provided proof of mechanism and evidence for single-agent clinical activity of MDM2 antagonism in leukemia by demonstrating complete remission (5 of 31 [16%] at the maximum tolerated dose), lysis of leukemic blasts and activation of p53 pathway targets in leukemic cells.

Targeted therapies

Roche is forging ahead with the development of therapies that target abnormal gene expression in diseases like cancer. Onartuzumab (MetMAb) is one of many promising compounds in our pipeline.

Onartuzumab is a targeted therapy that could be used in a number of different cancers, including lung cancer, breast cancer, colorectal cancer, glioblastoma, a type of brain tumour, and gastric cancer. Results so far strongly suggest that onartuzumab works best in patients who over express Met protein. It is being investigated in a late-stage trial for use in Met-positive advanced non-small cell lung cancer in combination with Tarceva, one of our existing lung cancer therapies. The mid-stage results, which were presented in 2011, showed the combination of onartuzumab and Tarceva tripled the time Met-positive patients lived compared with Tarceva alone.

Onartuzumab works by stopping a protein called the hepatocyte growth factor (HGF) from binding to Met. By stopping Met and HGF from coming together, cancerous cells find it more difficult to grow, replicate, survive and spread. We are also developing a tissue-based companion diagnostic test, cMET, which will allow doctors to identify those most likely to benefit from onartuzumab.

Companion diagnostic tests

Diagnostics plays a key role in the research and development of our targeted medicines. We have more than 200 Personalised Healthcare collaborations within the Group and more than 60% of our Pharmaceuticals pipeline projects are being developed with companion diagnostics.

The Diagnostics Division's tests allow our researchers to accurately identify the molecular abnormalities causing a disease. This allows researchers to make a drug tailored for specific patients. As a result the drug is more effective and the dosing is optimal, reducing unnecessary side effects.

The combination of specific diagnostic tests and targeted therapies has already improved the prognosis of many cancer patients. Companion diagnostic tests have also helped in the treatment of infectious diseases, like hepatitis C.

We are working on diagnostic testing that will shed more light on why certain tumours become resistant to a targeted drug therapy.

At Roche, we are confident we will also be able to use companion diagnostics in a number of other disease areas apart from cancer, such as immunology and neuroscience.

Combination therapies

The combination of cancer medicines is emerging as one of the most important and effective ways to help people with cancer live longer. By combining treatments it is possible to hit several pathways responsible for a tumour's growth. This also means medicines will be able to overcome the resistance a cancer may have built up to a certain treatment.

BRAF + MEKi – We are building on extensive clinical experience with our first-in-class BRAF inhibitor Zelboraf to investigate a number of combination approaches including Zelboraf with our investigational MEK inhibitor GDC-0973. Our scientists now believe that one reason why patients treated with BRAF inhibitors stop responding to therapy is because they have acquired resistance to drugs that inhibit the RAS-RAF pathway. We have initiated a phase III study exploring the potential of our investigational MEK inhibitor GDC-0973 with Zelboraf.

Avastin + onartuzumab – Preclinical studies have shown that the combination of Avastin and onartuzumab can have a synergistic effect in attacking cancer cell growth. Avastin works by targeting and inhibiting the vascular endothelial growth factor (VEGF), which is required for the growth of new blood vessels. By blocking VEGF, Avastin starves tumours of their blood supply. Onartuzumab targets the Met receptor, which also drives VEGF expression. In a phase Ib study the combination of Avastin and onartuzumab was generally well tolerated. Roche is looking at the simultaneous targeting of the VEGF and Met pathways across various tumour types, including triple negative breast cancer, metastatic colorectal cancer, glioblastoma and non-small cell lung cancer.

Looking to the future of oncology therapy

Roche is working on a new type of cancer treatment that should restore a patient's own immune system to attack the tumour. Anti-PD-L1 is Roche's first cancer immunotherapy programme in clinical development. The goal is to significantly improve durable survival in a number of human cancers. Anti-PD-L1 is a human monoclonal antibody engineered to restore a patient's existing immunity and generate new immunity.

Roche is uniquely positioned to be a leader in cancer immunotherapy based on our wealth of experience and knowledge in both immunology and oncology. We continue to research and develop our anti-PD-L1 molecule both as a monotherapy and in combinations with other treatments, incorporating bio-

Ongoing combination therapy trials

Phase I	Phase II	Phase III	Launched
Anti-PD-L1 + Avastin – Solid tumours	**Onartuzumab + Avastin** – Triple neg. mBC – mCRC – NSCLC, non-squamous 1L – Recurrent glioblastoma	**Perjeta + Herceptin** – Adjuvant HER2-positive BC (APHINITY)	**Perjeta + Herceptin** – HER2-positive BC
Anti-PD-L1 + Zelboraf (BRAF) – Metastatic melanoma BRAF mut+	**Anti-EGFL7 + Avastin** – NSCLC 1L – mCRC, 1L **Anti-CD22 ADC and Anti-CD79b ADC + MabThera** – hematologic malignancies	**T–DM1 + Perjeta** – HER2-positive BC 1L (MARIANNE) – HER2-positive BC EBC	
		Zelboraf BRAF + MEKi RG7421	

marker research to further enhance the understanding of the science behind cancer immunotherapy.

Another new way of treating cancer in the future could come from a rather unexpected source: the toxins from bacterial infection, or exotoxins. Exotoxins can kill cells, and one in particular, pseudomonas exotoxin (PE), could prove to be an important agent in the treatment of cancer as it is an extremely potent cell killer. So far these toxins have proven impossible to harness for therapeutic usage because the body's immune system has always rejected them.

In collaboration with the National Cancer Insitute (NCI), we are exploring the use of a de-immunised version of PE as a 'warhead' attached to antibody fragments or peptidergic binders. The whole molecule is called a cytolytic fusion protein (cFP). We have several such agents in development. The most advanced is being targeted to pleural mesothelioma, a cancer with very few treatment options. We aim to have the first cFPs in humans by 2014, and if this results in a clinical proof of concept we will be able to quickly develop a number of follow-on molecules targeting different cancers, allowing us to take advantage of the flexibility of this platform.

Neuroscience

Over the past ten years, scientists have gained a better understanding of the brain. Today Roche is working on new molecular entities that could become the next generation of medicines for a range of diseases including schizophrenia, multiple

Treating the untreatable

Roche is developing therapies for a number of central nervous system (CNS) disorders that until recently were believed to be untreatable.

'For people who had autism, for example, the traditional thinking was that nothing could be done,' Luca Santarelli, Head of Neuroscience, said.

New data has shown medicines could also be developed for illnesses such as autism, fragile X syndrome, Down's syndrome, refractory depression as well as the early stages of Alzheimer's disease.

With one of the strongest neuroscience pipelines in the industry, Roche has made considerable progress in this area over the last decade and the Group now has nearly a dozen compounds in development in CNS.

'There are no shortcuts in CNS development,' Santarelli said. 'Gantenerumab for Alzheimer's has been ten years in the making'.

Working closely with academic institutes and external biotech companies, as well as forming public-private partnerships has helped Roche to develop its presence in this field. But the development of companion diagnostics has also been critical, particularly for Alzheimer's as this is a very difficult disease to diagnose properly.

sclerosis, depression, neurodevelopmental disorders, Parkinson's disease and Alzheimer's disease.

We are tackling diseases of the central nervous system (CNS) by focusing on the biology of the illness, taking a similar approach to our development of cancer therapies. Biomarkers are also helping us to develop more targeted treatments for CNS disorders, such as Alzheimer's.

Alzheimer's disease

Two of our most advanced compounds for the treatment of Alzheimer's are gantenerumab and crenezumab.

With gantenerumab, we are aiming to treat patients with Alzheimer's around five years earlier than they are currently treated so that we can slow down or even prevent further damage to the brain. Gantenerumab, which was initially developed in partnership with MorphoSys, is being investigated in patients with prodromal Alzheimer's, who are showing signs of mild cognitive impairment and who have evidence of amyloid plaques in the brain. Early clinical studies have shown that gantenerumab can significantly decrease levels of amyloid in the brain. We are currently conducting a phase II/III trial with gantenerumab called SCarlet RoAD. We used a companion diagnostic to identify patients early and to ensure that all patients enrolled display Alzheimer's disease pathology. The first results of the SCarlet RoAD are expected in 2016.

Gantenerumab is one of three compounds selected for a worldwide trial investigating whether these antiamyloid agents can prevent Alzheimer's. The Dominantly Inherited Alzheimer Network trial is being conducted at the Washington University School of Medicine in St. Louis, USA.

Crenezumab is in two phase II trials (ABBY and BLAZE) for mild to moderate Alzheimer's. Results from these trials are due in 2013 and 2014. Crenezumab is also part of a US government-backed trial in pre-clinical Alzheimer's to determine whether it could help prevent or slow the disease. The study is investigating the use of crenezumab in a group of around 300 Colombians with a genetic mutation that results in them developing Alzheimer's in their forties. So far the drug has shown few side effects, meaning it can be used at higher doses, potentially increasing the amount that gets into the brain. Crenezumab is an antibody that targets both the solid bits of beta amyloid that make up plaques in the brain and the free-floating, soluble forms of the Abeta protein.

Alzheimer's disease

Alzheimer's has a devastating impact on the lives of patients and their families. It is the most common form of dementia and approximately 36 million people suffer from Alzheimer's worldwide. It is estimated that 66 million people will be affected by 2030. As many as 115 million people could have the disease by 2050 as the population ages.

Alzheimer's with notable clinical symptoms is most common in people above the age of 60, but people with certain rare genetic mutations may develop the disease earlier.

People with Alzheimer's have abnormal amounts of amyloid protein, or amyloid plaque in the brain. Build-up of this protein reduces the effectiveness of healthy neurons and gradually destroys them. Detecting the levels of this protein in spinal fluid can be used to identify the patients with Alzheimer's who are at high risk of converting into dementia in a few years' time.

We believe our approach of treating Alzheimer's at the early stages (prodromal) is pioneering. Roche currently has four compounds in clinical development for Alzheimer's.

Schizophrenia

Roche is working to improve the lives of people with schizophrenia, a chronic brain disease that affects approximately 26 million people and is among the 20 most common disabling conditions worldwide. The symptoms of schizophrenia fall into three main categories: positive symptoms, such as hallucinations and delusions; negative symptoms, such as lack of speech, lack of emotional expression, inability to begin and sustain activities and social withdrawal; and cognitive deficits, which include difficulties with memory, attention and decision making. Reduced signalling through the NMDA (N-methyl-D-aspartate) receptor is thought to be a possible explanation for all of these symptoms.

Bitopertin is a new, first-in-class, oral glycine reuptake inhibitor that is designed to improve NMDA receptor function. Phase III trials in the SearchLyte trial programme are investigating bitopertin in combination with standard of care antipsychotics in patients with predominant negative symptoms (DayLyte, FlashLyte, SunLyte) and those with sub-optimally controlled symptoms of schizophrenia (MoonLyte, TwiLyte, NightLyte).

Multiple sclerosis

We are developing ocrelizumab, a new therapy for multiple sclerosis (MS), a debilitating neurological illness. Ocrelizumab is a humanised, monoclonal antibody designed to selectively target CD20-positive B-cells, which are thought to play an important role in MS. It works with the body's immune system to eliminate the CD20-positive B-cells. Ocrelizumab is in phase III clinical trials for patients with the relapsing form of the disease (OPERA I and II), and patients with the primary progressive form of MS (ORATORIO) for which there is no approved treatment.

Diagnostics

In 2012 the Diagnostics Division made advances in lab automation, near patient testing and diabetes management. Our newly launched tests are further aiding the diagnosis of cancers, infectious diseases and metabolic disorders.

In the United States, our largest market, we launched a vitamin D test and three diabetes care devices: Accu-Chek Nano SmartView for discreet blood glucose self-testing, Accu-Chek Combo, a pump/metre combination and Accu-Chek Inform II for professional glucose testing at the hospital. In the rest of the world a key launch was the cobas b 101 system, which is used at the doctor's office or outpatient clinic to help identify and manage patients who have metabolic disorders.

Driving testing efficiency

We are further developing our diagnostic platforms and tests to enhance testing efficiency in clinical laboratories and research centres. We have a number of systems in early and late-stage development, including next-generation platforms for immunodiagnostic, clinical chemistry and coagulation testing. Our leading cobas series of fully automated analysers are being designed to help large labs further consolidate their work areas and handle expanding testing volumes. We are also developing the cobas 6800/8800, which is a novel molecular testing platform. It is expected to be the first to offer new levels of automation, throughput and cost-efficiency to molecular and blood screening laboratories.

Identifying those at risk

We are developing an immunoassay, Aβ42, to identify patients who are at a higher risk of developing Alzheimer's disease. We are also developing a genetic test, Apoliprotein E, to identify carriers of the ApoE4 genotype who may benefit from a dose adjustment of gantenerumab, as well as another immunoassay, Tau, which will be used as an exploratory surrogate marker for efficacy.

An immunoassay is any of various techniques for determining the levels of antigen and antibody.
(Oxford Medical Dictionary)

Developing new technologies

We are investing in new technologies that could make an important difference to the way certain diseases, such as cancer, are diagnosed. Two examples of this are microRNA and multiplexing from our Tissue Diagnostics business.

MicroRNA play an important role in almost all tumours. They control the expression of oncogenic proteins and can influence treatment resistance and whether a cancer spreads. Roche Tissue Diagnostics has developed the first fully automated staining technique that will allow researchers to detect microRNA and proteins in the tumour's microenvironment. This could help researchers better understand cancer and develop new targeted therapies.

Multiplexing is a technology that allows the simultaneous identification of up to nine different targets, such as mutated genes or proteins, from a single piece of tissue. This means that physicians will be able to get more answers at the time of initial diagnosis of a tumour, and there will still be tissue available for comparison, in case the cancer should return.

We also remain focused on developing faster, more efficient sequencing systems. Next-generation sequencing will allow scientists to examine (parts of) a person's genome[1] faster and more efficiently than before. We are continuing our collaborations with external partners on next-generation platforms. We also invested in sequencing workflow enhancements and initiated a collaboration with Precision System Science for

1 A genome is the total genetic material of an organism, comprising the genes contained in its chromosomes. (Oxford Medical Dictionary).

Diabetes Care: pumps and CGM

Roche continues to develop innovative and integrated diabetes management systems that help patients and caregivers to optimise therapy. We are focusing investments on insulin pumps and continuous glucose monitoring (CGM) where we see the greatest market potential for innovative, differentiated products. Our pipeline includes a next-generation insulin pump/blood glucose metre, Accu-Chek Insight, as well as a novel micropump. Following our decision to cancel the micropump's pilot launch in late 2012, we are further developing this product as a a combined metre and pump with proven Accu-Chek features. We are also developing a CGM system that provides real time continuous glucose monitoring by a small sensor under the patient's skin. The CGM system is in early development and delivered promising results in the first clinical studies.

an automated emulsion PCR[2] instrument, for preparation of genomic samples.

Providing medical value

We are developing tests that provide new answers in areas such as oncology, virology and metabolism. One such example is the cobas PIK3CA mutation assay which is designed to detect mutations in the PI3K (phosphoinositide 3-kinase) pathway. This pathway is mutated in more cancer patients than any other and plays a significant role in colorectal, gastric, breast and endometrial tumours.

A test for research use is being launched in early 2013, and the IVD test predicting the response to specific cancer therapies is being developed for launch in the coming years. Also in early development are tests to identify variations in gene expression in the PI3K pathway in tumour tissue. See more on companion diagnostics on pages 42 (cMET) and 45 (Aβ42, ApoE, Tau).

Delivering clinical evidence

We are also investing in and collaborating on clinical trials to demonstrate the medical value of our diagnostic products in helping physicians to better monitor and treat patients suffering from illnesses such as heart disease and diabetes.

In late 2012 we started the GUIDE-IT[3] clinical trial that investigates the benefit of our heart failure test, NT-proBNP, for therapy monitoring in heart failure patients. The pivotal trial is coordinated by the Duke Clinical Research Institute (main study) and funded by the US National Institutes of Health as well as Roche. NT-proBNP-guided heart failure care is expected to substantially reduce the occurrence of cardiovascular events, such as worsening heart failure, hospitalisation and death, as compared with current standards of care. See more on page 70.

We continue to study new diabetes management approaches based on innovative devices. The ABACUS[4] study investigated the use of our Accu-Chek Aviva Expert automatic bolus advisor, a functionality to calculate the appropriate insulin doses based on regular blood glucose monitoring, in insulin dependent patients. The study results, first presented in October, revealed that the use of the bolus adviser improved the ability to reach glycemic targets, supporting therapy adherence and patient wellbeing, without an increase of the number of hypoglycemic events.

Improving R&D productivity

Improving productivity in R&D is a priority for Roche. We are working to make our R&D practices more efficient in order to develop medicines in a sustainable way and reduce the time it takes to bring our products to market.

One approach is to design our trials to ensure shorter development times. By using biomarkers, for example, we are able to select the patients who are most likely to respond to our treatments. This means we can run smarter trials that are more likely to be successful. It also allows us to reduce the costs per trial per patient.

Another initiative, Trials to Patients (T2P), aims to better inform patients and their doctors about the benefits of participating in a clinical trial. We have also developed online recruiting tools to make it easier for patients to enrol.

If enrolment in clinical trials is increased through programmes like T2P, we will be able to accelerate drug development. For instance if 10% of cancer patients participated in trials, patient enrolment times could be cut to one year from the three to five

2 Polymerase chain reaction

3 GUIDing Evidence-based therapy using biomarker Intensified Treatment.

4 Automated Bolus Advisor Control and Usability Study.

years currently required, according to the National Cancer Institute.

As part of our efforts to streamline our R&D activities in 2012, we took the difficult decision to close our site in Nutley, New Jersey, United States. The closure will allow us to allocate resources to our expanding late-stage pipeline and to focus on the most promising agents.

Accessing external innovation

With approximately 150 active partnerships, and molecules from third parties accounting for around one-third of Roche sales, external innovation continues to make a valuable contribution to our pipeline and allows us to broaden our global innovation network.

Roche Partnering signed 55 new agreements in 2012, including three product transactions and 43 research and technology collaborations. In addition, nine product outlicencing agreements were signed. Among the team's main transactions in 2012 was the exclusive partnership with Versant Ventures and Inception Sciences to create a drug discovery incubator, Inception 3, for the treatment of sensorineural hearing loss. This deal structure is particularly innovative as it involves a venture firm, Versant, which provides equity financing, a pharmaceutical company, Roche, which contributes funding and other resources to the research, and a biotech firm, Inception, which provides an innovative technology platform as well as the drug hunting expertise of the Inception Sciences team.

In 2012 Genentech Partnering signed 14 new agreements including three product transactions, three research and technology collaborations, four academic collaborations, and four outlicencing agreements. In 2012 we entered a unique deal structure with US-based Constellation Pharmaceuticals, which includes a future option to acquire Constellation based on pre-negotiated terms. This major strategic agreement is based on the science of epigenetics and chromatin biology to discover and develop treatments for cancer and other serious diseases.

The Diagnostics Division signed more than 50 licensing agreements in 2012. We also made a tender offer for US group Illumina which was rejected.

The StemBANCC partnership

Roche is playing a leading role in StemBANCC, an exciting new academic-industry partnership that will help deepen our understanding of a number of complex diseases. The initiative will also improve the drug development process.

The StemBANCC project, which involves ten pharmaceutical companies and 23 academic institutions, is based on Nobel Prize winning technology that has revolutionised the way stem cells can be used in research.

For a long time it was believed that adult cells could only divide to make other cells of the same type, for example that skin cells can only make other skin cells, and liver cells can only make other liver cells.

But in recent years researchers have developed a way of reprogramming ordinary adult cells to create stem cells that can be used to generate any kind of cell. Such stem cells are known as induced pluripotent stem cells, and in 2012 scientists John Gurdon, Cambridge University, and Shinya Yamanaka, Kyoto University, were awarded the Nobel Prize in Physiology or Medicine for these findings.

These advances mean that we can now take blood or skin cell samples from patients and examine their diseases in a petri dish. This technology will also allow us to test potential small molecules and biologic treatments at a very early stage in the drug discovery process.

This project, which was launched by Roche and the Innovative Medicines Initiative at the end of 2012, will focus on diabetes, central nervous disorders, including dementias, autism and schizophrenia, as well as on peripheral nervous system disorders, especially pain. The partnership will run for five years.

Roche scientists have worked on induced pluripotent stem cells with partners at Harvard University, Massachusetts General Hospital for more than three years, and have created over 100 human induced pluripotent stem cell lines that can be used to model cardiovascular diseases. More recently we also joined forces with the Boston Children's Hospital and Harvard to use stem cells to model neurological diseases.

Conducting responsible R&D

Clinical trials

Clinical trials are critical for determining the safety and efficacy of new medicines. All of our clinical trials are compliant with Good Clinical Practice guidelines, an international quality standard. The information from our trials is shared with regulatory authorities and payers. Regardless of the outcome of a trial, Roche is dedicated to providing balanced information on the trial to healthcare professionals and to the public. We only perform trials in countries where we intend to market the medicine being tested.

In 2012, 326,642 patients were involved in our clinical trials.

Clinical trials

	2012	2011	2010
Number of clinical trials	2,280	2,336	2,253
Number of healthcare centres involved	35,720	35,647	33,698
Number of patients in phase I–IV clinical trials[1]	326,642	295,994	248,261

1 excludes non-interventionist screening programme.

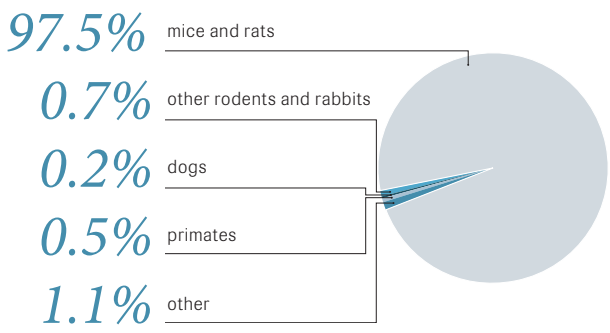
Details of our clinical trials are available at www.roche-trials.com, www.clinicaltrials.gov and through the International Federation of Pharmaceutical Manufacturers and Associations clinical trials portal and the US National Institutes of Health global registry.

Roche encourages its scientists to publish results of their work in medical journals and to present them at scientific and medical congresses. In 2012 more than 1,000 scientific articles by Roche scientists were published in leading journals such as *Nature, Cell, Science* and the *New England Journal of Medicine*.

Ethical practices

The Roche Science and Ethics Advisory Group (SEAG) is made up of independent external experts in bioethics and philosophy and offers advice and counsel on a broad range of ethical matters, including ethical approaches to biomedical and clinical research. SEAG follows a consultative approach on topics that are perceived as particularly sensitive or controversial by the public at large in order to take into account as many perspectives as possible.

Animals used in research (Roche and contract research organisations) in 2012



Bioethics

Roche has published several position papers on its R&D activities in areas such as genetics, stem cells and animal research. We routinely review and update these positions and our policies for research involving either humans or animals, taking into account scientific developments and public concerns.

The Roche Charter on Genetics ensures that our genetic research meets the highest standards and is socially responsible. We believe in the right of every individual to self-determination, privacy and confidentiality regarding the collection and use of genetic information.

Animal welfare

We take public concern about animal research seriously and throughout 2012 we have worked to maintain our already high standards of animal welfare. Wherever possible, we seek alternatives to the use of animals, such as computer simulation or *in vitro* testing using differentiated cells or stem cells. Without putting at risk the reliability and validity of research and test results, we follow the 3Rs approach:

- Reduce: the number of animals needed
- Refine: by tailoring procedures to minimise pain and discomfort
- Replace: with other methods that do not involve animals or use only cells or tissues of animals

Animal research remains indispensable to biomedical research for scientific and legal reasons. Regulatory authorities require all healthcare companies to test the safety and efficacy of new drugs in animals before they can be used in humans.

In 2012 we used 408,013 animals in our research, a 13% decrease from 2011. The number of animals used by contract research organisations working on Roche's behalf decreased to 64,314 compared with 68,606 in 2011. Approximately 97.5%

of the animals used were mice and rats. The overall decrease in 2012 animal usage is a direct reflection of the restructuring of the Roche organisation and the drug portfolio changes.

More on the web

- Roche's Pharmaceuticals and Diagnostics Pipelines: www.roche.com/pipeline
- Personalised Healthcare: www.roche.com/personalised_healthcare
- Group policies, positions and guidelines: www.roche.com/responsibility/sustainability/positions_policies_downloads.htm#guidelines
- Clincal trials and safety: www.roche.com/clinical_trials; www.roche.com/managing_medication_safety
- New products and technologies: www.roche.com/innovation_and_technologies
- Ethical standards: www.roche.com/ehtical_standards http://www.roche.com/about_roche/corporate_governance/code_of_conduct.htm
- Genetics and bioethics: www.roche.com/genetics_and_bioethics
- Animal welfare: www.roche.com/animal_welfare

Pharmaceuticals pipeline

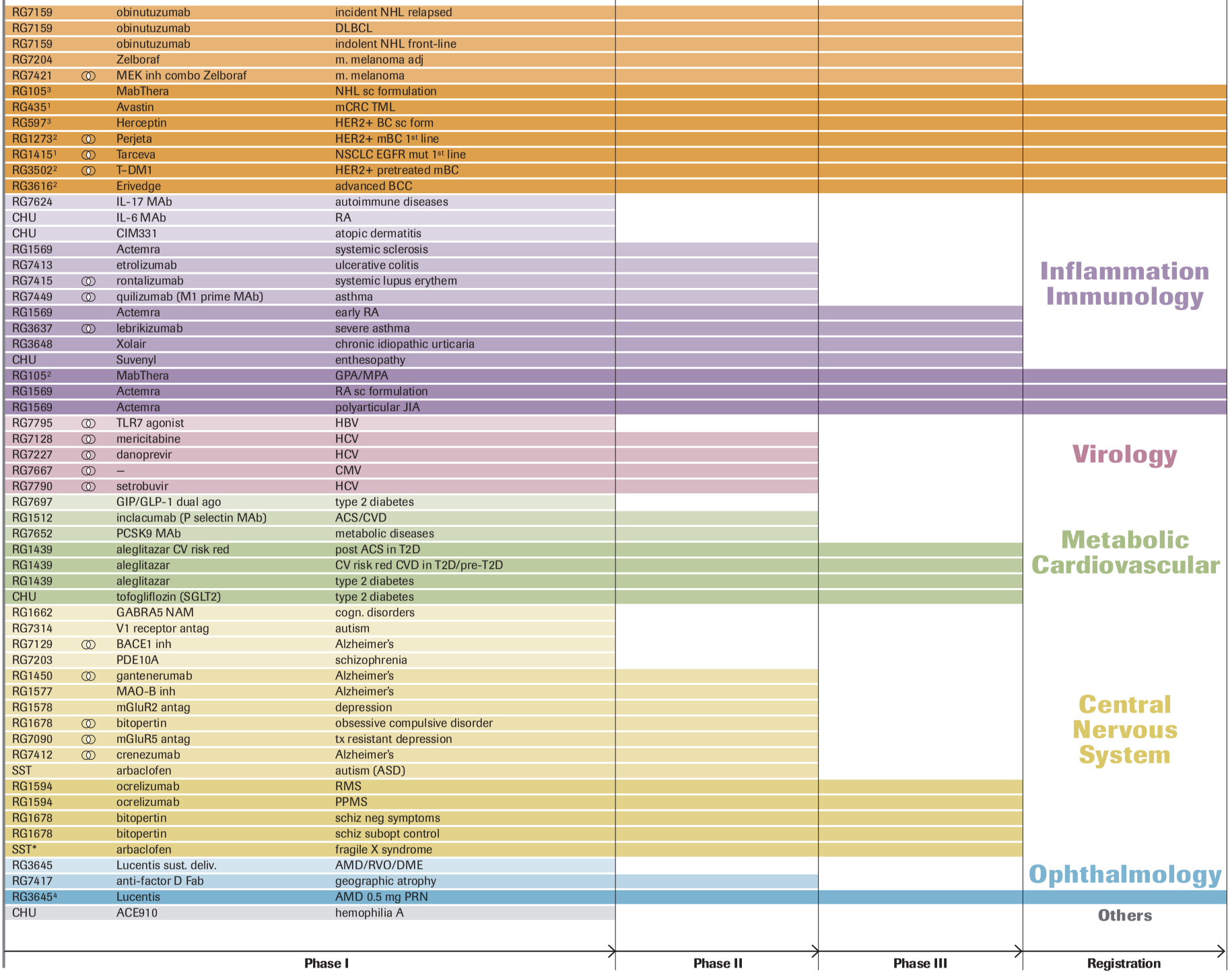
Oncology

1	Approved in EU, submitted in US
2	Approved in US, submitted in EU
3	Submitted in EU
4	Submitted in US
*	US only: ongoing evaluation for FDA submission
ⓟ	Personalised Healthcare project

RG-No	Roche Genentech managed
CHU	Chugai managed
SST	Seaside Therapeutics (opt-in)
RG105	MabThera is branded as Rituxan in US and Japan
RG1569	Actemra is branded as RoActemra in EU

ACS	acute coronary syndrome
AMD	age-related macular degeneration
BCC	basal cell carcinoma
CLL	chronic lymphocytic leukemia
CMV	cytomegalovirus
CRC	colorectal cancer
CVD	cardiovascular disease
DLBCL	diffuse large B-cell lymphoma
DME	diabetic macular edema
HBV	hepatitis b virus
HCV	hepatitis c virus
MAb	monoclonal antibody
mBC	metastatic breast cancer
NSCLC	non-small cell lung cancer
NHL	non-Hodgkin's lymphoma
PPMS	primary progressive multiple sclerosis
RA	rheumatoid arthritis
RMS	relapsing multiple sclerosis
RVO	retinal vein occlusion
sc	subcutaneous
T2D	type 2 diabetes

Project ID		Project/Product	Indication
RG7112		MDM2 ant	solid & hem tumors
RG7116		HER3 MAb	solid tumors
RG7155		CSF-1R MAb	solid tumors
RG7167	ⓟ	CIF/MEK inh	solid tumors
RG7204		Zelboraf + ipilimumab	met. melanoma
RG7212		Tweak MAb	oncology
RG7221	ⓟ	ANG2-VEGF MAb	oncology
RG7304	ⓟ	Raf & MEK dual inh	solid tumors
RG7356	ⓟ	CD44 MAb	solid tumors
RG7388		MDM2 ant	solid & hem tumors
RG7420	ⓟ	MEK inh	solid tumors
RG7440	ⓟ	AKT inhibitor	solid tumors
RG7446	ⓟ	PD-L1 MAb	solid tumors
RG7450	ⓟ	Steap 1 ADC	prostate ca.
RG7458	ⓟ	ADC	ovarian ca.
RG7598	ⓟ	ADC	multiple myeloma
RG7599	ⓟ	ADC	oncology
RG7600	ⓟ	ADC	oncology
RG7601	ⓟ	Bcl-2 inh	CLL and NHL
RG7602		ChK1 inh	solid tum & lymphoma
RG7604	ⓟ	PI3K inh	solid tumors
RG7636	ⓟ	ADC	metastatic melanoma
RG7666	ⓟ	PI3k inh	glioblastoma 2L
RG7741		ChK1 inh (2)	solid tumors
RG7853	ⓟ	ALK inhibitor	NSCLC
CHU		PI3K inh	solid tumors
CHU		WT-1 peptide	cancer vaccine
RG1273		Perjeta	HER2+ mBC 2nd line
RG1273		Perjeta	HER2+ gastric cancer
RG3502		T-DM1	HER2+ early BC
RG3502		T-DM1	HER2+gastric cancer
RG3616		Erivedge	operable BCC
RG3638	ⓟ	onartuzumab	triple-neg mBC, 1st/2nd line1L/2L
RG3638		onartuzumab	mCRC 1st line 1L
RG3638		onartuzumab	NSCLC non squamous 1st l
RG3638		onartuzumab	NSCLC squamous 1st line
RG3638		onartuzumab	glioblastoma 2nd line
RG7160		EGFR MAb	solid tumors
RG7204		Zelboraf	papillary thyroid cancer
RG7321	ⓟ	PI3K inh	solid tumors
RG7422	ⓟ	PI3K/mTOR inh	solid & hem tumors
RG7414		EGFL7 MAb	solid tumors
RG7593	ⓟ	CD22 ADC	hem tumors
RG7596	ⓟ	CD79b ADC	hem tumors
RG7597	ⓟ	HER3/EGFR	m. epithelial tumors
RG7686	ⓟ	glypican-3 MAb	liver cancer
RG435		Avastin	HER2+ BC adj
RG435		Avastin	HER2-neg. BC adj
RG435		Avastin	NSCLC adj
RG435		Avastin	high risk carcinoid
RG435		Avastin	glioblastoma 1st line
RG435*		Avastin	ovarian cancer 1st line
RG435*		Avastin	ovarian cancer platinum resist.
RG1273		Perjeta	HER2+ early BC
RG1415		Tarceva	NSCLC adj
RG3502		T-DM1	HER2+ mBC 3rd line
RG3502		T-DM1	HER2+ mBC 1st line
RG3638		onartuzumab	NSCLC 2nd/3rd line
RG3638		onartuzumab	gastric cancer
RG7159		obinutuzumab	CLL


RG7159 obinutuzumab incident NHL relapsed
RG7159 obinutuzumab DLBCL
RG7159 obinutuzumab indolent NHL front-line
RG7204 Zelboraf m. melanoma adj
RG7421 MEK inh combo Zelboraf m. melanoma
RG105[3] MabThera NHL sc formulation
RG435[1] Avastin mCRC TML
RG597[3] Herceptin HER2+ BC sc form
RG1273[2] Perjeta HER2+ mBC 1st line
RG1415[1] Tarceva NSCLC EGFR mut 1st line
RG3502[2] T-DM1 HER2+ pretreated mBC
RG3616[2] Erivedge advanced BCC
RG7624 IL-17 MAb autoimmune diseases
CHU IL-6 MAb RA
CHU CIM331 atopic dermatitis
RG1569 Actemra systemic sclerosis
RG7413 etrolizumab ulcerative colitis
RG7415 rontalizumab systemic lupus erythem
RG7449 quilizumab (M1 prime MAb) asthma
RG1569 Actemra early RA
RG3637 lebrikizumab severe asthma
RG3648 Xolair chronic idiopathic urticaria
CHU Suvenyl enthesopathy
RG105[2] MabThera GPA/MPA
RG1569 Actemra RA sc formulation
RG1569 Actemra polyarticular JIA
RG7795 TLR7 agonist HBV
RG7128 mericitabine HCV
RG7227 danoprevir HCV
RG7667 – CMV
RG7790 setrobuvir HCV
RG7697 GIP/GLP-1 dual ago type 2 diabetes
RG1512 inclacumab (P selectin MAb) ACS/CVD
RG7652 PCSK9 MAb metabolic diseases
RG1439 aleglitazar CV risk red post ACS in T2D
RG1439 aleglitazar CV risk red CVD in T2D/pre-T2D
RG1439 aleglitazar type 2 diabetes
CHU tofogliflozin (SGLT2) type 2 diabetes
RG1662 GABRA5 NAM cogn. disorders
RG7314 V1 receptor antag autism
RG7129 BACE1 inh Alzheimer's
RG7203 PDE10A schizophrenia
RG1450 gantenerumab Alzheimer's
RG1577 MAO-B inh Alzheimer's
RG1578 mGluR2 antag depression
RG1678 bitopertin obsessive compulsive disorder
RG7090 mGluR5 antag tx resistant depression
RG7412 crenezumab Alzheimer's
SST arbaclofen autism (ASD)
RG1594 ocrelizumab RMS
RG1594 ocrelizumab PPMS
RG1678 bitopertin schiz neg symptoms
RG1678 bitopertin schiz subopt control
SST* arbaclofen fragile X syndrome
RG3645 Lucentis sust. deliv. AMD/RVO/DME
RG7417 anti-factor D Fab geographic atrophy
RG3645[4] Lucentis AMD 0.5 mg PRN
CHU ACE910 hemophilia A
Inflammation Immunology
Virology
Metabolic Cardiovascular
Central Nervous System
Ophthalmology
Others
Phase I
Phase II
Phase III
Registration

Pharmaceuticals Division – major clinical trials in 2012

Product	Indication	Trial (phase)	Outcome
Actemra/ RoActemra	rheumatoid arthritis (RA)	ADACTA (IV)	statistically significant greater improvement in signs and symptoms as measured by mean change in DAS28 of RA in patients treated with Actemra monotherapy vs. adalimumab monotherapy
Actemra/ RoActemra	polyarticular juvenile idiopathic arthritis	CHERISH (III)	sustained clinically meaningful improvement with Actemra IV vs. placebo
Actemra/ RoActemra	early rheumatoid arthritis	FUNCTION (III)	statistically significant greater improvement of signs and symptoms of RA and greater radiographic progression inhibition with Actemra in combination with methotrexate vs. methotrexate alone
Actemra/ RoActemra (subcutaneous formulation)	rheumatoid arthritis	SUMMACTA (III)	comparable efficacy of Actemra SC formulation vs. intravenous formulation
Actemra/ RoActemra (subcutaneous formulation)	rheumatoid arthritis	BREVACTA (III)	statistically significant greater improvement of signs and symptoms of RA with Actemra SC vs. placebo
aleglitazar	reduction of major cardiovascular events in patients with type 2 diabetes who have experienced an acute coronary syndrome	AleNephro (II); renal safety study	average decrease in renal function in patients with stage 3 chronic kidney disease and type 2 diabetes is reversible, mild and stabilises over time
Avastin	metastatic colorectal cancer	ML 18147 (III)	significantly extended OS in patients who first received Avastin plus standard chemotherapy as initial treatment and then continued on Avastin with a different chemotherapy after their cancer progressed
Avastin	platinum-resistant ovarian cancer	AURELIA (III)	significantly improved PFS
Avastin	glioblastoma	AVAglio (III)	significantly improved PFS
Avastin	triple-negative adjuvant breast cancer	BEATRICE (III)	did not demonstrate a significant improvement in invasive disease-free survival versus adjuvant chemotherapy alone
dalcetrapib	patients with stable coronary heart disease following acute coronary syndrome	dal-OUTCOMES (III)	lack of clinically meaningful efficacy
Herceptin	HER2-positive early breast cancer	HERA (III)	1 year of Herceptin confirmed as standard of care
Herceptin (subcutaneous formulation)	HER2-positive early breast cancer	HannaH (III)	comparable efficacy of subcutaneous formulation versus intravenous formulation
MabThera (subcutaneous formulation)	treatment-naïve patients with follicular lymphoma	SABRINA (III)	minimum drug concentration confirmed as non-inferior versus IV administration; comparable safety and anti-lymphoma efficacy versus IV
Perjeta	HER2-positive metastatic breast cancer; combination with Herceptin and docetaxel (1L)	CLEOPATRA (III)	significantly improved PFS and OS
trastuzumab emtansine (T–DM1)	HER2-positive metastatic breast cancer (2L)	EMILIA (III); T–DM1 versus lapatinib and Xeloda	significantly improved PFS and OS

Pharmaceuticals Division – major regulatory filings in 2012

Product	Clinical data supporting filing	Indication or dosage form	Country
Actemra/RoActemra	CHERISH	polyarticular JIA	US, EU
Actemra/RoActemra	ADACTA	RA DMARD IR H2H	EU
Actemra/RoActemra	SUMMACTA, BREVACTA	DMARD IR, TNF IR	US, EU
(subcutaneous formulation)	MUSASHI	DMARD IR	Japan
Avastin	BRAIN	recurrent glioblastoma	Japan
Avastin	GOG-0218, ICON7	ovarian cancer	Japan
Avastin	ML18147	metastatic colorectal cancer (TML)	US
Herceptin (subcutaneous formulation)	HannaH	HER2-positive early-stage breast cancer	EU
Lucentis	HARBOR	AMD 0.5mg PRN	US
MabThera	RAVE, RITUXVAS	Granulomatosis with Polyangiitis (GPA) and Microscopic Polyangiitis (MPA) (two types of ANCA associated vasculitis)	EU
MabThera (subcutaneous formulation)	SABRINA, SparkThera, SAWYER	non-hodgkin's lymphoma	EU
Perjeta	CLEOPATRA	HER2-positive metastatic or recurrent breast cancer	EU, Japan
Tarceva	EURTAC	non-small cell lung cancer EGFR+ (1L); tablet 25mg, 100mg and 150mg	US, Japan and China
trastuzumab emtansine (T–DM1)	EMILIA	HER2-positive pre-treated metastatic breast cancer	US, EU

Pharmaceuticals Division – major regulatory approvals in 2012

Product	Clinical data supporting filing	Indication or dosage form	Country
Actemra	OPTION, TOWARD, LITHE	moderate to severe rheumatoid arthritis in adults who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARD)	US
Avastin	OCEANS	recurrent, platinum-sensitive ovarian cancer	EU, Switzerland
Avastin	ML18147	metastatic colorectal cancer (TML)	EU
Erivedge	ERIVANCE BCC/SHH4476g	advanced basal cell carcinoma	US
Lucentis	RIDE, RISE	diabetic macular edema	US
Rituxan	RATE	NHL, fast infusion	US
Perjeta	CLEOPATRA	HER2-positive metastatic breast cancer in patients (1L)	US, Switzerland
Tamiflu	WP22849, CASG 114	acute, uncomplicated influenza in infants two weeks of age and older	US
Zelboraf	BRIM2, BRIM3	BRAF V600 mutation-positive inoperable or metastatic melanoma	EU

Roche companion diagnostics on the market or in late development*

Disease area	Disease	Drug	Diagnostic test**	Technology	Application
Infectious diseases	CMV	Valcyte	CMV viral load	PCR	monitoring
	HBV	Pegasys and other antivirals	HBV viral load	PCR	monitoring
	HBV	Pegasys, peginterferon alfa-2b (Merck/SP)	HBsAg levels	immunoassay	monitoring
	HCV	Pegasys, peginterferon alfa-2b (Merck/SP)	HCV viral load	PCR	monitoring
	HCV	mericitabine (RG7128)	HCV viral load	PCR	monitoring
	HCV	danoprevir (RG7227)	HCV viral load	PCR	monitoring
	HIV	antivirals	HIV viral load	PCR	monitoring
	HIV	abacavir (GlaxoSmithKline)	HLA-B genotype	PCR	screening
Oncology	breast cancer	Herceptin, Perjeta	HER2 expression/ gene amplification	IHC, ISH	selection
	breast cancer	tamoxifen and other hormonal therapies	ER/PR expression	IHC	selection
	breast cancer	trastuzumab emtansine (T-DM1, RG3502)	HER2 expression/ gene amplification	IHC, ISH	selection
	cancer	compound (Merck)	p53 mutations	microarray	selection
	colon cancer	cetuximab (Merck)	KRAS mutations	PCR	selection
	colon cancer	panitumumab (Amgen)	KRAS mutations	PCR	selection
	gastric cancer	Herceptin	HER2 expression/ gene amplification	IHC, ISH	selection
	lymphoma	brentuximab vedotin (Seattle Genetics/ Millenium)	CD30 expression	IHC	selection
	melanoma	Zelboraf	BRAF mutation	PCR	selection
	NSCLC	Tarceva***, gefitinib (AstraZeneca)	EGFR mutations	PCR	selection
	NSCLC	onartuzumab (MetMAb, RG3638)	Met expression	IHC	selection
	NSCLC	crizotinib (Pfizer)	ALK	IHC	selection
	NSCLC	TG4010 (Transgene)	MUC1 expression	IHC	selection
Inflammation	asthma	lebrikizumab (RG3637)	serum periostin levels	immunoassay	selection
	rheumatoid arthritis	MabThera/Rituxan	RF, anti-CCP Ab	immunoassay	selection
Central nervous system	Alzheimer's disease	gantenerumab (RG1450)	aβ42 levels	immunoassay	selection
Others	osteoporosis	Bonviva/Boniva and other bisphosphonates	B-Crosslaps; P1NP levels	immunoassay	monitoring
	transplantation	CellCept	MPA levels	immunoassay	monitoring

* We have further projects with other pharmaceutical companies which are not disclosed for confidentiality reasons.
** not available in all markets;
*** selection of patients eligible for first-line treatment.
black type = on the market, grey type = in development. monitoring = monitoring of a patient's response to a particular treatment; screening = screening of patients for a particular genetic variation of HLA associated with hypersensitivity to abacavir; selection = selection of patients eligible for a particular treatment. ALK= anaplastic lymphoma kinase; anti-CCP = antibodies against cyclic citrullinated peptide; BRAF = B-isoform of the rapidly growing fibrosarcoma oncogene; CMV = cytomegalovirus; EGFR = epidermal growth factor receptor; ER/PR = estrogen receptor/progesterone receptor; HBV = hepatitis B virus; HBsAg = HBV surface antigen; HCV = hepatitis C virus; HER2 = human epidermal growth factor receptor 2; HIV = human immunodeficiency virus; HLA = human leucocyte antigen; IHC = immunohistochemistry; ISH = in situ hybridisation; KRAS = member of the Ras family of oncogenes; MPA = mycophenolic acid; NSCLC = non-small cell lung cancer; PCR = polymerase chain reaction; P1NP = procollagen type 1 N-terminal propeptide; RF = rheumatoid factor; SP = Schering Plough.

Diagnostics Division – major product launches in 2012

Area	Product name	Description	Market	Quarter
Instruments/devices				
Laboratories	BenchMark Special Stains	fully automated tissue stainer	WW	Q2
	VENTANA iScan HT	scanner that enables digital viewing of tissue slides	EU, US	Q2
	cobas p 312	pre-analytical system (decapping, sorting and archiving)	EU, US	Q1–2
	cobas p 630	pre-analytical molecular testing system	US	Q1
	cobas IT middleware solution 1.00	software to control the lab workflow until the test result	EU	Q1
Point of care	cobas b 123	blood gas analyser for critical care	US	Q2
	cobas b 101	analyser for HbA1c and lipid monitoring	EU	Q4
	Accu-Chek Inform II	wireless system for professional glucose testing in the hospital	US	Q4
Diabetes Care	Accu-Chek Nano SmartView	small, no-code blood glucose metre	US	Q2
	Accu-Chek Mobile	next-generation strip-free blood glucose metre	EU, Japan	Q2–4
	Accu-Chek Combo	insulin pump/blood glucose metre combination	US	Q4
Life sciences	LightCycler 96	system for real-time PCR analysis	WW	Q4
	SeqCap EZ products	for next-generation sequencing, prepare enriched regions of genome: SeqCap EZ Oncology and Neurology Panels and New Exome Products	WW	Q4
	GS FLX+ software v2.8	enables improved long-read sequencing performance on the GS FLX+ system	WW	Q4
	Cedex Bio HT	high-throughput analyser for metabolite testing in cell fermentation in biopharmaceutical production	WW	Q4
	cOmplete ULTRA	protease inhibitor tablets for use in molecular biology research	WW	Q1
	MycoTOOL	real-time PCR analysis kit for detection of mycoplasma	WW	Q1
Tests/assays				
Oncology	HE4	immunoassay for early ovarian cancer detection	US	Q4
	p16 Histology	IHC tissue test for early detection of cervical disease	WW	Q2
	ALK	IHC tissue test to identify patients eligible for lung cancer treatment crizotinib	EU	Q4
	10 other IHC tissue tests	for the detection of proteins in tissue samples including TTF-1 (lung and thyroid cancer) and hENT1 (various cancers)	EU, US	Q3–4
	10 ISH tissue probes	for the detection of genes in tissue samples, including EGFR, MYC, FGFR1, Chromosome 7 and 8	WW	Q1–3
	Ki-67, PR and p53 Algorithms	image analysis applications for antigens Ki-67, PR and p53, support breast cancer diagnosis in tissue samples	US	Q1–2
	GS GType TET2/CBL/ KRAS & RUNX1	gene sequencing primer sets for leukemia research	WW	Q1
Infectious diseases	HCV II	immunoassay to detect hepatitis C infections	EU	Q1
	HBc IgM	immunoassay to detect hepatitis B infections	US	Q1
	CT/NG	PCR test to detect chlamydia and gonorrhoea infections	US	Q1
	HIV-1, v2.0	PCR dual-target test to measure HIV viral load	US	Q3
	CMV	PCR test to monitor cytomegalovirus infections	US	Q3
Metabolism	Accu-Chek Aviva/ Performa universally coded test strips	require users to insert a code chip into their metre only once, with ongoing calibration of subsequent test strips	WW	Q2
	Vitamin D	immunoassay, measures vitamins D2 and D3	US	Q3

Diagnostics Division – key product launches planned for 2013

Area	Product name	Description	Market
Instruments/devices			
Laboratories	cobas 8100	next-generation modular pre-analytics	EU
Diabetes Care	Accu-Chek Insight	next-generation insulin pump and blood glucose metre	EU
	Accu-Chek Active	next-generation blood glucose metre with maltose-independent test strips	EU
Life sciences	GS FLX+ long amplicons	software for long-read targeted sequencing for DNA variant detection	WW
Tests/assays			
Oncology	Calcitonin	immunoassay, supports medullary thyroid cancer diagnosis and monitoring	EU
	proGRP	immunoassay, assists in the diagnosis of small cell lung cancer	EU
	EGFR	PCR test, supports therapy selection for non-small cell lung cancer	US
	ER	IHC tissue test for breast cancer diagnosis	US
	CINtec PLUS Cytology	immunocytochemistry test for diagnosis of cervical pre-cancer	EU
Infectious diseases	MPX 2.0	PCR next-generation blood screening, multiplex test for HIV, HCV and HBV	US
	HCV 2.0	PCR next-generation HCV viral load test	US
Trans-plantation	Cyclosporin, Tacrolimus	immunoassays for monitoring of immunosuppressive drug therapy	EU
Sequencing	SeqCap EZ Reagent Kits	for sample preparation for targeted next-generation sequencing	WW

black type = new product/first market launch; grey type = new product/launch in additional markets.

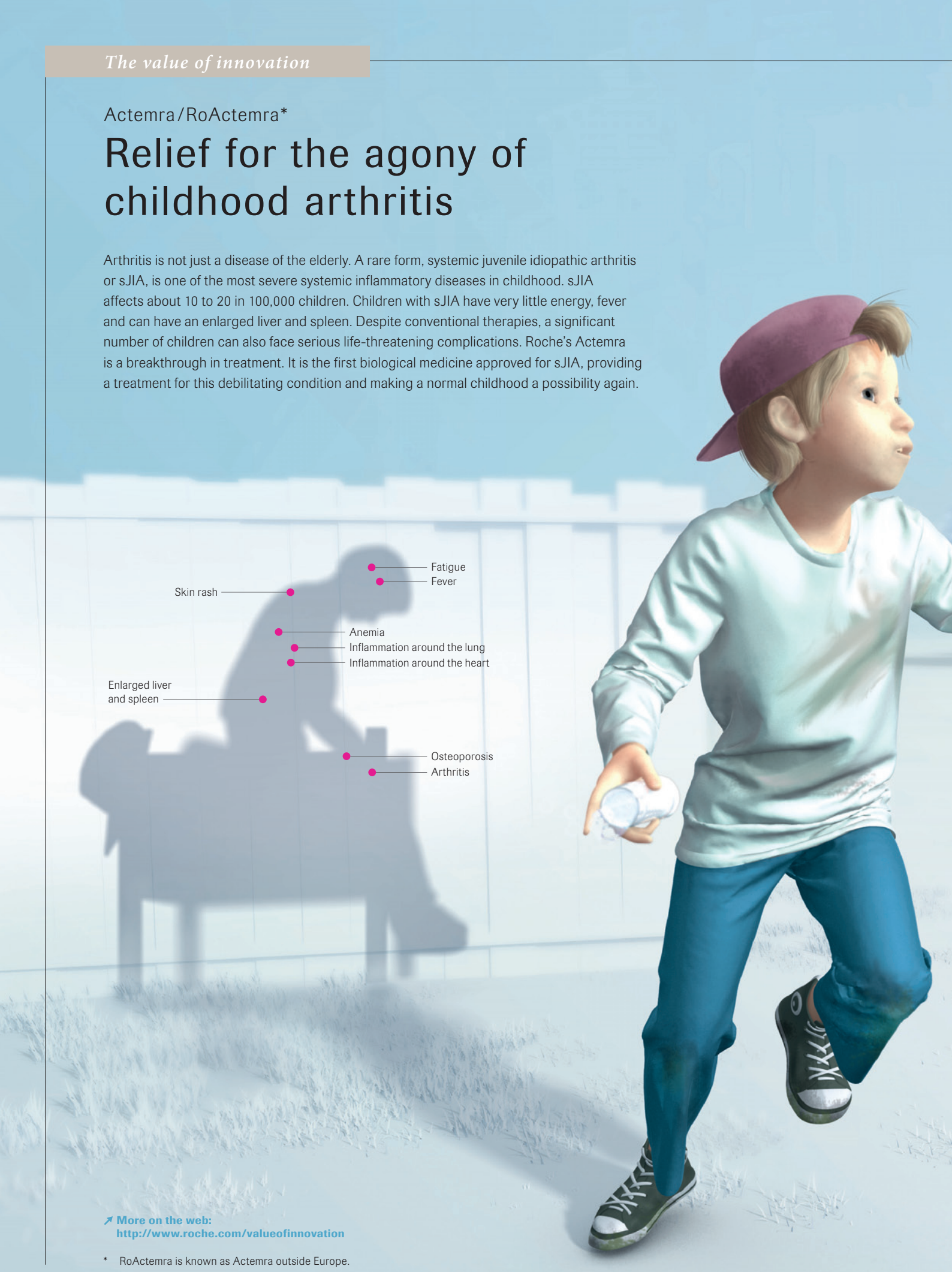
EU = European Union; US = United States; WW = worldwide.

ALK = anaplastic lymphoma kinase; CBL = Casitas B-cell lymphoma gene; CT/NG = *Chlamydia trachomatis/Neisseria gonorrhoeae*; EGFR = epidermal growth factor receptor; ER = estrogen receptor; GS = Genome Sequencer; HBV = hepatitis B virus; HCV = hepatitis C virus; HE4 = human epididymis secretory protein E4; HIV = human immunodeficiency virus; IHC = immunohistochemistry; ISH = *in situ* hybridisation; KRAS = member of the Ras family of oncogenes; p16 = protein p16INK4a; PCR = polymerase chain reaction; proGRP = pro-gastrin-releasing peptide; RUNX1 = Runt-related transcription factor 1; TET2 = member of the TET family of oncogenes.

Actemra/RoActemra*

Relief for the agony of childhood arthritis

Arthritis is not just a disease of the elderly. A rare form, systemic juvenile idiopathic arthritis or sJIA, is one of the most severe systemic inflammatory diseases in childhood. sJIA affects about 10 to 20 in 100,000 children. Children with sJIA have very little energy, fever and can have an enlarged liver and spleen. Despite conventional therapies, a significant number of children can also face serious life-threatening complications. Roche's Actemra is a breakthrough in treatment. It is the first biological medicine approved for sJIA, providing a treatment for this debilitating condition and making a normal childhood a possibility again.



↗ **More on the web:**
http://www.roche.com/valueofinnovation

* RoActemra is known as Actemra outside Europe.

Laura Gray was diagnosed with sJIA seven years ago:

'I used to be a particularly sporty person, but after being diagnosed that was a part of my life that was completely taken off the table and I couldn't do it anymore. Due to the illness I started missing quite a bit of school and got behind and lost friends from it because I couldn't keep up with them; out of sight, out of mind.
I can do an awful lot more now than when I wasn't on the drug. I'm currently learning to drive, I'm going for an interview at college, which was an option I hadn't considered when I was ill. I thought at the time that was something that was way, way off the table, but now these options have been opened up.'

26

manufacturing sites

MANUFACTURING AND PROCUREMENT

Initiated 240 million Swiss franc investment in diagnostics production in Penzberg, Germany.

Enabled rapid launch of new medicines Perjeta and Erivedge – available to US patients in one and three days after FDA approval, respectively.

Developed new biotech production methods and technologies, including production processes for our first antibody–drug conjugate, T–DM1.

Key figures

Manufacturing sites	26 17 Pharmaceuticals, 7 Diagnostics and 2 joint sites		
Employees	16,700 in manufacturing and logistics		
Portfolio	over 100 medicines	2,600 tests	140 instruments

Manufacturing, procurement and supply functions bring innovative medicines and diagnostics from the R&D pipeline to patients and healthcare professionals worldwide. At all stages of our global supply chain, from suppliers to manufacturers, warehousing and transportation, we require and apply rigorous safety, quality, ethics, labour, health and environmental standards. State-of-the-art processes and facilities ensure that these standards are fully met and that products are made available reliably.

In 2012 the Group's operations networks supported robust sales growth and new product development in the Pharmaceuticals and Diagnostics Divisions, enabling Roche to strengthen its leadership in oncology and *in vitro* diagnostics. In Pharmaceuticals, the network supported a broad product portfolio including new oncology treatments, as well as added new technologies and overcame technical challenges in biologics manufacturing. In Diagnostics, we supported strong growth in sales to clinical laboratories and streamlined parts of the network in line with business priorities.

Throughout the networks, we maintained a strong commitment to quality and compliance. We continued to improve our processes and develop new capabilities to best serve our product pipelines. In 2012 our sites successfully passed 104 regulatory inspections and we resolved issues from internal quality audits. We also continued to reduce our environmental footprint by implementing new logistics strategies.

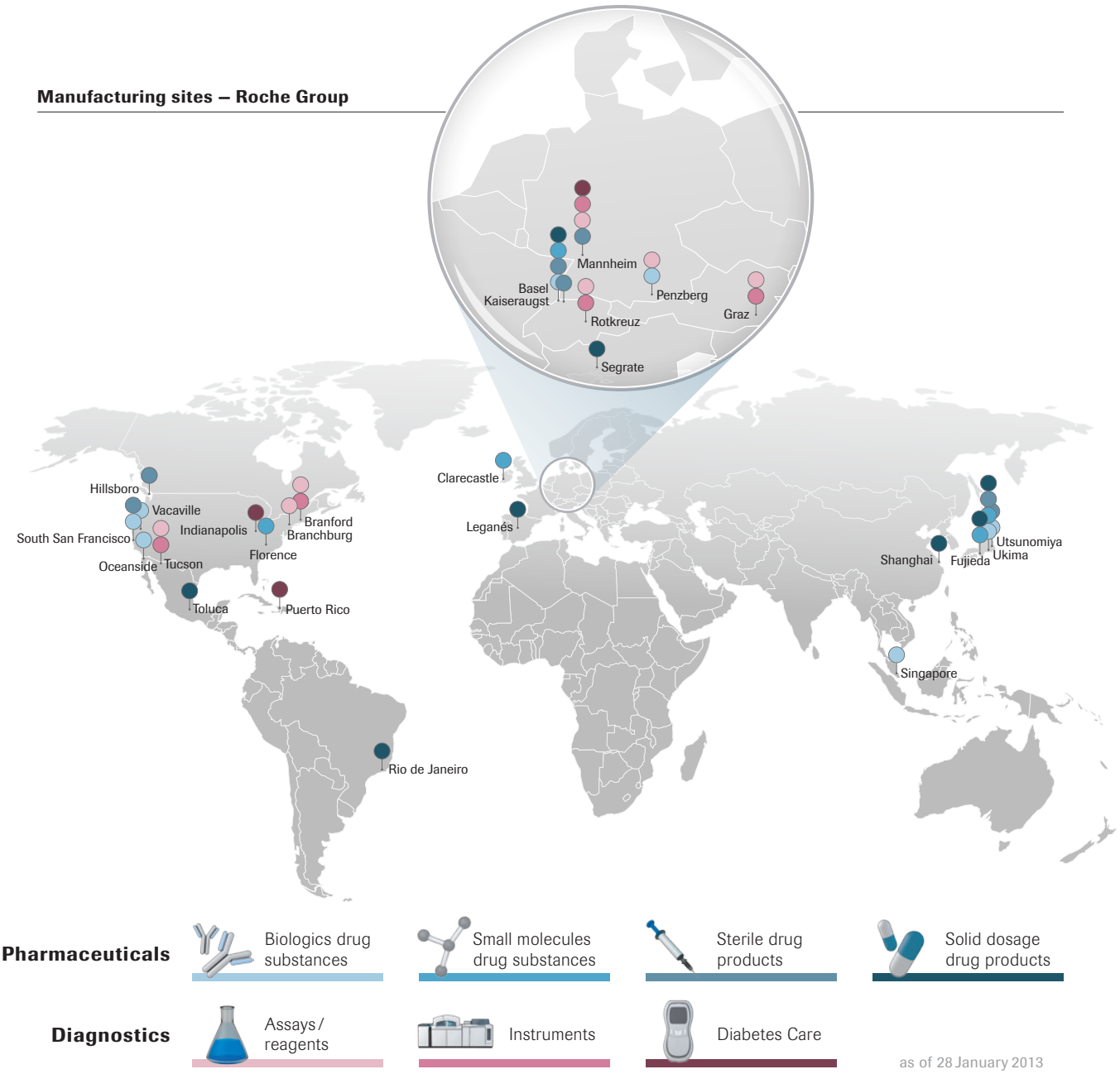
Capital investment

In 2012 we maintained robust capital investment programmes in our pharmaceutical and diagnostics manufacturing networks, adding capacity and improving production processes. Roche's leading engineering expertise was recognised for the fifth consecutive year as 'facility of the year', category winner for operational excellence, in the International Society for Pharmaceutical Engineering awards.

Investment highlights

- Penzberg, Germany (approx. 240 million Swiss francs budgeted, project initiated end of 2012):
  Expansion of raw material manufacturing for our Elecsys immunoassays, to be completed end of 2014, as well as increase of compounding, filling and lyophilisation capacity planned for 2016.
- Basel and Kaiseraugst, Switzerland (approx. 230 million Swiss francs). Three projects completed in 2012:
  – new Pharma quality control and assurance building
  – Pharma cold-chain storage capacity expansion
  – filling line upgrade for Herceptin subcutaneous formulation
  Ongoing projects to establish launch capacity for highly potent drug products and to upgrade the filling line for Rocephin formulation throughout 2013 and 2014.
- Shanghai, China (approx. 260 million Swiss francs budgeted): Ongoing Pharma site expansion, including new laboratory, warehouse, office and training facilities, to be completed in 2014. Additional manufacturing capacity for highly potent drug products and expansion of utility and infrastructure, to be completed in 2015.

Manufacturing sites – Roche Group



Pharmaceuticals manufacturing

Our network

Our pharmaceutical manufacturing network produces more than 100 medicines for commercial supply and clinical trials. With some of the world's most sophisticated biopharmaceutical production plants, the network hosts approximately 25% of global biologic production capacity[1], making Roche the largest manufacturer in the biotech sector.

Our manufacturing sites play a vital role at every stage of the product lifecycle, from discovery to commercialisation. To reduce the risk of supply interruptions and balance production capacity, we dual-register some manufacturing sites, which allows us to produce key pharmaceutical products at more than one facility. We also outsource certain production to contract manufacturing organisations (CMOs) to gain additional capacity, increase manufacturing flexibility, leverage specialised technologies and manage costs. For example, we partnered with multiple CMOs, including a manufacturer of specialised biologics and highly potent small molecules, to set up processes and facilities for the manufacturing of trastuzumab emtansine (T–DM1), an antibody–drug conjugate.

1 Worldwide mammalian cell culture capacity including CMOs. BioPlan Associates, Inc. Annual Report and internal analyses.

Erivedge launch: first in class, first to patients

At 8:00 am on Monday, January 30, 2012, Roche received FDA approval for Erivedge, setting off a remarkable coordinated effort by the Roche team and our contract manufacturers. With the active pharmaceutical ingredient sourced in Asia and Switzerland and the capsule produced in Canada, what remained was packaging and shipment.

The Roche artwork experts together with a printing company worked around the clock to complete the packaging design, based on the final wording of FDA approval, and prepare the actual packaging. With Roche staff on site at 3:00 am on Tuesday to oversee packaging, the initial two lots were loaded that afternoon on separate trucks to mitigate against damage or delay. By Wednesday morning, the new treatment was safely in our warehousing and distribution centre in Louisville, Kentucky (US). And when the FDA cleared it for shipment on Thursday, Erivedge was on its way to the distributors within a few hours.

Antibody–drug conjugates: Taking biotech to the next level

We are striking new paths in biotech manufacturing with antibody–drug conjugates, a new class of compounds, where our antibody substances are 'armed' with a toxin. While promising, this approach was long considered difficult to put into practice. A key challenge was to find the right composition for the chemical to link the antibody and toxin, and then to design and scale a production process that ensured the stability and expected safety profile of the medicine. It required new processes, new external partners and new quality specifications, which added complexity to an already complex biotech production process. The successful efforts of our manufacturing organisation, in collaboration with R&D, resulted in the technical dossier for the filing of Roche's first antibody–drug conjugate, T–DM1, in the EU and the US in mid-2012. It also laid the ground for the manufacturability of other medicines of this new class in our pipeline.

As part of Roche's emerging markets strategy, we work with local governments and other partners to establish and expand local production capacity to increase access to our medicines (*see Marketing and Distribution,* page 74).

Performance

Our primary objectives in 2012 were to maintain supply reliability and product quality, while supporting pipeline development and expediting the launch of new medicines.

Pharmaceutical manufacturing played a decisive role in the rapid launch in the US of breast cancer medicine Perjeta — available to patients one day following FDA approval — and skin cancer medicine Erivedge — in distribution three days after approval. In collaboration with R&D, we supported 108 development projects for new medicines, including manufacturing investigational products for approximately 600 global clinical trials that involved tens of thousands of patients.

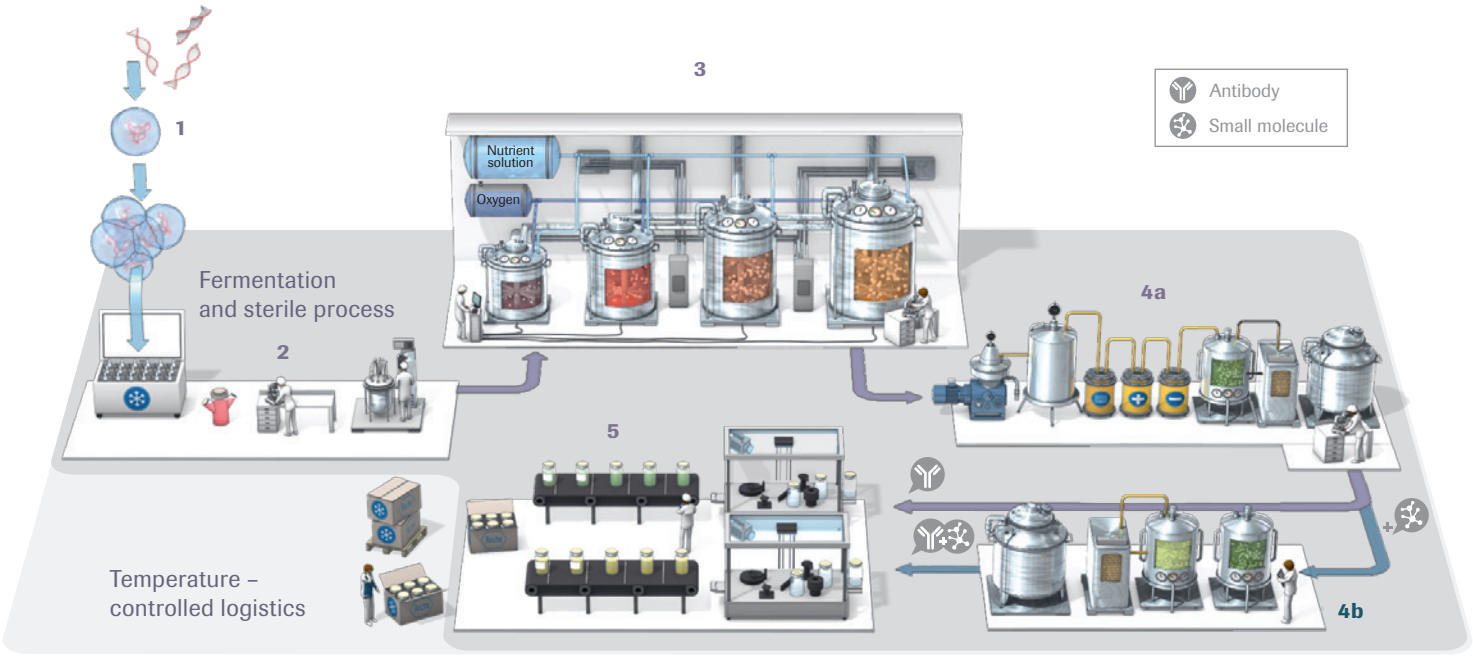
During the year we took active steps to safeguard operational reliability. Throughout the organisation, we increased inventory 'safety stock' levels, to ensure continuity of product supply in response to unforeseen increases in demand, especially for new product launches. This contributed to a total inventory increase of 18% in the division. We also increased oversight across the supply chain including suppliers and CMOs. To ensure an effective response in case of unexpected events, a new business continuity process for our manufacturing operations was put into effect.

Biologics manufacturing

Biologics (or biotech) manufacturing is a challenging process, as it involves living cells that are sensitive to even the slightest changes in their environment. A range of factors, from the nutrient solution and timing to the equipment used, can determine yield, amounts of unwanted by-products and even the structure of the active ingredient being produced. In 2012 we continued expanding our biotech capabilities, adding new methods and technologies. One innovative approach is for antibody–drug conjugates (ADC), where our antibody substances are 'armed' with a toxin. The process steps for biologics and ADC manufacturing are illustrated on the following page.

The inherently complex production process can occasionally present challenges that are unprecedented in the biopharmaceutical industry. In 2012 this included a one-time detection of the bacterium leptospira, during early-stage production of cancer drug MabThera/Rituxan. Importantly, our investigation of the issue, in cooperation with the health authorities, excluded the possibility of any clinically relevant risk to patients and sur-

Biologics manufacturing process



1 Cell line

Specific human genes are inserted into bacterial or mammalian cells to create a unique master cell line that yields the target antibody (biologics drug substance). This master cell bank is frozen for storage.

2 Culture

For production, cells are removed from the master cell bank, cultured in a liquid growth medium and transferred to larger vessels as the cells multiply.

3 Fermentation

The cell culture is transferred to progressively larger bioreactors. Special nutrient medium is added. Its unique composition is optimised for each cell line and enables production of the desired antibody.

4a Purification

The antibody is separated from the biomass (cells, culture medium and waste products) leading to a pure solution. The centrifugation, purification and concentration steps are specific to each desired antibody.

4b Conjugation

Additional steps for antibody-drug conjugates: The antibody is combined with a highly potent small molecule and again purified and concentrated.

5 Formulation, filling and packaging

The drug substance is formulated into a stable dosage form (sterile liquid or powder), filled into vials or syringes, and packed for shipping.

faced a new potential manufacturing risk. This groundbreaking work has been shared within the industry. We also experienced slower than expected cell growth in the newly scaled-up production process for our breast cancer treatment Perjeta. Our team ran a successful production campaign which enabled a timely launch, while committing to post-marketing production data reviews by the FDA to demonstrate resolution of the problem and maintain future supply.

Diagnostics manufacturing

Our network

The Roche Diagnostics manufacturing network handles all aspects of production, as well as procurement and logistics, for our industry-leading IVD product portfolio. This includes 140 different state-of-the-art instruments that perform more than 2,600 tests requiring 6,400 reagent kits, with 14,000 reagent and control components, and 160 consumables such as pipettes and cuvettes.

From 22,000 bits of steel, plastic and juices to a new DNA testing system

Roche's new mid/high-volume testing platform, cobas 6800/8800, is expected to be the first to bring exceptional levels of automation, throughput and cost-efficiency to molecular testing and blood screening labs. It also adds considerable complexity to development and manufacture.

To get from blueprint to pilot production, Roche production teams with backgrounds in biology, biochemistry, engineering and IT started in March 2007 to set up a process for transforming steel, plastic, software and juices into a new system including a variety of test kits. The closely coordinated effort included three manufacturing sites, Rotkreuz (Switzerland), Branchburg (US) and Penzberg (Germany), our R&D site in Pleasanton (US) and multiple global external suppliers. To manage the complexity, the team worked to ensure that exacting quality controls were built into production processes and that highest quality standards were applied internally and at supplier sites.

In December 2012 the first pilot molecular analysers were delivered to customers for field testing.

We manufacture the majority of our instruments and tests in-house, which allows us to maintain cost and quality advantages and leverage proprietary technologies and special expertise. We do, however, use external manufacturers to access unique technologies and control costs, such as for the production of hand-held blood glucose metres, large work stations, consumables, and an increasing number of sub-assemblies.

Performance

In 2012 we achieved our goals for saving costs and maintaining the supply of products to meet the division's above-market sales growth. For example, we delivered over nine million test kits for Roche's Elecsys immunoassay product line for highly automated blood testing in laboratories worldwide, an all-time high level of output and a major achievement for the business. We also supported the launch of 55 major diagnostic products in key markets (see table on page 56).

We continued transforming our network in line with business priorities. Under the Operational Excellence programme launched in late 2010, we further consolidated chemical raw materials and analytical services in Penzberg, Germany and closed our site in Burgdorf, Switzerland.

Additionally, we modified our manufacturing network based on changes to the product portfolio in two of our diagnostics businesses. We closed the Roche Applied Science Reykjavik, Iceland site, transferring its production of sequence capture devices to Madison in the US. We also initiated projects to streamline Diabetes Care operations and reduce costs, as that business unit adapts to a tough market environment.

Throughout 2012 we continued to pursue several long-term initiatives aimed at sustainable high performance:

- We established a continuous improvement culture and metrics in manufacturing quality performance *('right first time')* and put methodologies and tools in place to ensure more robust production processes *('design for quality and manufacturability')*, with first positive trends.
- We continued to optimise manufacturing capacity *('asset management')*, and initiated a major capital investment project at our site in Penzberg, Germany (see page 62).
- We started two new initiatives that are expected to generate significant savings over the next years: a *supply chain excellence* initiative to enhance the reliable and cost-effective supply of our products and to optimise inventory levels, and a *procurement excellence* initiative to ensure more strategic sourcing and improved supplier management, including a new supplier performance measurement tool.

Quality and compliance

Our overriding goal is to ensure that every person receives safe medicines and reliable diagnostic test results. To achieve this, we apply the same rigorous standards wherever a Roche product is manufactured or sourced. We, moreover, ensure that our quality management systems conform to all laws and regulations as well as the most recent norms and standards, including cGMP and those of ICH and ISO[2].

Harmonising and enhancing our quality systems

In 2012 Roche continued the global harmonisation of its quality management systems. In the Pharmaceuticals Division, we established a new system of over 100 global standards for areas such as quality management, risk management and preventive and corrective actions, with local implementation

2 Current Good Manufacturing Practices (cGMP); International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH); International Organization for Standardization (ISO).

ongoing. The Diagnostics Division's efforts to harmonise its multiple quality systems by 2016, were 40% complete at year-end. The harmonisation is expected to drive compliance and efficiency by, for instance, enhancing the manufacturing organisations' ability to manage quality performance and exchange best practices across the networks.

Assuring compliance

In 2012 regulatory authorities conducted 104 safety and quality inspections at the Roche Group's sites: 79 at our Pharmaceuticals sites and 25 in Diagnostics. The majority of these inspections resulted in no critical observations.

In collaboration with authorities, Roche Pharma resolved quality concerns regarding Mircera and Xenical production that were discovered in an internal audit and had interrupted supply as those products were held for release.

Roche Diagnostics continued to track the proposed revision to the In Vitro Diagnostic Directive in the EU, as well as preparing for a new FDA rule for Unique Device Identification for standardised coding of devices. We plan to implement new packaging design, barcodes and warehousing procedures in accordance with the final rule.

Collaborating with health authorities

Roche continues to collaborate with authorities and to provide expertise, including input on over 100 guidance documents, proposed regulations and laws. We are taking a leading role in implementing a 'quality by design' approach, which includes a strong focus on risk management and maximising quality performance in the design of production processes. Perjeta represented the first FDA submission in the industry of a biotechnologically manufactured drug based on these principles.

We are also the partner of choice for industry input on medicines with companion diagnostics (CDx) and work directly with the FDA on shaping the regulatory landscape on CDx. Roche, for instance, participated in over 45 meetings with the FDA and other regulators on CDx during 2011 and 2012.

Supply chain management

Our commitment to quality, innovation and sustainability extends throughout the supply chain. From responding quickly to market developments and ensuring reliable product supplies to reducing our environmental footprint, we maintain highly integrated and responsive global supply chains for both divisions.

Green warehousing

At the end of 2012, our Pharma warehouse in Mannheim, Germany, for refrigerated and normal storage, was externally rated as state-of-the-art in energy efficiency. Built in 2005, the warehouse had been constantly optimised and includes highly sophisticated environmentally friendly design features and processes. For example, energy consumption is minimised through an air conditioning and heating system oriented on working hours, window shutters reduce sunlight radiation by up to 20%, and the facility features a heat recovery system and special gate insulation. Packaging waste is recycled directly in the warehouse and pallets are reused, greatly reducing waste. Drawing on this role model and striving for the same kind of energy efficiency in all its warehouses, Roche developed a best practice action catalogue in 2012, that will be rolled out globally as of 2013.

Reducing environmental impact

Green logistics is an area of increasing focus within our supply chains, as we seek to systematically reduce air emissions, energy consumption and waste. In 2012 we contributed to Group-wide efforts to reduce environmental impact by further reducing the use of airfreight, and implementing six sea-freight lanes from supply hubs in Germany and the US to Saudi Arabia, South Africa, Singapore, Hong Kong, Israel and France. The change resulted in a 5% reduction of CO_2 emissions, or approximately 5,800 tonnes.

Additionally we addressed energy consumption and waste in our warehouses by reusing or recycling packaging materials. We are establishing goals to calculate and monitor achievements as well as fostering employee engagement by increasing awareness and training, including, for example, implementing a new e-learning tool in September 2012.

For more information, please see *Safety, Security, Health and Environment,* page 110 and following.

Procurement

Procurement teams work closely with business units along the value chain seeking innovative purchasing solutions to help them achieve their goals and generate cost savings that can be reinvested in the business. To create maximum value, we apply a 'total cost of ownership' concept with a holistic, long-term view on the benefits and costs of a purchasing decision.

While procurement is organised by division, procurement policies, processes and systems, along with large-volume spend and risk management, are closely aligned across the Group. The objective is to ensure sustainable performance and adherence to best practice and industry codes. Roche, for example, requires all suppliers to commit in all their activities to the sustainability principles of its Supplier Code of Conduct, which incorporates the principles of the Pharmaceutical Supply Chain Initiative (PSCI).

Aligning and building capabilities

In 2012 we implemented a new common standard to measure and report procurement savings. We continued to drive major joint sourcing projects such as research studies, temporary labour, production related purchases, credit cards and business travel. By pursuing this globally aligned approach, which retains local execution, we again realised substantial savings in line with business targets. We also negotiated a key contract with Google to provide employees worldwide with new uniform, cloud-based e-mail and calendar, which are expected to enhance connectivity and collaboration.

Procurement along the value chain

Supporting diverse needs with the right supplier partnerships

	RESEARCH AND DEVELOPMENT	MANUFACTURING	COMMERCIAL
Needs	Lab equipment, raw materials and services to invent and develop new drugs and diagnostics including services to run our clinical trials.	Reliable suppliers and logistics service providers for high quality product supply to patients and customers.	Marketing and other services for successful launch and commercialisation of our products through their lifecycle.
2012 examples of key supplier partnerships and initiatives	**Supplier diversity** Partnerships with small and diverse owned businesses in the local communities for specific R&D supplies. **Value outsourcing** Development of a new contracting model to outsource entire clinical programmes to external partners.	**Access to medicines** Contracting with an Indian manufacturer for local filling and packaging of Herceptin and MabThera, to improve access to these medicines in India. Involves transfer of significant process know-how.	**Making most of events** New approach on managing congresses, meetings and events with greater transparency on participation, prioritisation of events and tools for planning and booking. Enabled substantial cost savings.

We expect to generate further value and efficiencies by:

- Continuing to enhance organisational structures and capabilities in emerging markets to enable more pro-active and systematic management of local spending. For example, Roche Diagnostics started up a procurement office in Singapore in the beginning of 2012 to support the Asia–Pacific region and Roche Pharma rolled out its next-generation procurement system in China.
- Enhancing relationship management and oversight of suppliers, with a new procurement excellence programme in Diagnostics (page 66) and in frame of Pharmaceuticals' focus on supply reliability (page 64).
- Developing our people and exchanging knowledge such as with the new global learning and development platform by Pharma procurement, with a catalogue of customisable courses and access to internal and external resources.

Engaging with suppliers

We seek to build mutually beneficial and sustainable relationships with suppliers and actively engage and collaborate with them to manage performance and risk, ensure quality and compliance, reduce our combined environmental footprint and promote innovation. We thereby take into account the different business needs along the value chain (see illustration).

In June 2012 Roche launched the industry's first supplier relationship centre in South San Francisco (US), where Roche employees are co-located with representatives of five key suppliers dedicated to find innovative ways to generate mutual benefits. In 2012 we also rolled out a new e-learning module to help our suppliers to increase knowledge among their employees of sustainability, the Roche Supplier Code of Conduct and industry standards. A supplier day in Shanghai (China), with around 100 participants, provided a further opportunity for suppliers to learn more about sustainability and our audits. In partnership with the Institute for Supply Chain Management and Diversity Alliance for Science, Roche is also engaged in a programme to provide opportunities for innovative and competitive diverse suppliers.

Monitoring compliance

To ensure compliance with Roche and industry codes and standards, we conducted 115 supplier audits in 2012 across all regions, including five follow-up audits, 38 more than in 2011:

- 62 in the direct spend area (goods that go directly into production)
- 53 of service providers.

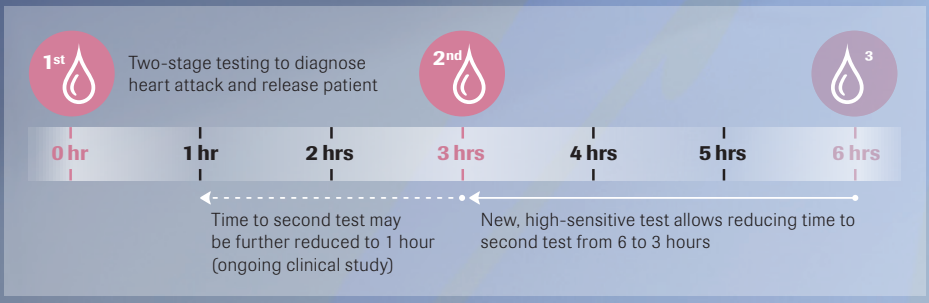
Roche also collaborated with other healthcare companies under the PSCI who developed a unified joint sustainability audit protocol. In 2012 ten suppliers were audited under this protocol by independent auditors.

The majority of suppliers audited in 2012 either met or exceeded minimum requirements. However, we decided to stop business with one supplier that did not meet minimum standards. The main findings in the direct spend area related to industrial hygiene and safety design, while findings for service providers occurred primarily in social and ethics areas.

More on the Web

- Biotech production: www.roche.com/biotechnology/production
- Pharmaceutical Supply Chain Initiative: www.pharmaceuticalsupplychain.org
- Supplier engagement: www.roche.com/stakeholder_engagement
- Supplier Code of Conduct: www.roche.com/roche_supplier_code_of_conduct.pdf

Chest pain
Approximately 10% of all emergency room consultations are for patients with heart attack symptoms. In the US alone, more than 5.5 million patients are seen in emergency departments every year for chest pain. Rapid, accurate diagnosis and early risk assessment are critical when a patient arrives.



1 Not available in the US and other markets
2 Also considering ECG information and clinical symptoms
3 For hospitals not using the high-sensitive test

Taking cardiac testing to the next level
Studies are ongoing to enhance the use and medical value of troponin T testing in clinical practice – in the emergency setting as well as beyond, for instance for regular check-up of patients at risk:

One-hour diagnosis of heart attack: This study is evaluating whether chest pain patients can be securely diagnosed with one Troponin T high-sensitive test at admission, and then have a final test after just one hour. This trial will help patients and take pressure off emergency departments, enabling rapid transfer to specialised treatment or early discharge (TRAPID-AMI study, started in 2011).

Patient monitoring after major surgeries: Another study assesses the use of the Troponin T test for patient monitoring after major non-cardiac surgery. About 200 million adults worldwide undergo major non-cardiac surgery each year. More than one million die within 30 days. Regular troponin T testing will help physicians to identify patients at risk, detecting cardiac injuries that might otherwise go unnoticed but could cause death (VISION study, started in 2007).

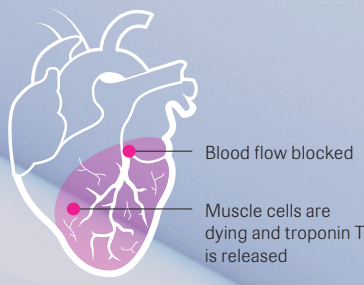
↗ **More on the web:**
http://www.roche.com/valueofinnovation

High-sensitivity cardiac test

Precise testing for life or death decisions

Diagnosing heart attack patients is one of the most challenging problems facing doctors in hospital emergency departments. A heart attack requires immediate and often serious intervention like heart catheterisation or coronary bypass surgery. A blood test that can accurately determine whether a patient is having a heart attack can literally mean the difference between life and death. Twenty years ago physicians had to rely on symptoms and electrocardiograms (ECG), which could miss over 50% of heart attacks. Roche has developed an Elecsys Troponin T high-sensitive test[1] which detects the presence of troponin T, a protein that is released into the bloodstream during a heart attack. The Troponin tests are reliable indicators of heart attack and the gold standard worldwide in cardiac critical care.

What is a heart attack?



Heart attacks are caused by the interruption of the blood supply to parts of the heart, causing heart cells to die. This is most commonly due to blockage of a coronary artery following the rupture of a substance called arterial plaque from the inner wall of the arteries.

Prof. Christian Müller, Cardiologist and Head of Outcome Research, University Hospital Basel:

'The high-sensitivity cardiac troponin is an indispensable test in the early diagnosis of a heart attack. It enables us to detect small heart attacks that we could have missed with the use of conventional tests. It is also of critical help in the allocation of resources in the emergency department because we can identify patients with cardiac disease early on and focus the right resources for patients from the outset.'

18,000

patients received treatment with one of the 25 top-selling Roche medicines in 2012

0,000

MARKETING AND DISTRIBUTION

Customised innovative market solutions to increase access to our medicines.

Launched an educational initiative in nine Asian countries to promote excellence in testing for HER2-positive breast cancer.

Started a programme with the Peruvian government to provide cancer care access for 12 million of the country's poorest citizens.

Key figures

Core Marketing and Distribution (M&D) expenditure in 2012

Roche Group	8,392 millions of CHF	+3% (CER)[1]	18.5% of sales
Pharmaceuticals	5,851 millions of CHF	+2% (CER)	16.6% of sales
Diagnostics	2,541 millions of CHF	+4% (CER)	24.7% of sales

1 Constant exchange rates (average full-year 2011).

Employees in M&D	28,381 Roche Group	17,631 Pharmaceuticals	10,750 Diagnostics

Tailored market strategies

Healthcare systems around the world vary greatly. In some regions, the most sophisticated new medicines and diagnostic tests are readily available, while in others healthcare infrastructure is so limited that even basic medical care is a luxury. Access to good medical care depends on many different factors including income levels, availability of medical professionals and political commitment, but common to most healthcare authorities is intense budget pressure and the need for sustainable healthcare solutions. This pressure is driving the market for ever more innovative ways to bring the most effective medicines to patients at an affordable cost.

At Roche, we focus on ensuring that our products demonstrate real benefits for patients, as well as represent a meaningful expenditure for healthcare authorities, wherever they may be. We are increasingly developing ways to bring value to healthcare systems to enable as many people as possible benefit from our medicines.

Demonstrating value

We work closely with healthcare authorities, insurers and other payers to demonstrate the value of our products and services and, in turn, gain appropriate reimbursement and market access. We collaborate with various authorities and policy makers and actively contribute to Health Technology Assessments (HTAs) that systematically evaluate the costs and benefit of our innovative medicines and diagnostics, in order to guide their most efficient and effective use. Our aim is to sustain medical innovation in order to meet medical need and help address the mounting pressure on healthcare budgets.

A priority for the Diagnostics Division is to support the development of reimbursement programmes that identify and establish evidence-based payment and coverage decisions, that provide effective and accurate assessments of the analytical and clinical validity of advanced molecular diagnostic tests. In particular, the Diagnostics Division in the United States is capitalising on these reimbursement programmes with proven results.

Another initiative Roche is heavily involved with (and co-founded) is the Green Park Collaborative, an international group, exploring the feasibility of developing guidelines for the design of clinical studies to meet the needs of HTA organisations and payers. The aim of the programme is to involve the payers earlier and improve the relevance of clinical research and to accelerate patient access to new drugs and technologies.

We are also actively participating in a joint initiative between the pharmaceutical industry and santésuisse, an association of Swiss health insurers, and other stakeholders to develop basic principles of future HTAs in Switzerland. We have established consensus on the valuation of health technologies, with the objective of improving quality and transparency in the healthcare system, as well as increasing efficiency and thus reducing costs. The project has triggered broad interest outside Switzerland, as an example of how stakeholders with typically conflicting interests can come together.

Access to healthcare programme highlights

7,800

children supported in seven African countries and India in monitoring their diabetes through a partnership with Novo Nordisk's Changing Diabetes in Children programme

1,250,000

infants tested for HIV through the AmpliCare initiative

56

countries where Roche does not file or enforce patents for any of its medicines

2,000

laboratory technicians to be trained in HIV diagnostics in a partnership with the US President's Emergency Plan for AIDS Relief

Right solution for the right market

In our view, 'one size' does not 'fit all' when it comes to bringing our products to market. Developing the right solutions for an individual market requires significant long-term commitment to understanding the needs and challenges in a country, as well as its healthcare system. We have a decentralised business model which empowers local management teams to work closely with healthcare providers and determine how best to customise solutions, appropriate for local market conditions.

Innovative pricing models

Part of this tailored approach to local healthcare systems is to develop reimbursement arrangements around value, rather than a uniform pricing structure. For example, we have programmes in place that differentiate price on the medical value of a drug, which can vary depending on the indication it is being used to treat. We also have 'pay for performance' payment models, for example in Italy, where refunds are given when disease has progressed earlier than anticipated, according to our pivotal trial programmes. These models have been successful in a number of markets in Western Europe.

In emerging markets, which are key to Roche's growth strategy, economic growth is not necessarily matched by improvements in healthcare infrastructure and funding. Within these markets there can also be striking differences in access to medical care. In the higher income private sector, people have access to quality healthcare, however in the public health system, where the majority of the population turn, the situation is very different. Our approach to these disparities is to work with governments to support public healthcare access and find solutions to bring our medicines to those in need. We are piloting several differential pricing programmes, in partnership with governmental organisations, which include providing diagnostic tests and education, as part of a packaged solution appropriate for individual country needs. An example of this is in South Africa, where in 2012 we worked with the government to enable MabThera, for the treatment of non-Hodgkin's lymphoma, to be reimbursed in the public healthcare system.

Second brands

In some emerging markets, we have also invested locally in partnerships to manufacture or finish some of our products in order to improve access to our medicines in underserved market segments. These products are commercialised under different brand names and can come in slightly different forms, for example in vials rather than syringes. This approach supports our long-term growth strategy in these markets, while providing an affordable solution for public healthcare authorities.

An example of this in 2012 was India, where Roche has developed second brands for cancer drugs Herceptin and MabThera/Rituxan. This was the first step in a wider initiative to implement manufacturing of Roche products in collaboration with a local partner, which has state-of-the-art facilities for biologics manufacture. This second brand strategy drives growth in India, while in partnership with the government,

Helping patients access new medicines

Our focus is on enrolling patients in clinical trials to obtain the data required to enable regulatory and reimbursement authorities to review and decide on whether these new medicines should be marketed and reimbursed. Approval by regulatory authorities is the only way to make medicines broadly available to patients for the use under the supervision of a qualified healthcare professional or doctor.

However, we recognise that it may not be possible for all patients who might receive benefit from the new medicine to enrol in the ongoing clinical trials, nor is it possible to have clinical trials for all potential disease settings available. Hence, under specific circumstances, Roche may provide patients with pre-approval access (PAA) to unapproved or investigational medicines outside the clinical trials process, before they are approved by regulatory authorities. This could be through an Expanded Access Program (in the US), a Pre-Approval Safety Study (in the EU or other countries) or through Compassionate Use.

Improving breast cancer diagnosis in Asia

Roche has launched the SPHERE (Scientific Partnership for HER2 testing Excellence) programme in Asia—Pacific, an educational initiative to promote and facilitate excellence in HER2 testing in breast cancer. HER2-positive breast cancer is a particularly aggressive form of cancer, which requires timely and accurate diagnosis.

This programme currently runs in nine markets in Asia — China, Korea, Taiwan, Hong Kong, Indonesia, the Philippines, Thailand, Vietnam and Malaysia. In 2012 alone, more than 1,000 laboratories and 9,000 pathologists, surgeons and technicians have been educated through this initiative.

SPHERE aims to increase the accuracy and reliability of HER2 testing across Asia, and in turn increase the chance of cure for those with the disease. The programme also looks to help SPHERE-trained centres monitor and improve their testing parameters, as well as build the first regional database on HER2 status in breast and gastric cancer.

increases access to medicines for patients below the poverty line. Another example of second branding is Egypt, where we launched a second brand of our hepatitis C drug to the public healthcare market in 2006. Since then, over 110,000 people have been treated, who might otherwise not have received treatment.

Patient assistance programmes

We also recognise that many patients, even in developed countries, still cannot afford treatment. Even those with insurance may not be able to pay for treatment if it is not fully covered by individual insurance plans. To mitigate this barrier to healthcare, Roche provides patient assistance programmes that assist both the underinsured and the uninsured with access to our medicines. In the United States, Genentech Access Solutions helped more than 100,000 underinsured and uninsured patients access appropriate medicines in 2012. The Genentech Access to Care Foundation provides free medicines to patients who are uninsured and who meet a specific set of financial and medical criteria.

In China, we have also launched a patient assistance programme for Herceptin, a breast cancer medicine, whereby treatment costs are reduced to increase the number of people benefiting from this drug in the public healthcare system.

Infrastructure development

In many areas of the world, healthcare infrastructure is rudimentary and significant challenges exist to improving it that are not just limited to fiscal constraints. At the most basic level, there are critical shortages of medical professionals and health facilities; low awareness of the causes of symptoms or of the prevention and treatment of disease; and even poor electricity supplies to keep hospital equipment running. To help resolve these issues, Roche collaborates with local stakeholders, governments and international health organisations, to support education and development of healthcare infrastructure as well as improve availability of medicines and provide diagnostic tests. In Peru for example, in 2012, Roche began a programme with the government to provide cancer care access for 12 million of the poorest citizens, providing diagnostics, pricing plans for medicines and support with education and infrastructure development.

In Algeria, Roche is supporting an initiative to bring breast cancer screening to women in rural areas, where mammography centres are few and far between. A fully equipped truck, locally referred to as the 'mamobile', with trained nurses and radiologists travels mainly in the Southern Sahara to give mammograms to local women. The programme is also piloting in Biskra, in the southeast of the country, where it will screen

as many as 40 women a day, with the aim of screening as many of the 89,000 women eligible in the province as possible. This programme is also being rolled out in other areas of the Middle East.

Customer satisfaction

We track customer satisfaction at regular intervals, usually annually or bi-annually, benchmarking our performance against our peers and industry averages. Through surveys conducted by Roche and third parties, we gauge customer satisfaction in our representative's knowledge and helpfulness during visits, the effectiveness of our medical support and clinical data distribution and the quality of our information and on our educational materials. In addition our Diagnostics Division looks at delivery times and service and technical support levels.

We analyse this feedback to identify the most appropriate communication channels and to establish sales and marketing plans, setting targets in areas that have been identified as important to our customers and where we see opportunities to improve our performance.

More on the Web

- Our products: www.roche.com/products
- Assessing the value of our products and pricing: www.roche.com/medical_value_patents_and_pricing
- Access to healthcare overview: www.roche.com/access_to_healthcare
- Genentech Access solutions: www.GenentechAccessSolutions.com
- List of patient groups supported: www.roche.com/patient-groups
- Responsible marketing: www.roche.com/business_integrity_and_responsible_marketing
- Roche's policies, guidelines and positions: www.roche.com/positions_policies_downloads.htm

Bespoke solutions for Chinese labs

Roche Diagnostics has been in China since 2000 and its clinical labs business is continuing to grow at 1.5 times the rate of the Chinese IVD market, with equipment sales to more than 2,000 hospitals in 440 cities. The IVD business has benefited from considerable investment in the country, as well as from the government's multi-billion dollar investment into healthcare infrastructure.

The ability to offer a broad range of modular instruments, from desktop solutions to large-scale equipment, is key to this growth, as Chinese customers primarily expand their labs step by step.

Equally important is the broad array of tests that can be run on the instruments, including over 100 immunoassays, which now represent our fastest-growing segment. We have also developed a flexible sales model with distributors, which ensures distributors have easier access to instruments. In addition, our service team has control over pre- and post-sales service to ensure high customer satisfaction levels.

Together this market strategy has not only secured our market leading position, but 26% growth in Diagnostics China for 2012.

Accurate diagnosis and personalised healthcare

Focusing healthcare budgets on targeted treatments

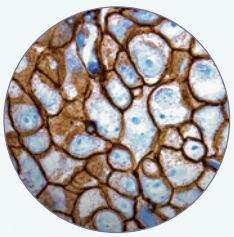
Rapid and accurate diagnosis is fundamental to the successful treatment of any cancer. Identifying those patients who will likely benefit from personalised treatment improves patient outcomes and saves time and money that could be better spent elsewhere. In breast cancer for example, 15–20% of all cases are of a very aggressive type, known as HER2-positive. Without treating this kind of breast cancer specifically with a HER2-targeted therapy, the patient is at increased risk of the cancer spreading as a general therapy may have a limited effect or no impact at all. Roche has developed a suite of HER2 tests, which provide rapid, reliable results enabling informed decisions for HER2-targeted treatment for patients.

Dr Alan Sokolow, former medical director of a US health insurance company, and now AccelusHealth:

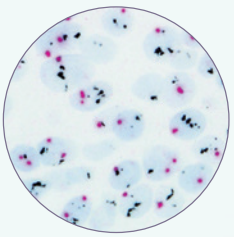
'For me, personalised healthcare and diagnostics have two clear advantages – they not only significantly improve health, but can also reduce healthcare costs. I would like to see more and more physicians adopting this approach and more recognition from payers, as they realise that the new tests and therapies deliver value and offer more quality and less waste.'

Quality HER2 testing is critical
An early step for patients confronted with breast cancer is usually a 'biopsy', taking a small amount of suspected tumour tissue and analysing it. To fully tap the potential of personalised healthcare, it is key to minimise the risk of false test results. Roche's two HER2 tests have shown in independent assessments to be more accurate and reliable.[1] Their automated processing on sophisticated tissue staining instruments not only helps save costs in the lab but also reduces the possibility of human error and ensures delivery of patient results as quickly as possible, literally overnight.

HER2 (4B5) IHC test[2]
marks HER2 proteins, first line of HER2 testing



HER2 Dual ISH test[3]
shows ratio of HER2 genes to chromosome 17, second-line testing in case of equivocal IHC test result

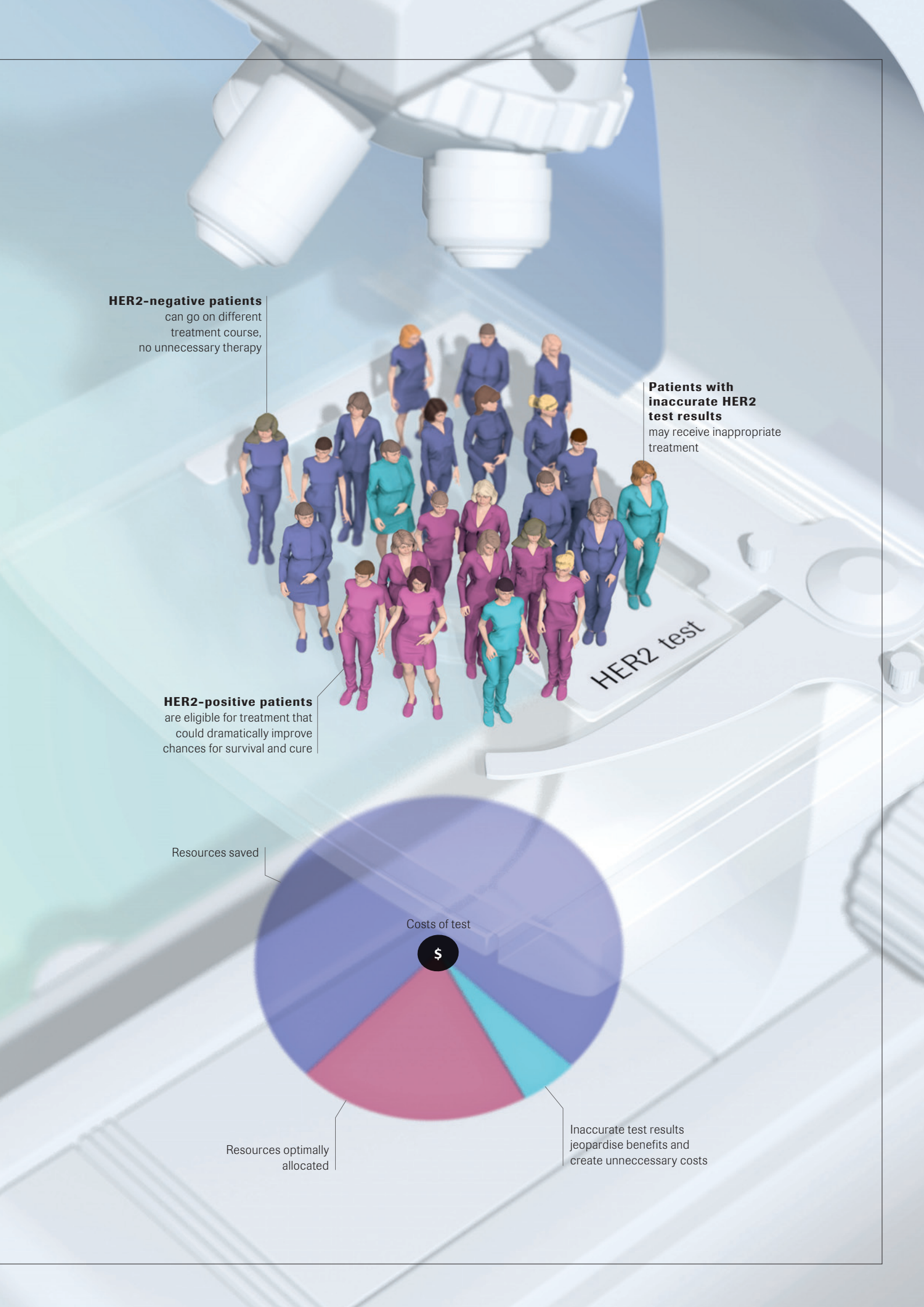


↗ **More on the web:**
http://www.roche.com/valueofinnovation

1 According to NordiQC (2012), other tests comparable to Roche's HER2 (4B5) IHC test show 15–50% more poor or borderline results. Mayr et al (2009) showed that a leading competitive HER2 IHC assay produced five false results while the VENTANA HER2 (4B5) test diagnosed all patients correctly. Superiority of the HER2 Dual ISH assay was proven by Loftin IR et al in a multi-site clinical study (2011), it reduces the inaccuracy rate by 4% compared to a competitive HER2 FISH assay.

2 PATHWAY anti-HER2/neu (4B5) Rabbit Monoclonal Primary Antibody.

3 INFORM HER2 Dual ISH DNA Probe Cocktail.


HER2-negative patients
can go on different
treatment course,
no unnecessary therapy
Patients with inaccurate HER2 test results
may receive inappropriate
treatment
HER2 test
HER2-positive patients
are eligible for treatment that
could dramatically improve
chances for survival and cure
Resources saved
Costs of test
$
Resources optimally
allocated
Inaccurate test results
jeopardise benefits and
create unneccessary costs

36,00

Swiss francs contributed to patient organisations in 2012

0,000

RESPONSIBLE BUSINESS

Launched Roche Compliance Pulse Check to evaluate progress in non-compliance cases.

Hosted a think tank on schizophrenia to better understand the needs of patients and their carers.

Worked with regulatory authorities to develop a strong framework for biosimilar approval.

Key figures

Contributions to healthcare institutions	176 millions of CHF
Contributions to patients organisations	36 millions of CHF

Integrity and sustainability in all aspects of our business
As one of the world's largest healthcare companies, Roche maintains the highest standards of business ethics and integrity.

Our commitment to responsible business behaviour goes beyond strict legal compliance. We demand conduct that is ethical and open and that forms the basis of our sustainable business and creates long-term value for our stakeholders.

We run our business in ways that are both profitable and responsible. We are committed to the Triple Bottom Line principle, by driving our social and environmental performance with the same diligence as our financial performance. In our sustainability management, we apply a materiality framework and continuously look for the positive impact that our sustainability initiatives have, or could have on our business.

Code of conduct

The Roche Group Code of Conduct guides our employees' business behaviour worldwide, covering topics such as corporate and personal integrity, social responsibility and compliance management. Employees complete mandatory training to ensure they understand the Code of Conduct, including where to find help and advice and how to raise a compliance concern over business practices or behaviour.

At Roche, we have developed a compliance programme that incorporates the key elements of a good practice compliance program with the clear purpose to embed compliance into the day-to-day business operations. We are convinced that compliance is closely linked to good leadership, our leaders are obliged to foster an environment of trust that encourages employees to speak up and are measured not only on business results, but on their ability to manage teams.

Roche also requires its external business partners to adhere to the same high standards as its employees. Local managers are responsible for monitoring and reporting compliance, as well as for responding quickly to any non-compliant behaviour. Our Supplier Code of Conduct clearly outlines our expectations of our suppliers. The Chief Compliance Officer serves as a contact person for all external stakeholders on issues relating to the implementation of and compliance with the Roche Group Code of Conduct.

Roche does not tolerate violations of its Code of Conduct. When a non-compliance allegation is confirmed, line managers are requested to take immediate corrective measures and to impose adequate sanctions on employees, such as warning letters, bonus cuts or termination of an employment contract. If a business partner does not behave appropriately, we do not hesitate to terminate the relationship.

Our employees can report concerns either to their line manager, the local compliance officer or the Chief Compliance Officer. Alternatively, they can report non-compliance issues anonymously to the Roche SpeakUp Line, which is accessible in 99 countries and 49 languages. We do not tolerate any retaliation against employees who have raised a compliance concern in good faith. In 2012, 71 alleged violations of our Code of Conduct were reported via the SpeakUp Line

In addition, local compliance officers must report material business ethics incidents to the Chief Compliance Officer. In 2012 there were 132 business ethics reports in areas such as fraud, theft, violation of good marketing practices, embezzlement, false records, conflict of interest, discrimination and harassment. Each allegation was carefully investigated, resulting in the termination of 108 employment contracts on account of unethical behaviour and two agreements with business partners for the same reason.

Compliance initiatives

We launched several supplementary initiatives in 2012, including the Roche Compliance Pulse Check and the setting up of the Healthcare Compliance Council (HCC). Compliance Pulse Check is a tool to enable local management, employees and compliance officers to assess progress on the handling and detection of non-compliance cases. HCC is headed by the Chief Compliance Officer and brings together compliance representatives of the Pharmaceuticals and Diagnostics Divisions, as well as compliance experts from various regions and affiliates. The HCC fulfils a coordination function intended to ensure a common interpretation of the healthcare provisions of our Code of Conduct and to support a consistent implementation of Roche's compliance programme throughout the Group.

Sunshine Act Regulations

In 2012 we further strengthened good business practice, putting in place a new global web-based system and process that contributes to Roche's ability to comply with new regulatory transparency requirements like the US Physician Payment Sunshine Act, as well as other similar disclosure regulations in Europe and elsewhere in the world. The system enables Roche to collect all contributions made to healthcare professionals by Global Functions and by cross-border engagements, and prepares Roche to be fully compliant with the Sunshine Act Regulations.

Stakeholder engagement

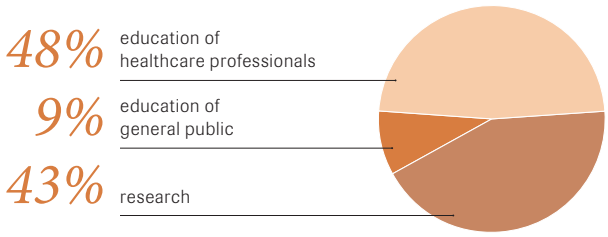
At Roche, we believe that open and constructive interaction with patients and healthcare professionals improves our ability to fit treatments to patients.

The pharmaceutical industry is governed by strict regulations and guidelines for the sale and marketing of products. Roche itself has rigorous internal processes in place to ensure that its employees adhere to the laws, regulations and industry codes of conduct that support good marketing practices. Our Code of Conduct sets out standards for adhering to regulatory compliance and for interacting and engaging with healthcare professionals. Our interactions with healthcare professionals are aimed at exchanging scientific information on the best use of Roche's products and services. All of these interactions are based on standards of integrity and fair remuneration for services. We are committed to benchmarking our achievements against best practice; this includes transparent reporting.

We continuously train staff who interact with healthcare professionals to increase awareness and understanding of our

Contributions to healthcare institutions

Total amount: 176 million Swiss francs



Code of Conduct, as well as industry and country-specific marketing codes, guidelines and best practices. In addition, Roche uses a Group-wide questionnaire to help local managers assess compliance with and awareness of responsible sales and marketing practices. All general managers, moreover, must sign a declaration of assurance acknowledging compliance with those practices.

The goal is to enable healthcare professionals to make decisions independently, based on all relevant data available, for delivering the greatest medical benefit to patients.

Education for healthcare professionals

Roche is dedicated to supporting the education of healthcare professionals through the highest quality programmes, with the aim of improving knowledge in disease and product areas where we have particular expertise. Through education, whether it be for doctors, nurses, healthcare officials or care givers, our main objective is to ensure the best care possible for patients.

To this end, we have a broad range of educational activities, from the publication of education and training materials, to the hosting or supporting of medical congresses. We focus on many different aspects of medical care, including new understanding about diseases, different treatment options, safety concerns, product use and healthcare in general. In diagnostics, we establish testing laboratories, train lab technicians, run pathology educational courses and set up quality control programmes.

Through these activities, we seek to exchange scientific information and knowledge to:

- improve understanding of emerging clinical data relating to therapies under investigation
- increase clinical, provider and payer understanding of the best treatment options, including safety and efficacy of various therapies for patients
- help clinicians communicate medical information more effectively to patients and caregivers

Patient support examples

- www.accu-chekconnect.com which offers tools and other resources for those living with diabetes, as well as clinical evidence and case studies for healthcare professionals.
- www.boniva.com offers osteoporosis prevention and care for patients using Boniva and the MyBoniva Program provides resources to help with compliance.
- www.herceptin.com offers guidance to those being treated with Herceptin for HER2-positive breast and gastric cancer and information on financial support, among other resources.
- www.cancerchampionprogram.org offers support and advice for cancer patients.

Education to enhance patient care

We provide courses in different formats, which can be digital, classroom, network-based, within a hospital or lab environment or as part of an existing medical event. For example, this year we organised symposiums and virtual medical conferences connected to the annual meeting of the American Society of Clinical Oncology (ASCO). ASCO is the world's largest clinical oncology event, which attracts thousands of healthcare professionals. In 2012, we also supported a continuing medical education symposium on clinical management of patients with acute coronary syndrome and type 2 diabetes at the European Society of Cardiology Congress.

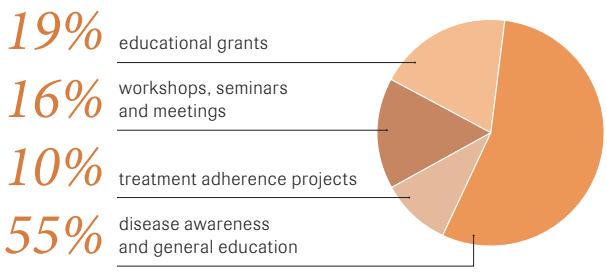
In parallel to these kinds of activities, Roche provides grants for independent medical education. This education is generally provided by an independent organisation, such as a community hospital, academic centre, society or association. In 2012 for example, we made available an unrestricted educational grant to enable an independent scientific presentation for rheumatic disease at the European League Against Rheumatism (EULAR) Congress.

Patients, caregivers and patient groups

Healthcare education and awareness can be as important to a patient's wellbeing as proper medical diagnosis and treatment. With that in mind, we produce newsletters, magazines and other publications aimed at helping people make healthy choices that prevent disease and increase general awareness of diseases. We organise disease awareness campaigns in association with patient groups and local hospitals and conduct screening programmes, like those in Algeria for breast cancer (see p. 76).

Contributions to patient organisations

Total amount: 36 million Swiss francs



Responsible use of medicines is also a priority area for us. We have websites for our products that have mechanisms to remind patients to take their medication, as well as provide access to trained nurses and information on how to live with a disease and medical side effects.

Additionally Roche operates counselling centres and telephone help lines and coordinates services to improve treatment compliance and rehabilitation. We also actively engage with patients and patient groups to gain insight into the challenges facing patients and their families.

In 2012 for example, we hosted a think tank on schizophrenia for patients and caregivers in Europe. The idea was to learn more about the issues and challenges facing caregivers, as well as patients, in order to shape planning and strategy for recommendation to EU policy makers. Roche has a new medicine, bitopertin, in development to address the negative symptoms of schizophrenia.

As transparency is essential to all interactions with patients, Roche publicly declares all patient group relationships and describes its activities at roche.com. We acknowledge both financial and non-financial support, as recommended by the European Federation of Pharmaceutical Industries and Associations (EFPIA).

Patient safety

Our products must not only be effective, they must be safe throughout their shelf life. Roche continuously monitors the safety of a drug from the time it is evaluated in clinical studies to its withdrawal from the market.

Our Drug Safety Committee is responsible for drug safety governance and for proactively ensuring patient safety, and

our employees are required to immediately report any issue relating to the safety or quality of our medicines. The quality of our processes and systems are regularly audited internally and inspected by major regulatory authorities.

All pharmaceuticals have a proactive safety management plan that is supported by a qualified physician who monitors overall safety. We have risk management plans in place, reviewed and approved by regulatory authorities. All adverse events are stored in a global database, reviewed by a qualified physician and reported promptly to appropriate regulatory authorities, as required. If there is a link to a Roche product, we evaluate whether the benefits of the medicine still outweigh the risks. We also maintain strict product recall procedures to ensure that we can withdraw products rapidly should quality or safety problems arise.

Despite these extensive safeguards, at the end of 2011, following an internal quality review, Roche identified some unreported potential missed adverse events from its Patient Assistance Program in the US. We immediately launched an investigation and notified the health authorities in January 2012, and have initiated a comprehensive corrective action plan.

In addition, a routine inspection by the UK regulatory authority in January and February 2012 identified other findings in Roche's safety related processes. Roche has fully cooperated with health authorities in clarifying the observations found in both cases and has implemented corrective and preventative action in agreement with health authorities. Based on Roche's assessments to date, no impact on the safety profiles of any of its products has been found and the European Medicines Agency and other health authorities have confirmed all medicines remain authorised without changes to the treatment advice for patients and healthcare professionals. All corrective and preventative action resulting from the inspections has been completed and newly defined processes are being implemented, which will become routine practice.

Counterfeits

Counterfeit products often look identical to authentic versions, making them difficult to detect, especially for patients. Counterfeit medicines can cause serious illness, or even death, if they contain harmful ingredients, and can deprive patients of proper treatment.

National health authorities, customs, police, intergovernmental agencies and international organisations such as the World Health Organization (WHO), take primary responsibility for the prevention and control of counterfeiting. Roche collaborates with these organisations to help prevent counterfeiting and supports authorities in their efforts to actively pursue and prosecute counterfeiters and their distributors.

Roche, in addition, has implemented internal anti-counterfeiting measures for the design, packaging and labelling of its products. We recommend buying prescription-only medicines exclusively from trusted sources such as doctors or authorised pharmacies.

Further, Roche participates in industry and governmental efforts to safeguard the medicine supply chain and protect patients. We, for example, worked closely with the EU Commission on development of the Falsified Medicines Directive, which aims to stop counterfeit medicines reaching patients by introducing harmonised, Pan-European safety and control measures, including unique product identification numbers, tamper-evident packaging and restrictions on repackaging. We also strongly advocate measures for increased public awareness of counterfeits.

We support anti-counterfeit organisations such as the Pharmaceutical Security Institute, the International Federation of Pharmaceutical Manufacturers and Associations, as well as the European Federation of Pharmaceutical Industry Associations and cooperate with other companies.

Roche acts immediately when potential counterfeits of our products are brought to our attention, including informing health authorities in the respective country where a counterfeit has been found.

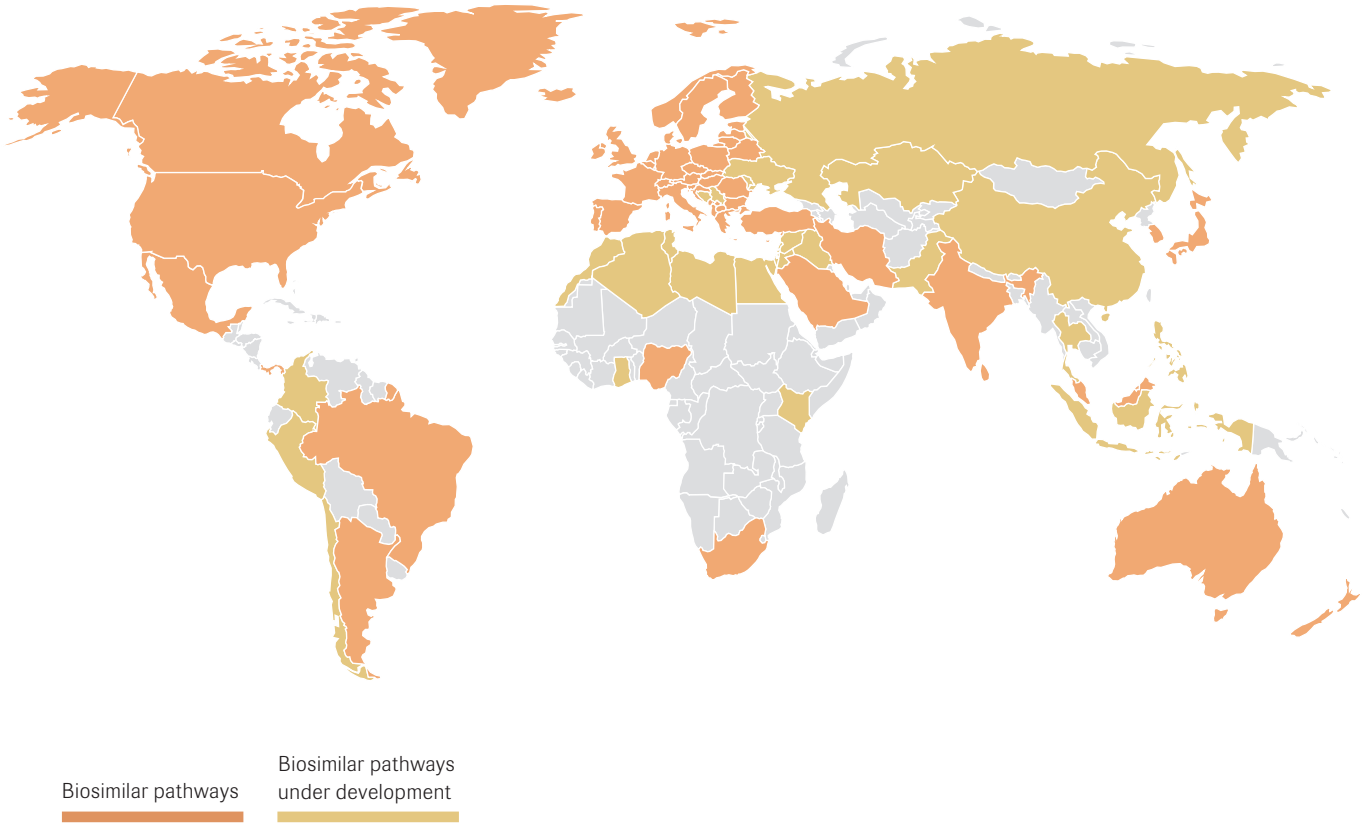
Internally, we draw on a number of departments and skills to fight counterfeiting. Roche has established a Roche Anti-Counterfeiting Commission, which consists of members of all affected departments, and is heavily involved in the coordination of many anti-counterfeiting activities. We also have investigative staff in Shanghai, China, and in high-risk regions such as Latin America and the Middle East.

Biosimilars

Similar biological medicinal products, or biosimilars, are now becoming a reality in some of our markets. Unlike generics of chemically synthesised medicines, the complexity of the biological production process means that these copycat products can never be identical to the original medicines and as such present a new set of safety and competitive challenges for the pharmaceutical industry.

Our view is that biosimilars must meet the same rigorous regulatory and quality standards as the innovator or original biological medical product, in order to ensure patient safety.

Protecting patient safety: biosimilars regulatory pathways



That means a product intended to be a copy of a licensed monoclonal antibody must demonstrate similar quality, non-clinical properties and clinical safety and efficacy in head-to-head studies. Otherwise, the product should be described as an intended copy biologic of a monoclonal antibody, not a biosimilar.

Roche is active in the support of the development of a strong regulatory framework for the approval of biosimilars and is engaged in discussions, primarily through associations such as the Emerging Biopharmaceutical Enterprises, the Biotechnology Industry Association of America and the International Federation of Pharmaceutical Manufacturers and Associations. Clear guidelines have now been implemented by the FDA, the European Medicines Agency and the World Health Organization, as well as in a number of key emerging markets such as India, South Africa and much of Latin America.

Risk and crisis management

Our Risk Management Policy sets out our approach for identifying, managing and reporting internal and external risks. We also use stakeholder feedback to help manage social, environmental and economic risks.

Using consistent methodologies and processes, we routinely perform risk assessments at all levels of our organisation. A Group Risk Report, which covers all material risks, is annually discussed with the Corporate Executive Committee and the Audit Committee of the Board of Directors. We regularly update our risk management processes to raise awareness and understanding of risk throughout the Roche Group.

The Group Risk Management team provides advisory services to sites, affiliates, project and product teams. It monitors risk patterns in specialist areas such as social media, IT security, compliance and sustainability. E-Learning programmes, class-

room training and workshops are in place to improve the understanding of risk and help employees manage them appropriately.

Additionally, we have established incident management teams throughout the Roche Group to ensure that we act quickly in an emergency. These teams regularly rehearse different crisis scenarios, alerts and escalation procedures. We continue to strengthen our business continuity management (BCM) to ensure that all our sites respond effectively to catastrophic events. A Business Continuity Management task force has established a Group BCM policy and guideline, together with templates facilitating a consistent and aligned local implementation. The Group-wide rollout of the new BCM framework will make sure that Roche's operations are resilient and capable of absorbing important disruptions.

Contributing to public policy

Roche actively engages in consultation with governments, industry bodies, regulatory authorities and other stakeholders on issues affecting the pharmaceutical and medical device industry. Our objectives are to help develop laws, regulations and policies for public health and to shape the debate in other areas. Priorities in 2012 included working with the EU on clinical trial regulation with the objective of supporting a harmonised and streamlined framework for clinical trials, as well as the facilitation of multi-national trials. In addition, we have been actively promoting discussion around the issues of parallel trade and reference pricing and the detrimental consequences for low-price EU countries. Our aim is to raise the issue of unequal access to high-value medicines and endorse the principle of differential pricing as a way to enable better access to pharmaceuticals for all citizens in Europe. Other areas of consultation with the EU included new rules on medical devices and IVDs, as well as data privacy and personalised healthcare.

Respecting human rights

Roche fully supports and implements the United Nation's Ruggie Framework 'Protect, Respect, Remedy' designed to prevent and address the risk of adverse impacts on human rights linked to business activities. In 2012 the Corporate Sustainability Committee assessed the risks and opportunities related to Roche's business and how best we can implement the UN framework. The committee subsequently established the Roche Position on Respecting Human Rights, which has been endorsed by the Corporate Executive Committee for use in internal and external communication.

Political Donations

Roche remains independent of any political affiliation.

In Switzerland, Roche spends around 7 million Swiss francs on contributions and donations to various organisations to safeguard its interests. These include payments to Interpharma, economiesuisse, scienceindustries, SwissHoldings and various chambers of commerce, financial assistance to trade unions and donations to political parties at the cantonal and federal level. Donations to political parties are each low-double-digit thousand franc sums and overall less than 4% of total contributions and donations.

Our employees in the US can make personal political contributions through Roche's Good Government Committee and Genentech's Political Action Committee (GenenPAC). Both are voluntary political action committees. In 2012, employees donated 293,144 US dollars to political campaigns through these committees.

More on the Web

- Roche Group Code of Conduct: www.roche.com/code_of_conduct
- Roche Supplier Code of Conduct: www.roche.com/roche_supplier_code_of_conduct.pdf
- Positions, policies and guidelines: www.roche.com/positions_policies_downloads.htm
- Roche Position on respecting Human Rights: www.roche.com/responsibility/employees/human_rights.htm
- Risk management and compliance: www.roche.com/risk_management_and_compliance
- Responsible marketing: www.roche.com/business_integrity_and_responsible_marketing
- List of patient groups supported: www.roche.com/patient-groups
- Roche clinical trials and patient safety: www.roche.com/clinical_trials; www.roche.com/managing_medication_safety
- Counterfeiting: www.roche.com/counterfeiting
- Patents and biosimilars: www.roche.com/patents
- Stakeholder engagement: www.roche.com/stakeholder_engagement

Working with the insurance industry in China

Improving health insurance coverage for cancer patients

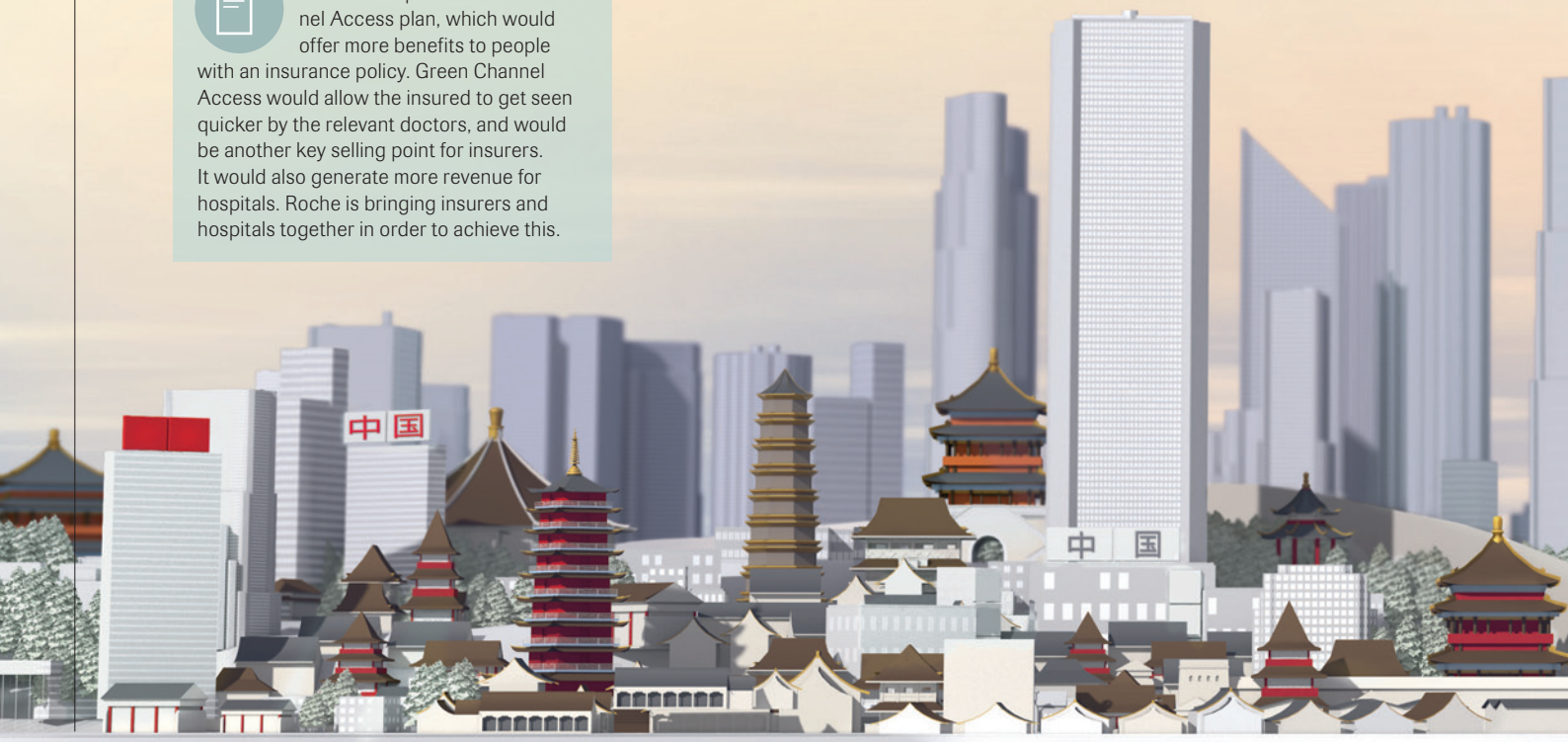
Cancer is a major killer across the world, yet healthcare coverage for cancer treatment in many countries is patchy, and in some cases non-existent. Roche is working with private insurers and clinics in Asia, Latin America and Europe to help them better serve cancer sufferers. Like many other countries, China is facing a sharp increase in cancer rates. Cancer is now the no. 1 killer in urban areas and the second leading cause of death in the country as a whole. An ageing population, pollution, heavy smoking and the adoption of Western lifestyles mean that cancer will remain a major health issue in China for the foreseeable future. Currently cancer patients in China have to pay for most of their cancer treatment themselves, sometimes even having to sell all they have to cover the costs. But in recent years Roche has started to work more closely with insurance companies there to help them establish insurance policies. In 2012, 10 million policies covering cancer treatment costs were sold in China.

Ryan Bi, Taikang Life Insurance Co., Ltd.:

'What our customers need most once they are diagnosed with cancer are the following: First, a way of paying for cancer treatment, which is where our insurance money comes in. Second, a treatment plan, which is very important and an area where we, as an insurance company, lack knowledge. With Roche on board, we will have exactly the help we need.'

Green Channel Access

The next step is the Green Channel Access plan, which would offer more benefits to people with an insurance policy. Green Channel Access would allow the insured to get seen quicker by the relevant doctors, and would be another key selling point for insurers. It would also generate more revenue for hospitals. Roche is bringing insurers and hospitals together in order to achieve this.



Challenges for the insurance industry		Support from Roche
No national overview of cancer treatment costs Difficult to calculate risk and price for policies	**Lack of data**	**Gathering data**	Analysing treatment costs to help insurance companies with their pricing policies
Sales forces do not fully recognise the importance of cancer coverage Insurance companies do not always value and understand the benefit of innovative treatment for the patient	**Depth of understanding**	**Educating**	Providing lectures on cancer Rolling out cancer awareness campaigns
Insurance companies do not always know where their clients can get good cancer treatment	**Knowledge gaps**	**Guiding**	Sharing information on what constitutes good cancer treatment

↗ More on the web:
http://www.roche.com/valueofinnovation

82,0

employees worldwide
(full-time equivalents)

989

OUR PEOPLE

Established seven Leadership Commitments as a standard for behaviour expected from every Roche leader.

Introduced innovative employee benefit programmes to support talent retention.

Hosted a diversity summit for 350 leaders to address the role of leaders in creating an inclusive and diverse workplace.

Key figures

Women in key positions 18.5% or +42% since 2009 on track to reach 2014 goal of 20%

Roche employees worldwide (full-time equivalents/FTE*)

	2012	2011	2010
Europe	36,511	35,509	35,811
North America	21,640	22,429	23,695
Asia	17,976	16,251	14,964
Latin America	4,563	4,506	4,633
Australia	737	755	858
Africa	662	679	692
Total	**82,089**	**80,129**	**80,653**

Employees (FTE) by function

	2012	2011	2010
Marketing and distribution	28,381	27,748	27,536
Research and development	18,279	18,449	19,039
Manufacturing and logistics	16,700	14,786	14,770
Servicing	14,442	15,041	15,160
General and administration	4,287	4,105	4,148
Total	**82,089**	**80,129**	**80,653**

Employees (FTE) by operating unit

	2012	2011	2010
Roche Pharmaceuticals	45,087	44,397	46,335
Chugai	6,965	6,908	6,852
Diagnostics Division	28,517	27,380	26,194
Other	1,520	1,444	1,272
Total	**82,089**	**80,129**	**80,653**

Employees by contract type

	2012	2011	2010
Regular (FTE)	79,923	78,013	78,537
Fixed term (FTE)	2,166	2,116	2,116
Full time (headcount)	79,132	76,911	76,767
Part time (headcount)	5,015	4,824	4,845

* Full-Time Equivalent (FTE) is used to reflect the actual working time of full and part-time employees. For example, two part-time employees working 50% would result in the equivalent of one FTE versus two employees (headcount).

People drive our business. The dedication and determination of our people to translate innovations in science into better lives for patients has enabled Roche to remain at the forefront of the healthcare industry for more than a century. We embrace the diversity of cultures and people across the Roche Group. Yet, no matter who we are, we share three fundamental values: integrity, courage and passion.

Building a great workplace

Roche is committed to constantly strengthening and maintaining an excellent workplace, one that fosters innovation and goes beyond offering attractive compensation and benefits. An excellent workplace is critical to our success and to the wellbeing of our people. We strive to build work environments and support systems that encourage collaboration and give our people what they need to develop personally and professionally.

We recognise that employees who are engaged are key to delivering the highest standards and the greatest levels of innovation. One way to track this engagement is through the use of employee surveys. Our first company-wide survey, the Roche Group Global Employee Opinion Survey (GEOS), was conducted in 2011 and put employee engagement at 62%, in line with industry average. Our strategic goal, however, is to reach an 80% employee engagement level by the end of 2014. A follow-up employee survey will be conducted in early 2013 to better understand where we are on our journey.

In 2012, in response to GEOS and other employee feedback, the Corporate Executive Committee (CEC) established an Employee Engagement Taskforce. This included a Leadership Work Stream which gathered input from more than 1,500 Roche leaders to develop Leadership Commitments. These commitments outline the behaviour expected from Roche leaders and will serve as a common standard for people leadership at all levels across the company. They are now being rolled out globally and will be integrated into key HR processes, from recruitment and development to performance management. Additionally, the taskforce identified ways to improve the visibility and transparency of employee career development (see Learning and development, p. 94).

The taskforce also backed a global programme to recognise individuals in timely and meaningful ways for their contribution, with locally and culturally tailored recognition awards ranging from a simple thank you to more formal rewards. A few programme elements were piloted in 2012 in South San Francisco and in Pharma Development globally, with worldwide implementation of the broader programme anticipated in 2013.

In 2013 we will also introduce a global wellbeing programme that builds on and aligns many existing local initiatives to ensure that all employees around the world have access to wellbeing initiatives. We will continue to identify and implement activities and initiatives both at Group and local level to address employee engagement.

Leadership Commitments

We believe every employee deserves a great leader. We therefore expect the following from every leader, regardless of their area of work or level of responsibility.

Every day I strive to lead by example, consistently demonstrating the Roche values of integrity, courage and passion. This means:

- I take a genuine interest in people.
- I listen carefully, tell the truth, and explain 'the why'.
- I empower and trust people to make decisions.
- I discover and develop the potential in people.
- I strive for excellence and extraordinary results.
- I set priorities and simplify work.
- I congratulate people for a job well done.

An employer of choice

Roche is consistently recognised globally as an employer of choice, reflecting its commitment to foster and maintain a collaborative working environment that embodies the Roche core values of integrity, courage and passion. The table below highlights some of the awards earned by Roche in 2012.

Key awards and recognition in 2012

Switzerland's Top Employers for 2012 — ranked 1st by CRF Institute	Roche Pharma Switzerland
Fortune 100 Best Companies to Work For – 14th consecutive year	Genentech South San Francisco
Science 2012 Top Employers — ranked 3rd	Genentech South San Francisco
Science 2012 Top Employers — ranked 8th	Roche*
Germany's Top Employers for 2012 — certified by CRF Institute	Roche Pharma Germany
Total E-Quality award winner by Total E-Quality Deutschland association	Roche Diagnostics and Roche Pharma (Germany)
2012 China's Top Employers — certified as one of China's top employers by CRF Institute	Roche Diagnostics (Shanghai) Limited
Denmark's Best Workplaces 2012 — 1st Place by Great Place To Work Institute	Roche Denmark
Best Employers Slovakia 2012 — ranked 2nd by Best Employer Study (Aon/Hewitt)	Roche Slovakia
Most Desired Employers 2012 — ranked 5th (Antal International)	Roche Pharma and Roche Diagnostics (Poland)
Universum — Ideal employers 2012 — ranked 2nd as Top employer for natural sciences	Roche Switzerland
Universum — Ideal employers 2012 — ranked 9th as Top employer for natural sciences	Roche Germany
Top 100 'Great Place To Work' for 2012 — ranked 71st by Great Place To Work Institute	Roche Brazil

* Excluding Genentech.

Roche talent pool

In 2012, 46% of our job vacancies were filled internally through our Taleo recruitment platform and Roche-hosted career websites in 91 countries, which drew 3.6 million visits (compared with 2.8 million in 2011). We received 504,811 applications for posted vacancies and registered 238,423 new candidates to our database of job seekers interested in becoming Roche employees.

Attracting and retaining top talent

Attracting and retaining highly skilled, passionate and motivated people, and helping them perform at consistently high levels, is vital to our ability to innovate and deliver superior business performance.

We are committed to recruiting top talent and increasing the diversity of our workforce, recognising that this sometimes comes with challenges in the marketplace. These include stiff competition for the best people in science and medicine, especially in emerging markets such as India, Brazil and China.

We respond to these market conditions by continuously adapting and adopting innovative talent acquisition strategies that reflect best practices. Using in-house recruitment teams and talent scouts, we employ the latest social media tools as well as retain some traditional routes of recruitment, such as business schools and universities, to connect and engage with talent to ensure they know about the opportunities available for working at Roche. The effectiveness of these efforts was recognised externally in 2012 when Roche received the Potential Park award for best online talent communicator in the UK, Asia and in Europe, and was ranked second in the US for its online recruitment techniques.

In emerging markets, our innovative approaches involve adapting and enhancing employee benefit programmes to meet local market needs. For example:

- In China, where turnover rates can be higher than in other countries, we started to phase-in new flexible benefits in 2012 that include cancer insurance for all Pharma employees and their families.
- In Singapore, our programme includes elderly care, nursing home expenses and an option called staycare, where employees can use some of their flexible benefits to fund local family activities such as tickets to the cinema or museum.
- In the UK, our flexible benefits include health insurance, vacation days that can be bought and sold, will preparation and bike purchases for personal fitness.

We also attract some of the best scientific talent by collaborating directly with academia through our postdoctoral programmes in Research and Early Development (gRED and pRED). In 2012, the gRED postdoctoral programme had 115 positions, whilst in pRED, we had 100 postdocs on projects which involved collaborations with outstanding academic groups in Europe, the US, Switzerland, China and Japan.

More generally, as a top employer, we pay close attention to the changing needs and expectations of the workforce. We actively promote flexible working models to our employees and encourage use of the latest technology to allow and embed this into Roche mainstream culture.

Attracting employees: staffing rates

	2012	2011	2010
New hires	10,043	8,463	8,279
Internal staffing rate	46%	43%	45%
External staffing rate	54%	57%	55%

Retaining employees: turnover

	2012	2011	2010
Total	**8.1%**	**10.1%**	**9.5%**
Europe	4.9%	6.8%	5.7%
North America	11.5%	15.1%	12.3%
Asia	9.3%	8.9%	10.0%
Latin America	11.5%	14.8%	19.3%
Australia	14.7%	18.2%	20.2%
Africa	14.2%	18.4%	16.8%

Reasons for leaving

	2012	2011	2010
Employee-initiated	57%	50%	46%
Employer-initiated	36%	41%	44%
Neutral	7%	10%	10%

Learning and career development

Our employees are encouraged to expand their expertise and pursue their professional passions. They take ownership for their development and are supported by their managers with continuous coaching and feedback. The company provides

tools and resources to support career development dialogues between employees and managers. These include online assessments to identify areas of strengths or development needs, overviews of key experiences required for certain roles and local career marketplaces to help employees who are considering a change in role, to learn about other career options.

A significant element of our employee development philosophy focuses on gaining experience and personal growth on the job. We believe employees build greater skills and capabilities to work in a global, innovative company by being exposed to new challenges and cultures. For that reason, we encourage employees to pursue development opportunities that may consist of a broader role, a challenging project or a temporary or international assignment.

We are working to further increase use of stretch assignments and international moves to develop employees. To encourage people, particularly women, to take international assignments, we offer extensive relocation support, helping families to settle and spouses to continue their careers.

Overall, the number of international assignments has risen sharply in recent years, from 340 in 2005 to 677 in 2012, primarily as a result of our expansion into emerging markets and the continuing globalisation of our organisation. The percentage of women among all employees on international assignment, has increased from 21% in 2005 to 29% in 2012.

In addition to on-the-job development for all employees, Roche provides formal development opportunities and mentoring and coaching programmes. Most large Roche affiliates and sites have training curriculum available across a broad range of skills. In emerging markets, we are making significant investments in employee development through organisations such as the Roche China Academy and the CEMAI Training Center that both provide formal technical, sales, and leadership training to employees in those regions.

We maintain a special focus on the development of future leaders as part of Group-wide talent management, including a full suite of development programmes for leaders at every stage of their career. In 2012 we introduced a programme for top executives, Catalyst, which focuses on leading through change and reinforces our Leadership Commitments. Our global programmes are supplemented by divisional or regional programmes, such as Leadership Development Forums where participants test their leadership skills against simulated real-life challenges. These intense three-day programmes include senior leaders, who observe and assess each participant's strengths and point out areas for improvement.

We also introduced a 360-degree feedback tool for leaders in late 2012 and will launch it globally starting in 2013. This tool will help leaders build an understanding of their key strengths and development gaps.

Learning and development

	2012	2011	2010
Total training investment (million CHF)	129	116	150
Training spend per employee (CHF)	1,538	1,417	1,829
Total number of training hours (million)	2.25	2.08	1.87
Average training hours per employee	27	26	23
Number of post graduate students and interns*	1,122	1,050	780

* Excluding Chugai.

Succession management

We maintain specific succession plans for each of our top 428 key positions at corporate and operating group level. We monitor these continuously to ensure we have a broad and deep talent pipeline and where a special skill set or broad experience is required, we have also identified an external pipeline of talent.

The strength of our internal talent pipeline continued to grow in 2012, for example, two key Corporate Executive Committee positions were filled internally. In the broader organisation a further 1,900 positions have been identified for succession planning as we continue to make this our strategic priority.

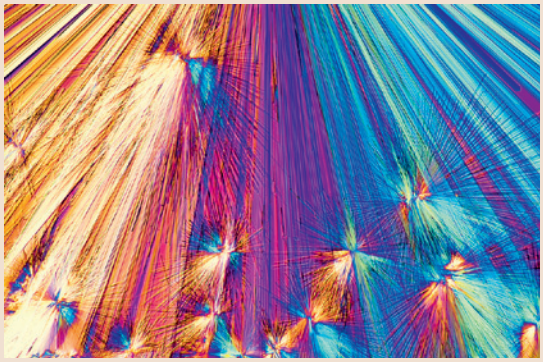
Embracing diversity

We believe that a diverse and inclusive workforce provides the inspiration and innovation on which our business depends. We embrace diversity by fostering an inclusive environment that enables differing views, skills and experiences to be exchanged freely and openly.

Today 46% of our employees are women and worldwide, our employees represent more than 139 different nationalities. At our global headquarters in Basel alone, we have more than 88 different nationalities.

Diversity summit for 350 leaders

One example of Roche's many diversity initiatives included the 2012 Roche Diversity Leadership Summit which in May brought 350 leaders to Basel to challenge perceptions and address the role of leaders in fostering a diverse and inclusive workplace. The one day event included presentations on diversity and entrepreneurship, women in leadership, flexible working, cultural diversity and thinking styles, among other topics. Among attendees, 98% rated the summit positively; 94% would recommend it to their colleagues.



Gender diversity remains among our top priorities. At the end of 2012 the number of women in our top key positions went up slightly to 18.5% compared to the previous year. The total number of high potentials identified in 2012 indicates an increased rigour in our high-potential process with a continued focus on diversity. We expect to continue making progress in 2013 and remain on track to achieve our overall 2014 gender goal of increasing the percentage of women in our top key positions to 20%.

Leadership pipeline

	2012	2011	2010
Number of high-potentials	4,137	4,690	4,681
Percentage of women high-potentials	38%	39%	38%
Percentage of women in global leadership programmes	36%	33%	32%

In support of this goal, we have introduced several initiatives to help women throughout their careers. These range from basic measures such as granting parental leave and permitting flexible work schedules to enhancing mentoring and sponsorship programmes and maintaining ties with leadership networks.

In 2012, for example, Pharmaceuticals North America held a women's leadership summit and launched gWISE, the Genentech Women in Science and Engineering network, while Diagnostics North America started the Women in Leadership Network. We also hosted the Healthcare Businesswomen's Association European Leadership Conference at our Basel headquarters in 2012. The conference featured a panel of executives from numerous healthcare organisations and fostered networking among women leaders from companies across Europe.

Roche has networks at several sites that help foster a diverse and inclusive environment, including:

- Basel. OPEN – Out, Proud & Equal Network – launched in 2012 to encourage a culture of respect and equality for everyone regardless of their sexual orientation.
- Basel. A family and career networking group for employees with family responsibilities, whether as parents or caregivers for relatives, in support of better work-life balance.
- South San Francisco. African Americans in Biotechnology.
- South San Francisco. STAGES – Strengthening Ties Across Generations.

Additionally, in 2012 in Italy, Germany, Israel and Spain, we increased support for employees by introducing on-site childcare and holiday care for children. Roche France established a Charter of Diversity, which includes childcare, flexible work options, equal opportunities and a commitment to providing resources for the disabled. The Charter also included a plan to retain and hire older employees to consult on working conditions, training and skill development and the transition to retirement. At Roche Turkey, women now represent 38% of all employees and 60% of top positions. Roche Turkey won the prestigious Prism Award in 2012 for its efforts in this area from the International Coaching Federation.

In 2012 we raised awareness throughout the Group for diversity with the Do ONE Thing for Diversity & Inclusion, a grassroots campaign to encourage people to lead or take part in at least one activity in support of diversity and inclusion.

Gender diversity

	2012	2011	2010	2009
Women in total workforce	46%	46%	46%	46%
Women in line management	38%	35%	37%	37%
Women in top 120 executive positions	17.5%	15%	15%	9%
Women in key positions	18.5%	18%	16%	13%

Reward and recognition

A competitive compensation and benefits programme is one aspect of Roche's strategy to attract talented people, to motivate and retain current employees, and to encourage strong performance. In 2012 the company paid 11.3 billion Swiss francs in remuneration to its employees.

We reward performance through a transparent and consistent process that encourages fairness, continuous feedback, dialogue and development. Throughout 2012, we also continued to align remuneration policies and processes across all business units. We established common tools and language for employee performance appraisals to help our leaders give meaningful feedback and to encourage productive dialogue. This included the use of a multi-rater tool for employees which resulted in 99,500 feedback requests being sent out between September and November alone. Other activities included practice labs for managers on providing performance feedback to ensure that the Roche Compensation & Performance Management principles are applied effectively and consistently throughout the Group.

Additionally, we added more flexibility to the Group-wide compensation portfolio by empowering managers to use annual bonuses and long-term incentives to acknowledge extraordinary employee contributions.

We also agreed to change our long-term incentive programme for leaders to maintain the competitiveness of our compensation plans and address feedback for a stronger alignment of incentives with share price performance. The revised plan, which takes effect in 2013, underscores our belief in employee ownership by enabling employees to earn equity through a combination of Stock-settled Stock Appreciation Rights and restricted stock units.

Enabling HR excellence

We recognise that strong employee performance can be enabled by aligned and integrated processes and systems. In 2012 we finalised the implementation of our Common Human Resource Information Solution (CHRIS), which will serve as the foundation for complete and comprehensive services to manage employee information and key human resources processes.

CHRIS is available in ten languages to 195 Roche legal entities with 77,409 employees operating in 108 countries. In January 2013 the compensation and performance modules on CHRIS were extended to an additional 152 affiliates in 104 countries with over 27,000 employees.

Fair employment practices

We treat our employees fairly throughout the employment cycle. This includes supporting those affected by organisational changes. For example, the consolidation and streamlining of research activities in pRED resulted in the reduction of around 1,000 positions with the transfer of 80 positions to Switzerland and Germany. To support our impacted employees, we ensured that comprehensive packages of support measures were in place including severance payment programmes, outplacement services, counselling, access to an on-site Career Lab, retraining and redeployment options.

Roche is an equal opportunity employer. As such, we do not tolerate any form of workplace discrimination.

The Roche Employment Policy governs human rights and labour relations at every Roche site, setting out our inclusive workplace philosophy and exacting employment practices. The Chief Compliance Officer monitors implementation of and compliance with this policy in association with HR managers and compliance officers at each Roche site. Roche is committed to enforcing this policy at all sites, to using it as the foundation on which our employment processes are designed and monitored, and expects all employees to act in accordance with the policy.

In 2012 we updated the policy for implementation in January 2013.

We respect our employees' right to freedom of association and collective bargaining. Currently, approximately 8,640 employees are trade union members and more than 32,433 belong to other labour groups. Additionally, the Roche Europe Forum represents the interests of around 36,590 employees in 26 countries.

More on the Web

- Employees: www.roche.com/employees
- Global careers portal: careers.roche.com
- Employment policy: www.roche.com/employment_policy.pdf
- Group policies, positions and guidelines: www.roche.com/positions_policies_downloads.htm
- Commitments to employees: www.roche.com/commitments
- Health and safety: www.roche.com/environment

cobas HPV and CINtec tests

Better screening for cervical cancer

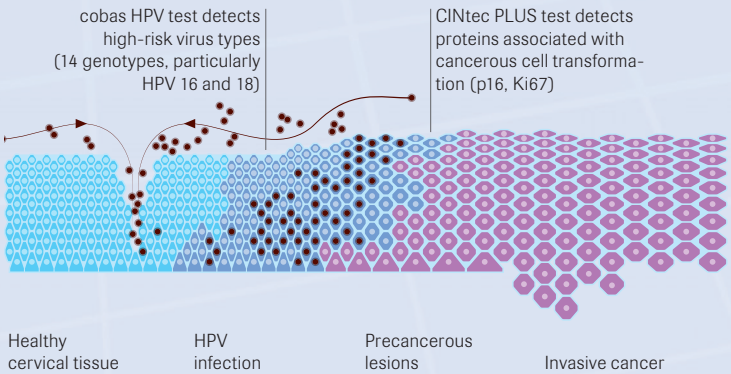
Cervical cancer develops slowly over years. While screening programmes based on the Pap smear[1] have reduced the number of cervical cancer deaths in many countries dramatically, the test is not foolproof, and many women are missed. The Pap test examines cells of the cervix for abnormalities, yet the disease is almost always caused by a persistent infection with high-risk human papillomavirus (HPV) genotypes. Most HPV infections are harmless, therefore it is important to pinpoint those infections that are most likely to cause cervical cancer. Roche's cobas HPV test detects high-risk HPV to identify those women at greatest risk of developing cervical disease. Our CINtec products help better identify precancerous lesions, enabling doctors to remove unhealthy tissue before cancer can fully develop and to protect patients from unnecessary treatment. This gives women peace of mind that they are safe or that they receive the appropriate care to prevent the cancer.

1920s

No screening – cervical cancer detected late through symptoms and usually meaning death sentence

Women at risk for cervical cancer

From virus to cancer



A high-risk HPV type is the root cause in almost all cases of cervical cancer. Infection with HPV is fairly common, and in most cases the body is able to clear the virus on its own. For some women, however, the infection is not resolved and persists, which can lead to cervical cancer. Of the more than 40 relevant types of HPV, 14 types are considered high risk. But just two types – HPV 16 and 18 – are responsible for approximately 70% of cervical cancers.
The cobas HPV test provides individual test results for HPV 16 and 18, along with a pooled result for the other 12 high-risk genotypes, and thus enables instant identification of those women who are at the highest risk and need immediate intervention.

Incidence and screening

Each year there are about 470,000 new cases of cervical cancer, and more than 250,000 succumb to the disease. Incidence is highest in developing countries which lack screening programmes. Even in developed regions, thousands of women still die from this cancer.

Cervical cancer prevention programmes are predominantly based on the Pap test, with vaccination and modern HPV screening slowly being adopted. Forerunners are Italy, which introduced HPV primary screening in several regions in 2011, and Sweden, which introduced a pilot programme in Stockholm in early 2012.

1 Test invented by and named after US physician George Papanicolaou.

Christine Baze, cervical cancer survivor and patient advocate:

'When I was 31 years old I was diagnosed with invasive cervical cancer. Despite the fact that I had been going for Pap smears every year. Ten days later I was having a radical hysterectomy and then I had five weeks of daily pelvic radiation, four rounds of chemotherapy and three rounds of internal radiation. When I was diagnosed we only had the Pap to work with and now screening has got better and more accurate with the addition of the HPV test. It's pretty amazing to think about how the doctors and the patients get more accurate information. The thing I want women to know is that they can take care of their bodies. Have the most accurate screening possible!'

1940s

Screening based on Pap smears – annual test misses around 50% of women with precancers

2012

Screening based on molecular testing – two-stage approach identifies over 90% of women with precancers

- stage 1: check for the cancer's root cause – HPV high-risk infections (cobas HPV test)
- stage 2: check for precancerous lesions (CINtec PLUS test)

↗ **More on the web:**
http://www.roche.com/valueofinnovation

20,0

employees participated in the 2012 Roche Children's Walk

COMMUNITY INVOLVEMENT

Inaugurated a second Transnet-Phelophepa Healthcare Train to bring primary healthcare to remote regions of South Africa.

Supported humanitarian and social projects in the aftermath of Hurricane Sandy.

Partnered with organisations in the Philippines to supply affordable solar powered lights for people living in the shanty town of Tondo.

Key figures

Breakdown of giving by area, 2012

Humanitarian and social projects	92%	**Arts and culture**	4%
Science and education	3%	**Community and environment**	1%

Since Roche was formed more than a hundred years ago, the company has directed human and financial resources to community projects and philanthropic initiatives that make a lasting impact.

We direct our giving to four areas of priority: humanitarian and social projects, science and education, arts and culture, and community and environment. No matter the size of the project or cost, we focus on outcomes. The philanthropic activities we support and engage in must generate tangible long-term benefits to people and their communities, as measured by:

- Innovation, by applying creative and effective solutions to society's challenges
- Sustainability, by delivering enduring impact in a dynamic, resource-constrained world
- Collaboration, by drawing on the strengths and skills from Roche and the partnering organisation to individually tailor activities to the needs of each project

Our aim is to participate in projects as a collaborator, contributing our expertise and resources from the earliest possible stage, while sharing in the long-term risks, commitments and investments necessary to achieve lasting benefits.

Responsibility for most philanthropic activities is delegated to our more than 100 local affiliates operating in over 150 countries. By selecting and managing our engagement locally, we can better tailor activities to local priorities and respond quickly when an urgent need arises.

Our activities are guided by Roche's global Donations and Non-commercial Sponsorship Policy. Philanthropic donations may only be made to registered or accredited independent non-governmental organisations, multilateral organisations or not-for-profit charities.

Lighting up in the Philippines

What do you get with sunshine and an old plastic bottle filled with water and chlorine? A 55-watt solar bulb that refracts sunlight. The so-called solar bottle bulb is powerful enough to light up a small, dark home. Plus, it's environmentally friendly, inexpensive and easy to make.

Roche Philippines, with its employees, entered into a partnership with MyShelter Foundation and the Philippine Christian Foundation to reduce dependence on electricity and open-flame lighting for people living in Tondo, a shanty town.

The Liter of Light Project uses plastic soda bottles encased in corrugated tin, filled with water and bleach, and mounted in the roof to allow light to pass through into the home. The solar bulbs, which take about an hour to install and can last up to five years, not only improve living environments for families but also allow children to read.

Employee involvement

At Roche, we encourage our employees to involve themselves in the communities where they work and live, both as means to give back and to engage in personally enriching experiences. From site to site we often support employee community service by offering flexible work schedules, brokering volunteer assignments and coordinating group projects. We, however, refrain from exerting any influence on the type or amount of volunteer work that our employees engage in.

As part of our activities to improve health in the world's poorest countries, we offer a secondment programme to employees, which enables them to contribute their skills to assignments with humanitarian organisations in least developed countries as well as in low and lower middle income economies. The programme allows employees to participate for three to twelve months in a project dedicated to improving health. In 2012 Roche secondees contributed to projects in India, South Africa and Haiti.

Since 2003 our employees have united in a common cause: The Roche Children's Walk. More than 110,000 walkers from Roche sites around the world have participated in this one-day event that raises money for schools and orphans in Malawi. In 2012 over 20,000 employees from 113 Roche sites in 52 countries participated.

Humanitarian and social projects

The largest part of our philanthropic giving is directed toward humanitarian and social projects, as we believe that improving human services and support systems is the most effective way to help build stronger, healthier communities.

Our preference is to provide support yielding outcomes which can be maintained on a long-term basis at the local level. For example, in countries that do not have adequate healthcare infrastructure, such as trained healthcare workers, hospitals or general health awareness, we find that investments in education and prevention are usually a more sustainable solution than medicine or diagnostic donations.

In this spirit, Roche supports projects such as those run by the United Nations Children's Fund (UNICEF) in Malawi. Our funding has helped build classrooms and pay for school materials like desks, books and other literacy resources. In addition, we have joined UNICEF in supporting primary school teacher training and the building of a new teacher training college in southern Malawi. Additionally, Roche provides financial support to the European Coalition of Positive People for its work in Malawi to help children orphaned to HIV/AIDS day centres, skills training, nutrition and educational assistance.

In the aftermath of Hurricane Sandy, which struck the Northeast US in October 2012, the Genentech Foundation and the neighbouring Roche facilities in New Jersey quickly provided major donations to the American Red Cross for shelter, recovery assistance, emergency transportation and meals. The Foundation is a US-based, private charitable foundation established in 2002 by Genentech. It provides financial support to qualified non-profit US charitable organisations in community support, health science education, patient education and advocacy.

A clinic on rails – Phelophepa

Described by locals as a 'miracle train', the Transnet-Phelophepa Healthcare Train is a clinic on rails that brings primary healthcare to remote regions of South Africa where there is only one doctor for every 5,000 residents.

Phelophepa means good, clean health. Since its launch in 1994, Roche has been the main external sponsor of Transnet-Phelophepa, funding its primary healthcare, community outreach and other ancillary services.

From modest beginnings as a three-car train, the service was expanded in 2012 to two 18-coach trains. With both trains running 36 weeks a year, Phelophepa can deliver medical services and healthcare education to reach over 550,000 people annually, including more than 90,000 patients in need of care. Train staff also visit schools, providing vital health checks, medicines and education to children.

Illuminated DNA

DNA, or deoxyribonucleic acid, is an essential part of every organism. It's not normally found in a chandelier. But the idea of creating a chandelier modelled on crystallised DNA intrigued Dutch designer Lucas Maassen. So from DNA fragments crystallised by Roche's Molecular Biology Laboratory, a magnified glass version of this crystal, which normally is only visible under the microscope, was produced by a crystal manufacturer.

One thousand glass orbs later, 'Valerie, My Crystal Sister', representing the sister that Maassen never had, was assembled by his parents on 12 June 2012 at the Vitra Design Museum in Weil am Rhein, Germany, during the Art Basel show. The work, a true collaboration of Lucas Maassen and Roche scientists, was part of the Confrontations: Contemporary Dutch Design exhibition at the Museum.

Science and education

As a business founded on excellence and innovation in science, we help to develop future scientists and public understanding of life sciences by supporting programmes that enhance science education, draw talent to science careers and engage outstanding young scientists and their teachers.

In Switzerland, Roche is an active supporter of Swiss Youth in Science, a foundation that raises awareness and appreciation of science among children and young people. We support the foundation's national competition, study weeks and the Swiss Talent Forum, a think tank for young adults, among other activities.

Simply Science is a website designed to generate interest among young people in life science. Hosted by a Swiss foundation of the same name, the website is piloting an innovative national secondary school class competition, Science on the Move. Roche is the sole corporate sponsor of the competition, which aims to promote science study and science careers by broadening the understanding of life science research.

Roche Diagnostics in Germany is helping teachers make classroom experiments more attractive and more vivid with Blue Genes, a kit containing two DNA experiments and precise descriptions for lesson planning. Provided for a nominal fee, the experimental kit complements theoretical instruction, giving teachers and students a hands-on opportunity to learn the basic techniques of molecular biology.

In 2012, Roche Ireland supported a primary school faced with terminating its computer programme, as it did not have the funds to upgrade its outdated computer lab.

The school's computer room officially re-opened in May with donated computers from Roche Ireland, enabling the school to again provide students with new skills, including literacy, numeracy and word processing.

Arts and culture

Roche actively cultivates and supports ground-breaking contemporary art and cultural projects. We favour creative activities that explore the parallels between innovation in the arts and in science.

Roche Commissions offers contemporary music artists the challenge and opportunity to forge new frontiers in their field. Started in 2003, every second year a recognised contemporary composer is selected on the recommendation of the artistic director of the Lucerne Festival, our partner in Roche Commissions. The commissioned work is then premiered at the Lucerne Festival in the summer. In 2012, composer and conductor Matthias Pintscher was granted the sixth Roche Commissions award for his composition, 'Chute d'Étoiles.'

We also support creative expression through monthly Roche 'n' Jazz events. Together with the Roche-founded Museum Tinguely and the Bird's Eye Jazz Club, we bring inventive jazz to the community of Basel. Through Roche Continents, 100 students of science, music and fine arts from across Europe are selected to spend a week in Salzburg, Austria during the Salzburg Festival to attend workshops that explore the common ground of creativity in art and science.

Gene sequencing at the zoo

Kumari, an Asian elephant calf at the Smithsonian National Zoo, lived only 16 months before dying of persistent internal bleeding. While searching for the cause of the bleeding, pathologists at the zoo discovered an aggressive herpes virus that is specific to elephants, the elephant endotheliotropic herpes virus (EEHV).

Since then, the zoo has launched a study of EEHV and other animal diseases, using a powerful gene sequencing device donated by Roche, the GS Junior System. Installed at the Smithsonian Conservation Biology Institute, the system will support research into the causes of high mortality rates among elephants living in captivity and the growing number of EEHV cases in the wild. Scientists now believe the disease may be connected to the loss of the animals' natural habitat.

Community and environment

As an organisation and as individuals, we are committed to using our resources to support local communities and protect natural resources. In the US, the Genentech Gives Back Week is an opportunity for employees at this Roche affiliate to support their communities. In 2012 employees helped with donations in the form of cash, goods and employee time to 115 non-profit organisations, participated in 150 volunteer projects and donated 590,000 air miles and 75 barrels of educational supplies, clothing and food.

Latvia has one of the highest infant mortality rates and one of the lowest birth rates in Europe. Roche Latvia, in collaboration with neonatology and obstetrics experts, initiated Save 100 Newborns, aiming to reduce infant mortality rates by half. Based on situational and data assessments, a series of recommendations were made, ranging from improving medical information quality to improving the usage of ultrasound examinations. The Ministry of Health adapted the new policies and implemented the proposed recommendations.

More information can be found on www.roche.com.

Examples of Community Involvement indicators and measures of success in 2012

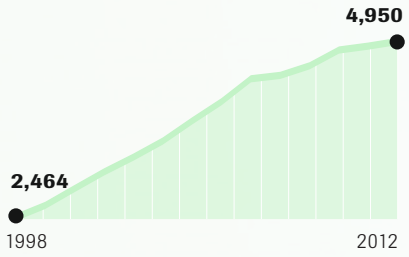
	Humanitarian and social projects	Science and education	Arts and culture	Community and environment
Roche employee engagement	• Logistics consultations • Volunteers with disabled • Employee walkers raising funds for vulnerable children • Secondee days	• Scientists as workshop trainers • Science/technology educational materials • Volunteer tutors or mentors	• Roche experts workshop leaders • Hours of collaboration	• Workforce volunteers in local programmes • Team building events with service agencies
Community beneficiaries	• Individuals screened • Student teachers trained • Children enrolled in secondary school • Disabled children assisted	• Teachers in professional development workshops • Children aided by tutoring • Secondary students conducting research	• Museum visitors • Arts and science students joint projects • Children in creativity workshops • Concert audiences	• Individuals/families assisted with community services • Family counselling sessions • Homes renovated
Infrastructure and system changes	• Social service centres renovated • Prototype schools constructed • Mobile health clinic operations and construction	• Placement of students • Teaching methods adopted • Visits/hits to online resources • Training course graduates	• Creativity workshops established • Performance of commissioned music • Ongoing museum operations	• Cultural groups sustained • Recreation programmes established • Public sites cleaned up

From mining to biotech – Roche Penzberg

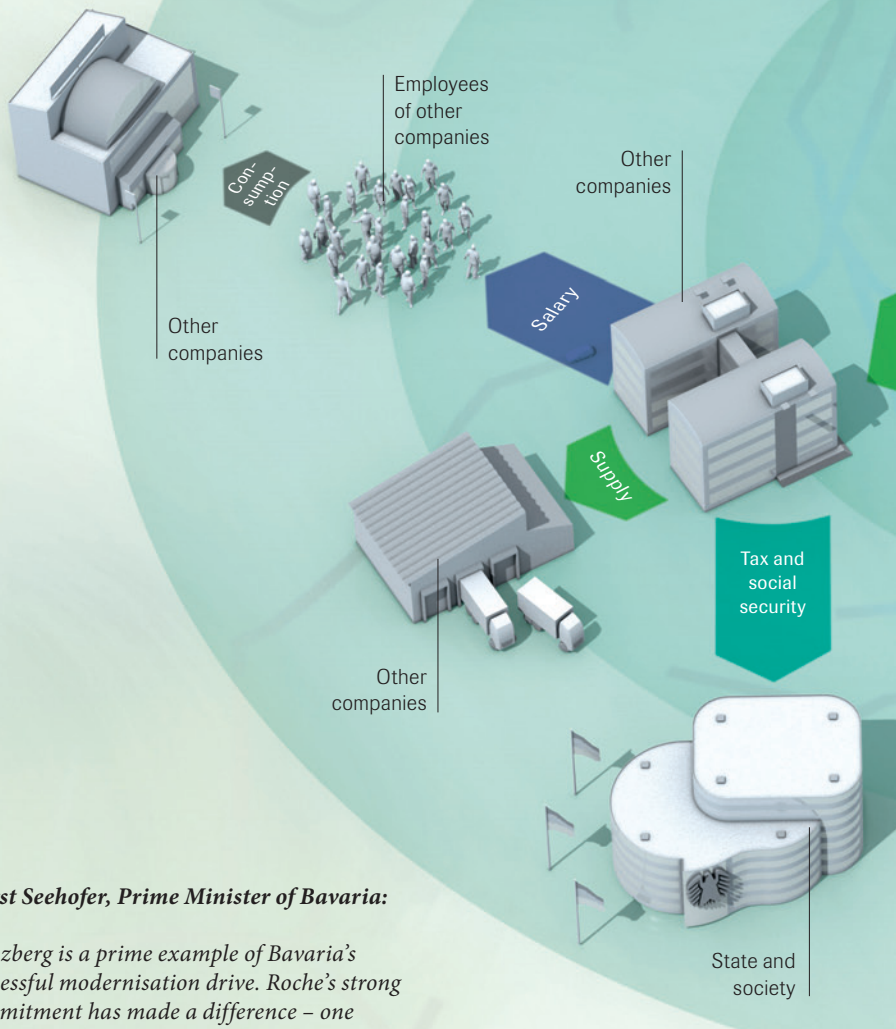
Innovation creating value for the local economy

The Roche Penzberg biotech hub is located on the site of a former coal mine on the outskirts of the Bavarian town of Penzberg (Germany). Roche bought the site in 1998 and since then has invested over 1.8 billion euros in this state-of-the-art facility, creating 2,500 additional jobs. Of its 5,000 employees, more than 30 % holds a university degree.
The impact on the local economy of an innovation-driven company, like Roche in Penzberg, is enormous, creating far above-average wealth for the community. People employed by Roche Penzberg are extremely well qualified, with high salary levels, bringing increased tax receipts and more consumer spending. In order to make its products, Roche needs not only high-qualified labour, but also supplies of goods and services. As a result, innovation triggers a substantial multiplier effect not just for the local economy, but for Germany as a whole.

Increase of employment since 1998



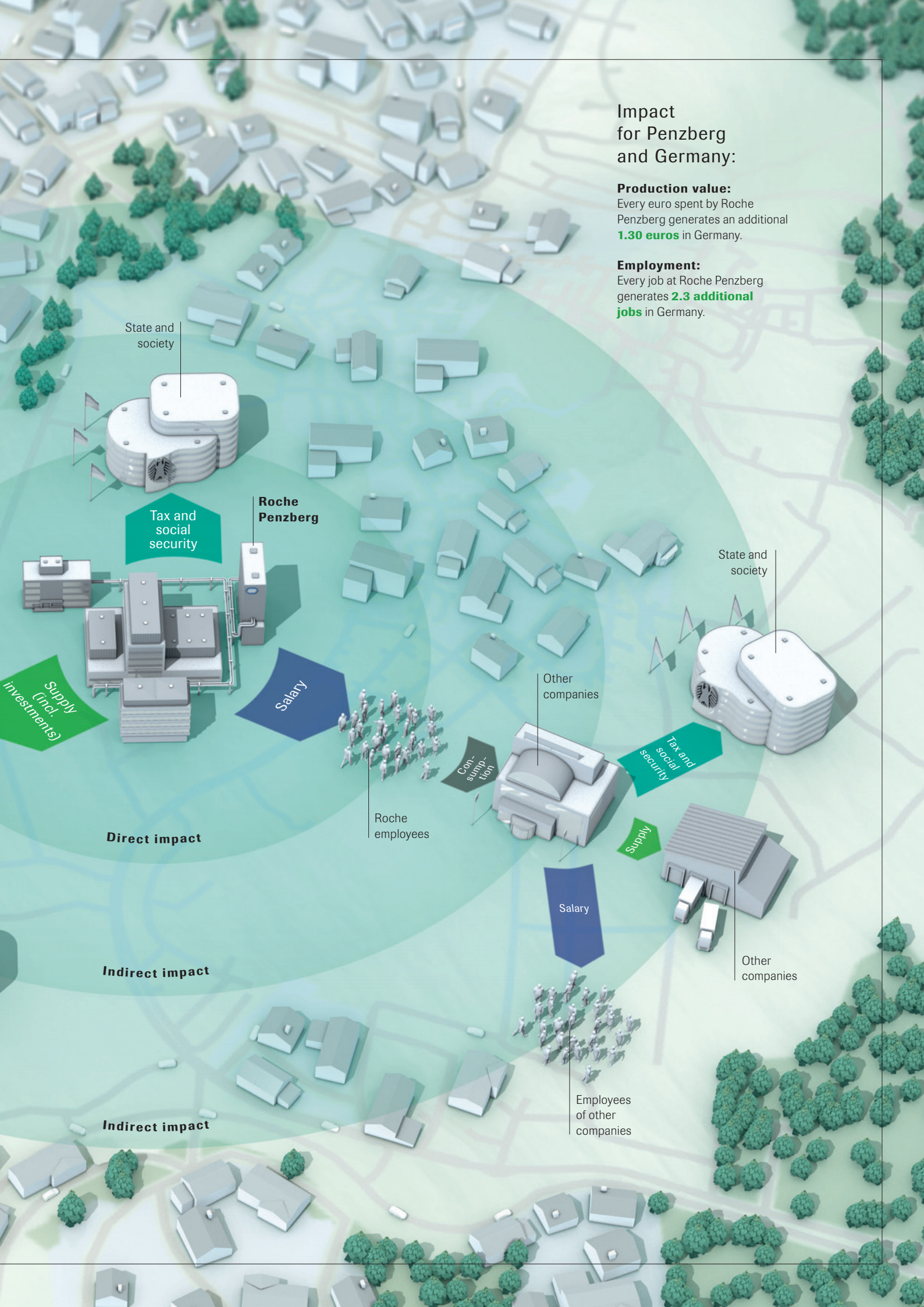
- 1.8 billion euros invested since 1998
- Biggest payer of business tax in the Penzberg region
- Distinct external network of academics and biotech companies
- Complete biotech value chain: from science to patients



Horst Seehofer, Prime Minister of Bavaria:

'Penzberg is a prime example of Bavaria's successful modernisation drive. Roche's strong commitment has made a difference – one that has also benefited our country. What was once a small mining town in rural Upper Bavaria is now an internationally networked location for research and innovation, generating a sizeable number of highly qualified jobs.'

↗ **More on the web:**
http://www.roche.com/valueofinnovation


Impact
for Penzberg
and Germany:
Production value:
Every euro spent by Roche Penzberg generates an additional 1.30 euros in Germany.
Employment:
Every job at Roche Penzberg generates 2.3 additional jobs in Germany.
State and society
Tax and social security
Roche Penzberg
Supply (incl. investments)
Salary
Roche employees
Direct impact
Other companies
Con-sump-tion
Tax and social security
State and society
Supply
Salary
Other companies
Indirect impact
Employees of other companies
Indirect impact

2.6

percent reduction in greenhouse gas emissions

SAFETY, SECURITY, HEALTH AND ENVIRONMENT

Increased energy efficiency per employee by 3.7%.

Reduced ecological impact per employee by 6.2%.

Decreased water consumption by 8.6%.

Key figures

Roche accident rate (RAR)	0.072	+7.3% on track to reach 2015 goal
Energy efficiency	158 GJ/employee	–3.7% on track to reach 2014 goal
CO_2 efficiency	11.80 t/employee	–6.9% on track to reach 2014 goal
Total environmental impact	6.45 million impact points/employee	–6.2% on track to reach 2015 goal

At Roche, we refer to safety, security, health and environmental protection as SHE, and approach it with the same sense of responsibility, and just as methodically, as we do issues concerning quality, productivity and cost-efficiency.

We strive for continuous improvement in SHE wherever possible and economically viable. We seek sustainable long-term improvement throughout our organisation by changing behaviour, adapting equipment to the most recent standards and developing innovative processes.

Relevance and materiality

To maximise the value of SHE reporting, we strive to provide information that is balanced and relevant to stakeholders. We have identified the following topics that we believe are material to our business and, thus, sufficiently important to be reported:

- people, with respect to health, integrity, wellbeing
- environment and the conservation of resources
- material assets and functional efficiency
- business continuity and cost of SHE
- compliance with external and internal regulations

With regards to SHE, we have looked at each of the above material issues. We have considered potential future developments, analysed the need and feasibility to act, defined performance indicators and set goals or targets.

Materiality is influenced by external and internal factors. For instance, external regulations and laws may affect strategy, as will reporting conventions within the industry and stakeholder expectations. Internally, an organisation's policies, strategies and goals determine the materiality of an issue. We have considered all of these factors when identifying the SHE areas for inclusion in our reporting. Based on this analysis we have identified the following priority SHE topics:

- occupational accidents and occupational illnesses
- energy consumption and use of sustainable energy
- total eco-balance (ecological impact of our operations) and total toxicity of our waste water
- the closing of gaps identified during our internal SHE audits
- compliance with all SHE laws and regulations
- improvement of the SHE performance of our suppliers and service providers
- reduction of the total SHE risk load
- SHE education of our employees

Improving and monitoring performance

Employee engagement and training

Prevention is the key to effective SHE management. With around 600 employees in safety, health and environmental protection, SHE teams at each Roche site identify risks, develop mitigation plans and communicate policy and guidelines to employees and other stakeholders.

We believe that education, awareness and training are the best ways to foster employee engagement in and responsibility for SHE. With this in mind, we conduct regular training sessions, regional conferences and workshops and provide online tools in local languages to most employees. In 2012 our employees participated in more than 205,000 hours of SHE training.

We regularly review the effectiveness of our SHE management system and encourage employees to identify areas for improvement. Using a database of SHE best practices, our employees frequently share knowledge and exchange new ideas for pro-

cedures. During 2012, 43 proposals from the database were adopted by other areas within our organisation.

The annual Roche Responsible Care Award recognises the best contributors to and applications of good SHE practices by employees. We received 115 entries for the 2012 award and will announce the winners in the first quarter of 2013.

Audits and assessments

We assess SHE performance by comparing our results against laws and regulations, internal standards and those set by organisations such as the International Chamber of Commerce's Business Charter for Sustainable Development, International Organisation for Standardisation and the chemical industry's Responsible Care programme.

We conduct internal audits every three years at the chemical, pharmaceutical and diagnostics manufacturing sites that are critical to our operations, stipulating necessary SHE improvements after each audit. The audit frequency for other facilities is determined by risk potential, strategic importance, past performance and other site-specific circumstances. Plant management and local SHE officers conduct more frequent spot checks and inspections to assess compliance with SHE standards.

We expect contract manufacturers, suppliers and service providers to meet the same SHE standards as we do. To ensure compliance with these standards, we, or third-party auditors retained by us, periodically inspect the operations of our suppliers and issue recommendations for improvement. In the event of unsatisfactory SHE performance, we may terminate a contract or refuse to award a new contract to a supplier.

SHE audits

	2012	2011	2010	2009
Internal audits				
Follow-up	17	23	24	27
First time	9	3	4	2
External audits*				
Follow-up	10	5	5	4
First time	48	42	31	34

* Of direct materials suppliers.

Of the 17 internal follow-up audits in 2012, most sites improved their performance. Recommended SHE improvements following these audits included increasing the involvement of line management and improving risk analysis.

ECOmpetition

Started in 1995, the Roche ECOmpetition gives employees an opportunity to contribute ideas and suggestions for improving our sustainability culture and performance. It also raises awareness of environmental protection and encourages sustainability by identifying cost savings from environmental protection activities.

ECOmpetition submissions have resulted in significant improvement in a variety of areas, including energy conservation, waste reduction, decreased consumption of water and raw materials, and reduced air pollution. Additionally, a number of submissions have addressed the social aspect of sustainability. Suggestions for improving certain manufacturing processes have resulted in major cost savings, and other ideas, including measures to reduce energy consumption of air-conditioning systems, have proved useful at multiple sites.

For the sixth edition of ECOmpetition in 2012, 18 winners were selected from 264 entries. Reducing energy consumption got the most interest as well as improving logistics both with respect to packaging and transportation concepts. A most interesting idea references the use of a (heat-driven) Sterling engine for cooling purposes.

Seeing the light, turning it off

Genentech in South San Francisco, has a goal of reducing energy use in the 50-building campus by 15% within five years. To help achieve it, members of Green Genes, a nearly 1,500-member employee club that supports green practices, elected to find ways to eliminate or reduce unnecessary lighting.

Sparked by an idea from a member of the Green Genes Energy Team, the club formed the Army of Darkness in 2010. Volunteers audited buildings where they worked, documenting lighting controls, conditions and operating hours. Even though many campus buildings were equipped with occupancy sensors that automatically turn off lights, the audit found ineffective lighting controls, areas with no light switches and lights that were always on. Many of these issues were resolved quickly and easily, others were scheduled for lighting system upgrades. The Army of Darkness' efforts have contributed to lighting projects saving an estimated three million kilowatt hours per year.

Further details can be found in the chapter *Manufacturing and Procurement,* page 60.

Minimising our environmental footprint

As part of our commitment to sustainable development, we proactively seek to employ new, more sustainable technologies and processes which minimise our impact on the environment.

We have established a Group-wide goal for eco-balance. However, management at each Roche site may establish strategies and objectives for reducing environmental impacts that are best suited to local circumstances.

Our total environmental impact per employee in 2012 was 6.45 million impact points, a 6.2% improvement on 2011. We have targeted to improve our eco-balance by 15% from 2010 levels by 2020.

Eco-efficiency

Eco-efficiency aims at minimising ecological damage while maximising efficiency of the firm's production processes. This can be achieved by using less energy, materials and water, decreasing the elimination of hazardous emissions or by-products and increasing recycling. We quantify eco-efficiency by the eco-efficiency rate (EER), a ratio of sales to expenditures on environmental protection and environmental impact points in accordance with the Swiss Federal Office for the Environment (FOEN). The more efficiently business activity is increased (sales), while expenditure on environmental protection is limited and environmental harm reduced, the higher the EER value and, thus, eco-efficiency.

We seek to improve our EER by reducing material and energy consumption and waste and by using renewable resources. In 2012 these and other efforts resulted in our EER improving to 0.565, or 4.8% from 2011.

Eco-efficiency rate (EER)

	2012	2011	2010	2009
Sales (million CHF)	45,499	42,531	47,473	49,051
Environmental expenditure (million CHF)	147.8	140	194	186
Environmental impact (10^6 environmental impact points)	545,022	563,742	591,592	572,983
EER (x 1000)	0.565	0.539	0.414	0.460

In addition to expending 147.8 million Swiss francs for environmental purposes, our expenses for safety and security amounted to 265.3 million Swiss francs. Hence, the total expenses for SHE measures in 2012 were approximately 413 million Swiss francs, compared with 429 million Swiss Francs in 2011, a decrease of approximately 3.6%.

Increasing energy efficiency

Our goal is to reduce total energy consumption – fossil fuels and electricity – in gigajoules (GJ) per employee by 10% by 2014 from 2009 levels, and by 20% by 2020 from 2010 levels. Our long-term goal is to reduce energy consumption per employee by approximately 50% from the 2005 baseline levels.

We also plan to increase the proportion of sustainable energy we use to 20% of total energy consumed by 2020. Our strategy for achieving this objective is to first improve energy efficiency aggressively before substituting fossil fuels with sustainable energy.

Energy conservation is a priority throughout the Group, first, because it is the main source of greenhouse gas emissions, such as CO_2, and second, because reducing energy consumption lowers operating costs. Our systematic approach to energy management includes:

- constructing energy-efficient buildings
- retrofitting heating, cooling and air conditioning installations

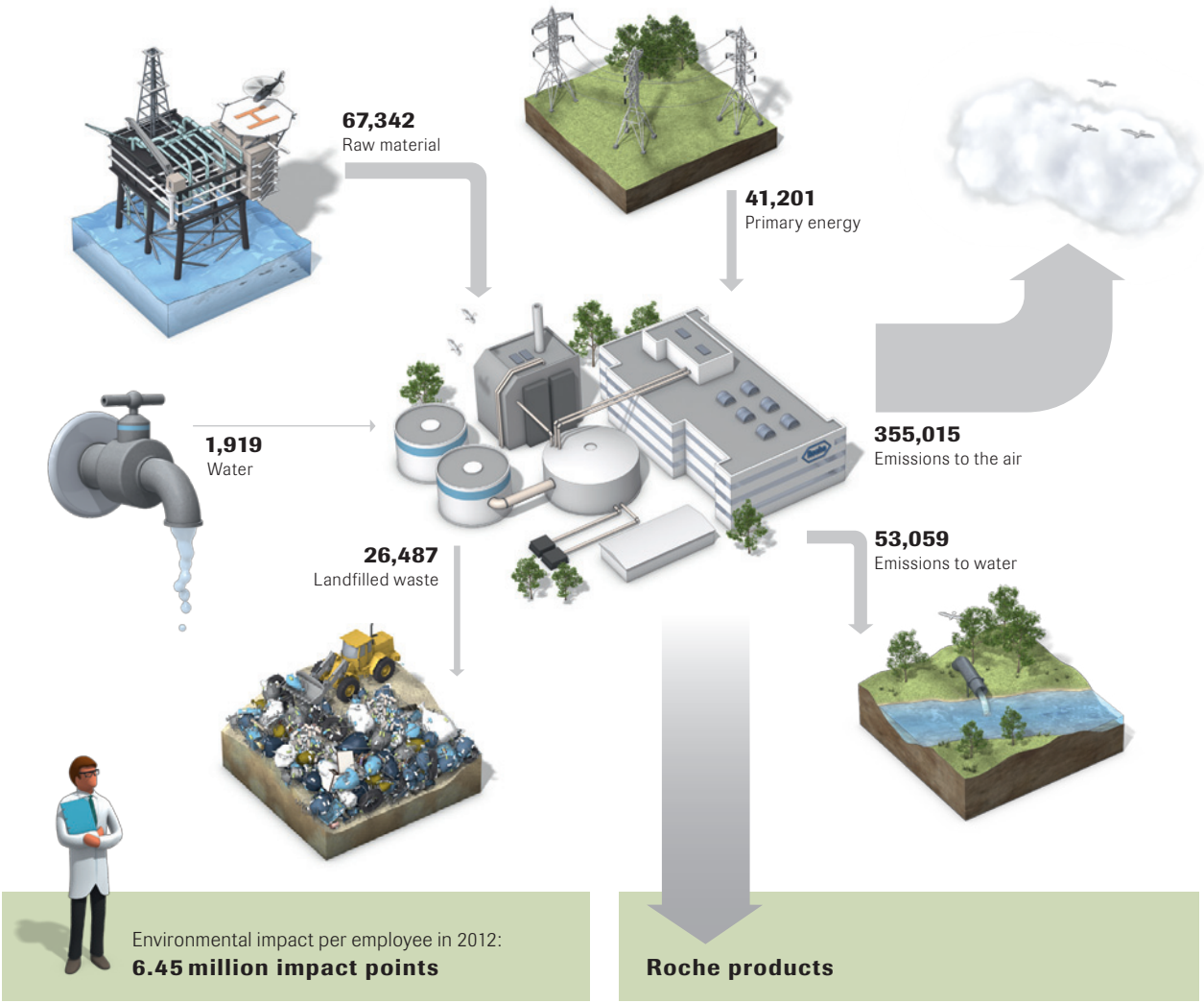
Eco-balance and impact points

The Roche eco-balance refers to the consumption of energy and resources and the pollution caused by our business activities. It thus describes the total environmental impacts of our operations.

By allocating environmental impact points (weighting factors) to ecologically relevant parameters – the consumption of resources, such as raw materials, water and energy, and the waste and emissions to air, water and soil – we obtain a view of the demand we place on the Earth's ecosystems. These points are added and then related to the total number of employees, which enables us to monitor our environmental impact per employee (million impact points).

Eco-balance

all numbers are in impact points (see box)



- adjusting the range of acceptable temperatures in offices and other workplaces
- purchasing energy-efficient equipment, including hybrid and diesel-efficient cars
- changing work processes
- reviewing employees' travel needs

In 2012 we continued to focus on the responsible use of resources and continuous reductions in energy consumption. Our activities resulted in improved energy usage in several areas:

- 2.8% reduction of energy use in buildings and stationary equipment (gas, fuel oil, waste, electricity)
- 4.8% decrease in car fuel consumption (in the Central and Eastern European, Middle Eastern, African and Indian countries the fuel reductions resulted in savings of approx. 1 million Swiss francs)
- 3.9% increase in the use of sustainable energy, bringing total sustainable energy to 9% of consumption.

These improvements resulted in an overall decline in energy consumption of 0.7% in 2012. Together with a slight increase in the number of employees, energy consumption was 158 GJ per employee, which surpassed our 2012 target of 163 GJ.

A project team at Roche Indianapolis improved organisational efficiency and reduced international air travel of leaders of three business units. Three face-to-face meetings were cancelled, 113 person days of productivity were gained, including avoiding 73 travel days, and 30 international and 11 domestic

flights avoided, resulting in a saving of approximately 763 gigajoules of energy or approximately 54 tonnes of CO_2 emissions and some 120,000 Swiss francs. However, overall in the area of business travel, our reduction efforts were less successful, as energy consumption from air travel increased by 10.6%.

Lowering greenhouse gas emissions

Greenhouse gas (GHG) emissions at Roche originate from the generation and use of energy. Our goal for improving energy efficiency and reducing energy consumption, therefore, also applies to GHG emissions: a 10% reduction, measured in tonnes per employee by 2014 from 2009 levels and a 20% reduction by 2020 from 2010 levels. We expect to achieve further reductions by substituting fossil fuels with energy from sustainable sources.

We actively seek to decrease GHG emissions by establishing internal energy standards that ensure new plants and buildings are designed for maximum energy efficiency, while optimising and retrofitting existing assets.

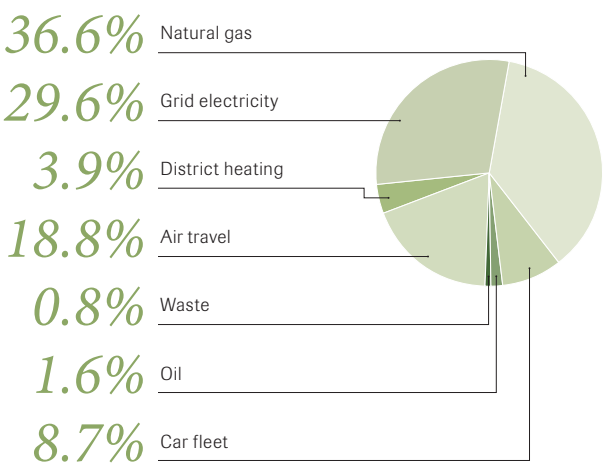
We are reducing the amount of fuel we use to heat, cool and operate our sites and, thus, were able to reduce GHG emissions by 2.6% in 2012 as a result of energy saving measures.

Introducing new technologies

Fuel cell technology was chosen as the best option for the refurbishing of the energy supply at Roche Molecular Diagnostics in Pleasanton, California. The project engineering team received the 2012 Innovation Award from senior management of Roche Molecular Diagnostics.

Fuel cells produce electricity and heat from hydrogen in an electrochemical reaction – not combustion – similar to a battery. To get optimum overall efficiency, heat exchangers recover the heat, which is then used to heat the buildings at the Pleasanton site. This process of producing usable electricity and heat is commonly known as cogeneration (cogen) or combined heat and power (CHP). Depending on the amount of heat used at the site, the typical efficiency rate of the fuel cells ranges from 65% to 75%, whereas the electricity-to-heat ratio is approximately three to two.

Energy use by type



Greenhouse gas emissions CO_2 equivalent

	2012	2011	2010	2009
Total emissions (million tonnes)	1.004	1.031	1.077	1.053
Total emissions per million CHF of sales (tonnes)	22.06	24.23	22.69	21.47

Energy use terajoules

	2012	2011	2010	2009 Baseline
Total energy use	13,280	13,372	14,495	13,898
Total energy use per million CHF of sales	0.292	0.314	0.305	0.283
Total energy use per employee	0.158	0.164	0.176	0.176

Reducing halogenated hydrocarbon emissions

Halogenated hydrocarbons are used as refrigerants in cooling equipment. When chlorinated, these compounds deplete the ozone layer, whereas when fluorinated or partially fluorinated they have a considerable global warming potential. All of them are persistent and, thus, stay in the atmosphere over a long period of time. For example, chlorodifluoromethane, commonly used as a propellant and refrigerant, remains in the atmosphere for approximately 15 years.

We plan to reduce halogenated refrigerants by 90% at all Roche sites by 2015. Sites acquired in recent years, such as those of Genentech and Ventana, are working towards separate timelines.

Since 2004 we have made significant progress reducing emissions of halogenated hydrocarbons, eliminating all halons and reducing fully halogenated compounds by 90%, excluding Genentech sites and Ventana.

Recent acquisitions and the lack of alternatives in some countries make complete elimination of these chemicals by 2015 unrealistic. We nevertheless continue to examine alternatives and work with refrigeration suppliers to make further reductions.

Halogenated hydrocarbons tonnes

	2012	2011	2010	2009
Inventory	172.1	181.9	205.2	179.8
Emissions	2.6	3.8	3.8	6.5

Minimising other air emissions

We minimise emissions to air through a variety of technologies and practices. Our priorities are to avoid pollutants, reduce quantities of pollutants and control remaining pollutant emissions in line with our eco-balance goals. Our overall objective is to keep emissions to the low levels we have achieved in recent years.

Our emissions strategy prescribes a continuous improvement programme at our manufacturing sites. This includes flue gas scrubbers to reduce nitrogen oxides (NO_x) and sulphur dioxide (SO_2) and various incineration and freezing processes to reduce the release of volatile organic compounds (VOCs), which may also reduce energy use.

In 2013 the Basel site will commission an installation that will freeze out VOCs from waste air discharged by manufacturing buildings and equipment. The process uses liquid nitrogen and will replace an energy intensive process of incinerating waste air. A similar installation will be completed at our chemical manufacturing plant in Florence, USA by end of 2013.

Our emissions to air are at very low levels but fluctuate from year to year. This can result in significant variability. In 2012, for instance, Group NO_x emissions increased by 14.4% to 254 tonnes because of prolonged use of an emergency generator at a single site.

Emissions to air tonnes

	2012	2011	2010	2009
VOCs	122	124	164	177
Particulates	20	20	33	27
Nitrogen oxides	254	222	262	286
Sulphur dioxide	5	8	7	9

Managing waste

Waste is a parameter of our eco-balance. Our waste reduction targets, therefore, are reflected in our goal to improve the Group's eco-balance by 15% by 2020. We maintain waste reduction goals for individual sites, however, we have not set a Group-wide goal, primarily because of large year-to-year fluctuations in waste from construction and demolition activities.

Roche, as other pharmaceutical and diagnostics companies, produces relatively low volumes of chemicals and, thus, generates small quantities of chemical waste. We nevertheless continue to reduce already low volumes of waste as our production of biotech products increases and chemical-based products declines. The Genentech Hillsboro site in Oregon, USA, for example, diverted more than 68% of its solid waste from landfills, earning the 2012 Recycle at Work Award from local government.

Production of pharmaceutical and diagnostic products rose by 5.4% overall in 2012. Chemical waste was down by 14.8%, while general waste increased by 9.2%.

We accept responsibility for all waste generated at our operations, including that previously deposited at our sites or landfills. We permit landfilling only as a last resort and, even then, only for inert materials such as slag or incineration ash. Depending on the availability of suitable local waste-treatment plants, we may dispose of non-hazardous general waste in authorised landfills.

In Switzerland, Roche and other companies continued to clean up hazardous waste landfills at Kölliken and Bonfol. As a former user of the Kesslergrube landfill in Grenzach, Germany, Roche is studying possible remediation options. We are also evaluating various remedial options at our former site in Belleville, New Jersey, USA.

In June 2012 Roche announced the planned shut-down of operations at its approximately 100-acre site in Nutley, New Jersey. As a consequence and in view of a future sale of the property, Roche has accelerated its existing efforts, under state regulatory oversight, to fully investigate and remediate

the soil and groundwater conditions at the site. Early remediation activities that are either completed or underway include groundwater treatment, soil excavation and operation of soil-vapour extraction systems.

As a potential responsible party, Roche is involved in several investigations and remediation projects at different environmental sites throughout the US.

Waste tonnes

	2012	2011	2010	2009
General waste produced	26,346	24,121	27,249	19,828
General waste per million CHF of sales	0.58	0.57	0.57	0.40
Chemical waste produced	25,703	30,170	29,020	27,605
Chemical waste per million CHF of sales	0.56	0.70	0.61	0.56

Conserving and protecting water resources

Roche supports global efforts to promote water protection, conserve water reserves and improve access to clean drinking water. Our long-term goal is to reduce total wastewater toxicity by 10% in 2020 from a 2015 baseline. In the meantime, we continue to investigate reliable performance indicators and measurement methods for establishing that baseline and strive to stabilise water consumption throughout the Group.

Over half the water we draw is used in cooling circuits. As this water is not chemically contaminated, we discharge it after analysis. The rest is purified in treatment plants before it is released to waterways.

Even though we do not operate sites that consume large volumes of water in areas of water scarcity, we still adopt conservation and reduction programmes according to local conditions and needs. For example, our Californian sites use drought resistant landscaping. At other sites we reduce water consumption by:

- collecting and recycling water from cooling towers, creating a closed-loop system
- reusing cleaning water for next 'first rinse' and recycling used water
- reducing cooling requirements and improving cooling processes
- improving heat recovery

We record organic emissions into water as total organic carbon (TOC) after processing in a wastewater treatment plant. We only discharge wastewaters and pollutants if they comply fully with relevant regulations, including pre-treatment requirements. At above 90%, the elimination rates in our wastewater treatment plants are already high. We seek to further minimise contamination of water by:

- reducing discharges of toxic and poorly biodegradable substances and heavy metals
- reducing the generation of wastewater
- treating or pre-treating wastewater, with ozone in some cases, for non- or poorly degradable contaminants

As a result of continuous efforts to reuse reject water from reverse osmosis in cooling towers or boilers and from improved cooling processes, our water consumption decreased by 8.6% in 2012 to 3 million cubic metres. At the Penzberg site, Germany, for instance, a self-powered high-efficiency wastewater treatment plant earned several awards for innovation and environmental responsibility. Other local programmes have identified opportunities to reduce water consumption. At the Genentech South San Francisco site, an evaluation identified improvements to the reverse osmosis portion of a water purification plant that could save an estimated 38 million gallons and approximately 504,000 Swiss francs per year. Furthermore a pilot study has been launched to treat and reuse wastewater from a neutralisation cascade that, if successful, could save an additional 60 million gallons as well as approximately 795,000 Swiss francs per year.

Water usage and discharge

	2012	2011	2010	2009
Water withdrawn (million cubic metres)	19.8	20.4	19.6	18.6
Water used (million cubic metres)	3.0	3.3	3.6	2.8
Wastewater discharged to treatment plant (million cubic metres)	5.6	5.7	6.3	5.2
Organic matter discharged to watercourses after treatment (tonnes)	140	228	242	154
Heavy metals discharged to watercourses after treatment (kilogrammes)	374	288	463	426

In 2012 we transferred 5.6 million cubic metres of water to treatment plants, resulting in the discharge of 140 tonnes of organic matter. In addition, we discharged 374 kilogrammes of heavy metals, of which most were leaching from metal pipes, from our operations into watercourses.

Heavy metal emissions from Roche sites are at very low levels. Thus, new processes or other activities may have significant effects on amounts emitted. For example, cleaning of galvanised equipment before it was dismantled at our Mannheim site, Germany, resulted in a 30% increase in zinc washouts.

TOC emissions could be reduced substantially in the Roche Rio de Janeiro plant by modifying processes, using new cleaning agents as well as a different production programme.

Water management

Water is considered the basis of all life. It is equally important for industrial activities. Thus, the production of pharmaceuticals and diagnostics is only possible with sufficient amounts of clean water. The availability of high-quality water is critical to our business, as almost all processes in chemical, biotech, pharmaceutical and diagnostics manufacturing involve water as a reagent, solvent or cleaning agent. Globally, poor quality of water is resulting in higher costs for purification and risk of product contamination in the pharmaceutical industry. In addition, water is used as an energy carrier in refrigeration and heating installations.

Appropriate water management is, thus, a must for all Roche operations, and all Roche Group sites are working on programmes to reduce water consumption and to recycle or reuse water. In this context, we completed an assessment of the exposure of Roche businesses to water risks during the last two years. The focus was on the availability of water in sufficient amounts and of acceptable quality.

A first evaluation using the water tool of the World Business Council for Sustainable Development identified six sites that could eventually face water scarcity in the near future. The tool uses statistical information from bodies such as the Food and Agriculture Organization of the UN, the World Resources Institute and the University of New Haven.

A second evaluation concentrated on the future development of the site and the surrounding area where water competitors could negatively influence future growth. Finally, two sites were identified that need an in-depth water analysis with respect to their development and improvements of the water supply.

Water management is a local issue and therefore Roche has purposely decided not to set a global target surrounding water management but to encourage local targets. Only locally can water management be closely and, therefore, more effectively monitored.

Supporting biodiversity

Roche supports the principles of resource stewardship defined in the Convention on Biological Diversity (CBD) and its three main objectives covering the conservation of biological diversity, sustainable use of its components, and fair and equitable sharing of the benefits from the use of genetic resources.

We avoid the use of non-commodity natural resource materials as a source for products or the discovery and development of pharmaceuticals. If, however, we discover or develop a commercial product derived from natural plant, microbial or animal genetic materials, our use of those resources will be guided by the principles and goals of the CBD.

We, otherwise, do not operate facilities in areas that are protected or have high biodiversity values. All Roche sites require access to city infrastructure and, as such, are located in urban environments.

Safeguarding employees and property

Health and safety

Employee health and safety is our first priority. Our primary objectives are to keep the Roche accident rate (RAR) below 0.07, reducing it to below 0.06 by 2020, and to reduce the Roche illness rate (RIR) to less than 0.01 by 2020. (RAR corresponds to the number of working days lost due to occupational accidents per employee and year at a Roche site. RIR corresponds to the number of working days lost due to occupational illnesses per employee and year.)

We maintain an integrated programme of employee consultation, workplace inspections and training across all business areas. Our approach is to promote a strong safety culture that empowers all of our employees to report and address safety issues. We expect similarly rigorous policies from our contractors. We also encourage the safety and wellbeing of our employees by selling discounted, protective equipment for recreational activities and conducting bicycle safety checks, among other activities. In 2012 at Roche Leganés, Madrid, Spain, an optician worked on site adjusting lenses and selling

glasses for four days. At Roche Pleasanton, USA, a volunteer ergonomics team, known locally as Ergo Angels, performs drop-in ergonomic evaluations for employees.

These and other ongoing efforts to further improve workplace safety have resulted in a decline of approximately 37% in the number of work-related accidents per million working hours from 2005 to 2012. Employees reported 440 occupational accidents in 2012, a 12.8% increase in frequency compared with 2011, while the resulting number of lost days increased 10.3% from 5,471 to 6,036. Overall, the Roche accident rate went up by 7.3%, from 0.067 to 0.072.

Although the number of reported cases of occupational illnesses increased to 147 in 2012 from 141 cases in 2011, the number of working days lost declined to 1,494 from 2,047. As a result, the Roche illness rate decreased by 28.0% to 0.018 from 0.025.

Our occupational accident and illness profile remains consistent, with slips, falls and repetitive strains representing the majority of work-related incidents in 2012. However, we have to report one work-related fatality. An employee fell while cycling from one building to another on the campus and tragically died a few days after the accident.

Employee safety and health

	2012	2011	2010 Basis	2009
Roche accident rate	0.072	0.067	0.065	0.074
Roche illness rate	0.018	0.025	0.014	0.008
Number of work-related accidents	440	390	432	392
Cases of work-related illnesses	147	141	182	217
Work-related fatalities	1	0	0	0
Work-related accidents per million working hours	2.92	2.67	2.97	2.92

Security

Our goal is to protect our employees and visitors, physical assets, intellectual property and products from harm or loss. In 2012 Roche started an information security awareness campaign addressing, as a first priority, employees working in R&D departments. Theft or loss of business critical information is regarded as a significant business risk for Roche. A small specialist team comprised of members from Global Competitive Intelligence, IT Security, Legal Data Compliance and Group Security briefed employees at Roche Diagnostics Rotkreuz and Roche Basel on these topics. The campaign will be continued in 2013 at the remaining R&D sites and extended to other operational areas as needed.

Further security activities in 2012 included conducting the Western Europe Security Workshop in Mannheim, Germany, where site security officers together with the Chief Security Officer discussed priority issues such as product counterfeiting and information security.

Pharmaceuticals in the environment

We consider the entire lifecycle of our drugs, taking steps to minimise the release of pharmaceuticals into the environment at all stages.

Traces of pharmaceutical products can enter the environment in a variety of ways, including the manufacturing process, improper disposal of unused medicines and through natural process following normal patient use. Patient use, however, is generally recognised as the primary contributor.

Evidence suggests that the exposure to these trace concentrations in surface, ground and drinking water does not pose harm to human health. The risks to aquatic life are thought to be greater. Scientific studies have not identified any short-term effects from exposure to low-level concentrations of pharmaceuticals, but more research is being conducted to evaluate potential long-term impacts. We, therefore, recognise the need for further research into possible effects and support scientific work in this field.

We design our manufacturing sites to reduce the risk of active ingredients entering wastewater. We also support pharmaceutical take-back programmes and employ proactive measures to prevent the release of our products into the environment by:

- offering financial incentives to ensure that unused or outdated products are returned by retailers and others in the supply chain
- establishing policies that require returned or waste pharmaceutical products to be incinerated rather than disposed in landfills
- supporting research into the effects of our pharmaceuticals in the environment
- providing environmental risk assessments to authorities for all new medicines

Legislation and compliance

We meet all local laws and regulations, although, our policies are often more rigorous than external standards.

We are fully on track with the registration of our chemical materials according to the European legislation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and requirements from the Globally Harmonised System of Classification and Labelling of Chemicals.

For nine consecutive years prior to 2012, we incurred no significant fines for SHE-related violations. During 2012, however, we were assessed small fines for two minor infractions with respect to a worker accident in 2010, resulting in four lost days, and a breach in a management regulation relating to having a specific risk assessment for a particular process.

SHE Goals

Education

	Basis	Target date
Improve SHE education by increasing SHE training per employee to an average of four hours per year		2020

Safety

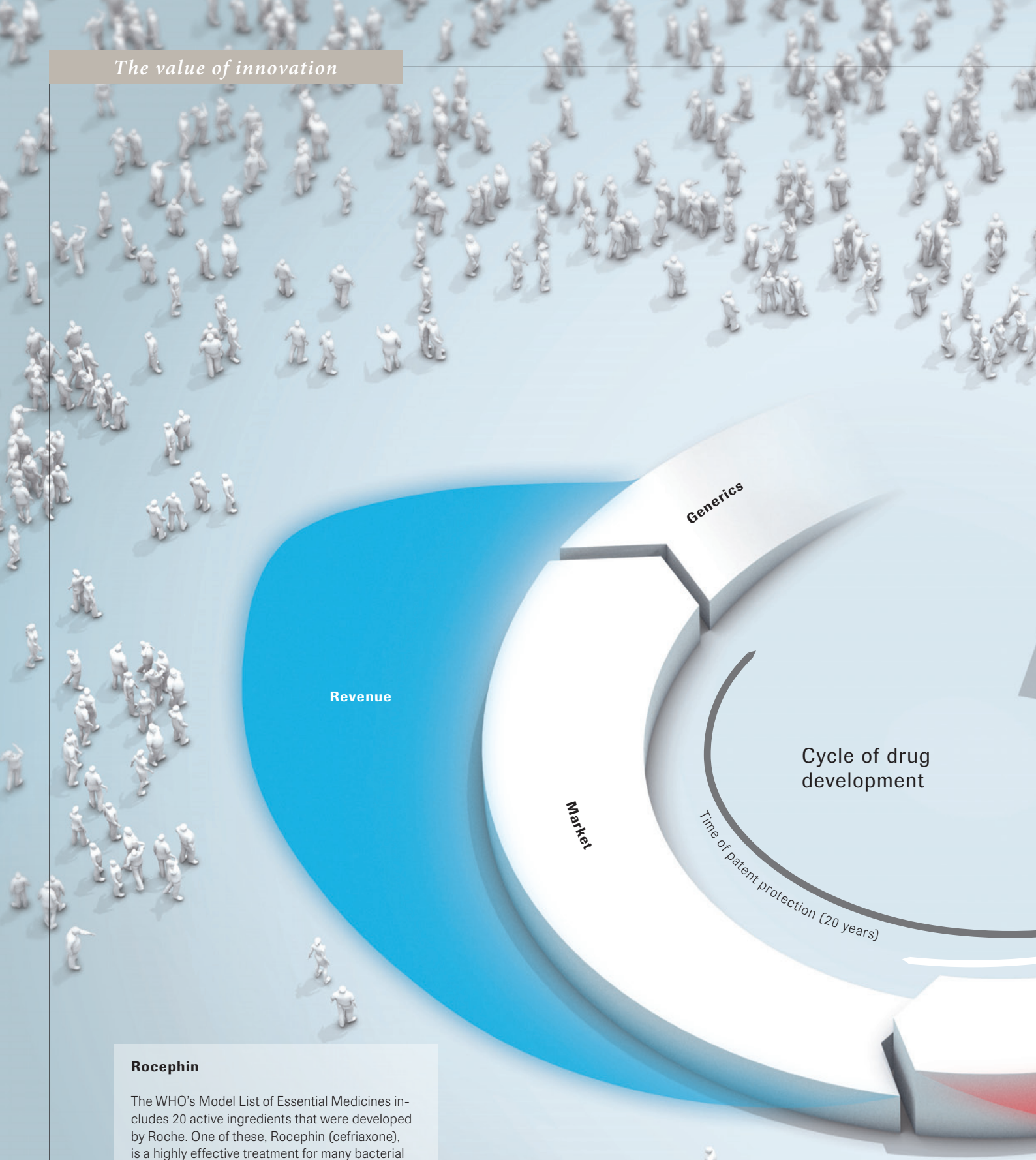
	Basis	Target date
Improve Roche accident rate by 12% (RAR < 0.07) until 2015 and by 24% (RAR < 0.06) until 2020	2010	2015 2020
Reduce number of occupational accidents causing lost working days (cases per 200,000 working hours) by 12% (< 0.6) until 2015 and by 27% (< 0.5) until 2020	2010	2015 2020
Keep Roche illness rate below 0.01	2010	2020
Bring number of cases of occupational illnesses causing lost working days (cases per 200,000 working hours) below 0.32 until 2015	2010	2015

Environmental protection

	Basis	Target date
Improve energy efficiency (GJ/employee) by 10% until 2014 and by 20% until 2020	2009 2010	2014 2020
Increase share of sustainable energies in total energy consumption to 20% until 2020		2020
Reduce CO_2 emission per employee in line with improving energy efficiency by 20% until 2020	2010	2020
Reduce total environmental impacts (calculated as eco-balance according to Swiss Federal Office for the Environment, BAFU) per employee by 15% until 2020	2010	2020
Reduce total waste water toxicity by 10% until 2020	2015	2020

More on the Web

- Environmental protection: www.roche.com/environment
- EER and eco-balance: www.roche.com/fact_sheet_eco_efficiency.pdf
- SHE goals: www.roche.com/she_goals
- SHE performance: www.roche.com/she_performance
- SHE services: www.roche.com/she_services
- Policies, guidelines, position papers: www.roche.com/responsibility/environment/she_management/policy_guidelines_and_audits.htm



Rocephin

The WHO's Model List of Essential Medicines includes 20 active ingredients that were developed by Roche. One of these, Rocephin (cefriaxone), is a highly effective treatment for many bacterial infections, including purulent meningitis.

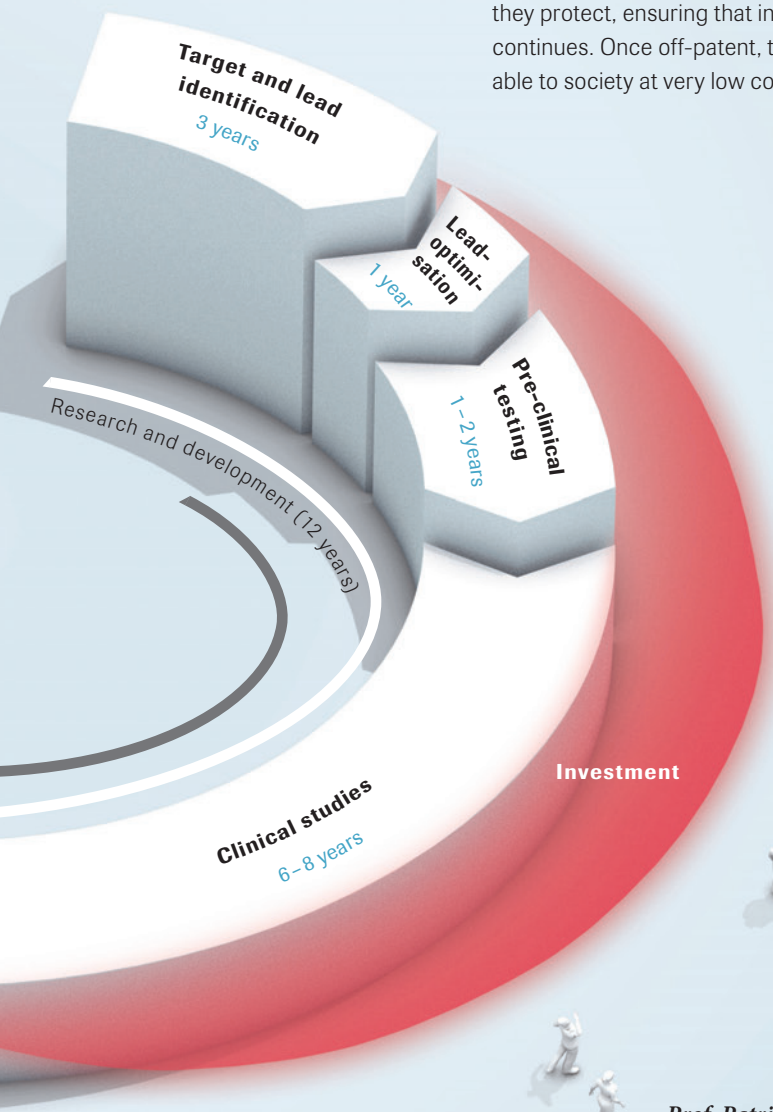
After its approval in 1982, Rocephin quickly became Roche's top-selling drug and the world's number one injectable antibiotic. Generic production of ceftriaxone was, naturally, an attractive proposition. The patents expired in the time between 1997 and 2005. By 1999 there were 2,012 ceftriaxone generics on the market, produced in 38 different countries.

↗ More on the web:
http://www.roche.com/valueofinnovation

Innovation in the pharmaceutical industry

A lasting contribution to world health

The discovery and development of new drugs is very high risk. Development can cost a billion Swiss francs or more and take between eight and twelve years to complete. Only one in five drug candidates, on average, receive regulatory approval. Even then, a patented drug can be copied easily and quickly because its composition must be declared.
For innovation to continue to drive medical breakthrough, investment in research and development has to be compensated and new drugs must be adequately protected, which is where patents come in. Patents temporarily confer an exclusive right to market the products they protect, ensuring that innovation is rewarded and the search for new treatments continues. Once off-patent, these products can be replaced with generics and made available to society at very low cost in perpetuity.



Prof. Patrick Aebischer, Président École Polytechnique Fédérale de Lausanne:

'Patents are essential for research in the life sciences. They protect knowledge as a raw material and provide incentives for high-risk investments.'

1896

after its foundation 116 years ago, Roche over the years specialised as a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics

6

CORPORATE GOVERNANCE

Roche is committed to serving all its stakeholders. As a basis for the successful implementation of this commitment to all stakeholders our Corporate Governance principles accordingly put the focus of our business activities on sustainable value creation and innovation and prescribe a management culture conforming to recognised standards of corporate governance and a policy of transparent communication.

REMUNERATION REPORT

Roche's success depends on the abilities and dedication of all its people. Recognition of this forms the basis of our performance-oriented remuneration policy and system.

Corporate Governance

Roche is committed to serving all its stakeholders. As a basis for the successful implementation of this commitment our Corporate Governance principles accordingly put the focus of our business activities on sustainable value creation and innovation and prescribe a management culture conforming to recognised standards of corporate governance and a policy of transparent communication.

A strong Board of Directors, which represents the interests of the shareholders and all other stakeholders, and highly skilled managers that act with integrity are extremely important.

In 2012 the Dow Jones Sustainability Indexes designated Roche 'Supersector Leader' in healthcare for the fourth consecutive year. Sustainability is at the core of our business practices and this award reflects our commitment to running our business in a way that is ethical, responsible and creates long-term value for stakeholders.

This Corporate Governance Report sets out the structures, processes and rules which Roche takes as the basis for well-functioning corporate governance. In doing so, Roche complies with all relevant corporate governance requirements, in particular with all applicable laws, the Swiss Stock Exchange (SIX Swiss Exchange) directives (including the commentaries thereto) and the Swiss Code of Best Practice for Corporate Governance promulgated by the Swiss business federation 'economiesuisse'. The company's internal governance framework, particularly its Articles of Incorporation and Bylaws, embodies all the principles needed to ensure that the company's businesses are managed and supervised in a manner consistent with good corporate governance, including the necessary checks and balances.[1]

The printed Annual Report contains selected links to the Roche website (www.roche.com). Readers are thus provided not only with a 'snapshot' of our company at the reporting date but are also directed to sources which they can consult at any time for up-to-date information about corporate governance at Roche. Whereas each annual report covers a single financial year ending 31 December, our website contains information of a more permanent nature, as well as the latest Roche news. The company's Articles of Incorporation, Bylaws and the curricula vitae of the members of the Board of Directors and the Corporate Executive Committee are published on our website.

For further details please refer to the following report.

Board of Directors

At the 94th Annual General Meeting (AGM) of Roche Holding Ltd, on 6 March 2012, shareholders re-elected John I. Bell, André Hoffmann and Franz B. Humer as members of the Board of Directors for the term of two years as provided by the Articles of Incorporation.

At its organising meeting immediately following the AGM, the Board of Directors has determined the structure and composition of its committees as shown on page 13.

At the AGM on 5 March 2013, the Board of Directors will nominate Andreas Oeri, Pius Baschera, Paul Bulcke, William M. Burns, Christoph Franz, DeAnne Julius, Arthur D. Levinson, Peter R. Voser and Beatrice Weder di Mauro for re-election to the Board for the term of two years as provided by the Articles of Incorporation.

Bruno Gehrig, Vice-Chairman of the Board of Directors, and Lodewijk J.R. de Vink, both long-term members of the Board of Directors, have decided to retire as members of the Board of Directors. The Board of Directors thanks both members for their long and valuable contribution to the successful continuing development of Roche.

At the AGM on 5 March 2013, the Board of Directors will additionally nominate Severin Schwan for election to the Board for the term of two years as provided by the Articles of Incorporation.

1 http://www.roche.com/about_roche/corporate_governance.htm

Corporate Executive Committee

Sophie Kornowski-Bonnet, former General Manager of Roche Pharma in France, has been appointed Head of Roche Partnering at the Group's headquarters in Basel and joined the Enlarged Corporate Executive Committee as a new member on 1 February 2012 reporting to Severin Schwan, CEO of the Roche Group. She succeeded Dan Zabrowski, who took over as Head of Roche Applied Science in the Diagnostics Division, located in Penzberg, Germany, as of 1 February 2012. Dan Zabrowski is a member of the Diagnostics leadership team and has been reporting to Roland Diggelmann, COO Division Roche Diagnostics, since 1 September 2012.

Jean-Jacques Garaud, Head of Roche Pharma Research and Early Development (pRED) and member of the Enlarged Corporate Executive Committee, retired from Roche on 30 June 2012. Effective 1 July 2012, Mike Burgess, Discovery and Translational Area (DTA) Head for Oncology and Head of Large Molecule Research, assumed the ad-interim position of Head of Roche Pharma Research and Early Development (pRED) and sits on the Enlarged Corporate Executive Committee. John C. Reed has been appointed Head of Roche Pharma Research and Early Development (pRED) and member of the Enlarged Corporate Executive Committee succeeding Mike Burgess and reporting to Severin Schwan, effective 2 April 2013.

Effective 1 September 2012, Daniel O'Day was appointed COO Division Roche Pharmaceuticals, succeeding Pascal Soriot following his resignation. At the same time, Roland Diggelmann, Head of the Asia–Pacific Region for Roche Diagnostics, succeeded Daniel O'Day as COO Division Roche Diagnostics.

Information on each member of the Board of Directors (including the years in which they were elected and the years in which their terms end) and on each member of the Corporate Executive Committee is listed on pages 12 to 15 and page 126 'Board of Directors and Corporate Executive Committee'.

Information relating to Corporate Governance

1 Group structure and shareholders

- Roche's operating businesses are organised into two divisions: Pharmaceuticals and Diagnostics. The Pharmaceuticals Division comprises the two business segments Roche Pharmaceuticals and Chugai, whereas Genentech as the former third segment has been integrated into Roche Pharmaceuticals. The Diagnostics Division consists of the following five business areas: Applied Science, Diabetes Care, Molecular Diagnostics, Professional Diagnostics and Tissue Diagnostics. Business activities are carried out through Group subsidiaries and associated companies. Detailed information on Roche Holding Ltd and on significant subsidiaries and associated companies (including company name, listing information, domicile, share capital, and equity interest) are listed in the Finance Report, Note 33 to the Roche Group Consolidated Financial Statements ('Subsidiaries and associates', page 133).
- Major shareholders are listed in the Finance Report, Notes 27 and 32 to the Roche Group Consolidated Financial Statements ('Equity attributable to Roche shareholders' and 'Related parties', pages 117 and 131) and in Note 4 to the Financial Statements of Roche Holding Ltd ('Significant shareholders', page 158).
- André Hoffmann, Vice-Chairman of the Board of Directors, and Andreas Oeri, member of the Board of Directors and Chairman of the Board's Corporate Governance and Sustainability Committee, serve in their respective capacities on the Board and its committees as representatives of the shareholders group with pooled voting rights and receive the remuneration set forth in the Remuneration Report on page 136 and in the Finance Report, Note 32 to the Roche Group Consolidated Financial Statements ('Related parties', page 131) and Note 6 to the Financial Statements of Roche Holding Ltd ('Board and Executive remuneration', page 159). No other relationships exist with the shareholders with pooled voting rights.
- There are no cross-shareholdings.

2 Capital structure

- Information on Roche's capital structure is provided in the Finance Report, Notes to the Financial Statements of Roche Holding Ltd (page 157). Additional details are contained in the Articles of Incorporation of Roche Holding Ltd.[2]

2 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm

- Changes in equity are detailed in the Finance Report, Notes to the Financial Statements of Roche Holding Ltd (page 157).
- The company has a share capital of 160,000,000 Swiss francs, divided into 160,000,000 fully paid bearer shares with a nominal value of 1 Swiss franc each. There are no restrictions on the exercise of the voting rights of these shares. Upon deposit, shares can be voted without any restrictions.
- There is no authorised or conditional capital.
- In addition, 702,562,700 non-voting equity securities (NES) have been issued in bearer form. They do not form part of the share capital and confer no voting rights. Each NES confers the same rights as one share to participate in available earnings and in any liquidation proceeds following repayment of the share capital. Roche's NES and the rights pertaining thereto (including the provisions protecting the interests of NES holders) are described in §4 of the Articles of Incorporation of Roche Holding Ltd.
- Information on debt instruments which have been issued and on outstanding bonds is provided in the Finance Report, Note 26 to the Roche Group Consolidated Financial Statements ('Debt', page 111).
- Additional information on employee stock options is provided in the Finance Report, Note 10 to the Roche Group Consolidated Financial Statements ('Employee stock options and other equity compensation plans', including detailed information on the 'Roche Option Plan' and the 'Roche Restricted Stock Unit Plan' page 85 ff.).
- Roche has issued no options apart from employee stock options, Stock-settled Stock Appreciation Rights (S-SARs) and options issued in connection with debt instruments.
- Neither the options awarded to employees nor the debt instruments which have been issued have any effect on Roche's share capital.

3 Board of Directors and Corporate Executive Committee

- Information on each member of the Board of Directors (including the years in which they were elected and the years in which their terms end) and on each member of the Corporate Executive Committee is listed on pages 12 to 15. Curricula vitae of all current and of former members (of the last 5 years) of both bodies and other information (including information on board memberships) are available and continuously updated on the Internet.[3]
- The Annual General Meeting elects the members of the Board of Directors in staggered elections in which each nominee is voted on separately (see §18 of the Articles of Incorporation of Roche Holding Ltd[4] and the Minutes of the 94th Annual General Meeting of Roche Holding Ltd, held 6 March 2012[5]).
- With the exception of Franz B. Humer, William M. Burns and Arthur D. Levinson, none of the members of the Board of Directors has been a member of Roche's Corporate Executive Committee or served in an executive capacity at any Group subsidiary during the three financial years preceding the current reporting period.
- The internal organisation of the Board of Directors and the division of authority and responsibilities between the Board and management, the remits of the Board committees, and the information and control mechanisms available to the Board in its dealings with corporate management, are governed by the Bylaws.[6]
- The Board of Directors of Roche Holding Ltd is organised so as to ensure that the Group conducts its businesses responsibly and with a focus on long-term value creation. To this end, the Roche Board has delegated certain responsibilities to several committees[7]. Their composition and chairpersons as of 1 January 2013 are described on page 13. Each committee's authorities and responsibilities are defined in detail in the Bylaws of the Board of Directors.[8]
- All the committees except the Presidium are chaired by independent directors.
- According to the Bylaws of the Board of Directors, a Board meeting may be convened without the Chairman present at the request of any of its members. The Roche Board meets once a year to assess the Chairman's performance. This meeting, which is not attended by the Chairman, is chaired by one of the Vice-Chairmen.
- As part of the Management Information System, the Board of Directors is informed about the most important issues, sales performance etc. on a monthly basis. The Board has access to an electronic information platform which provides timely information to the Board of Directors and the Board's committees as does the system of controls as set forth below.

3 http://www.roche.com/about_roche/management/board_of_directors.htm and http://www.roche.com/about_roche/management/executive_committee.htm

4 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm

5 http://www.roche.com/about_roche/corporate_governance/annual_general_meetings.htm

6 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm

7 http://www.roche.com/about_roche/corporate_governance/committees.htm

8 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm

- The Board of Directors has established a system of controls which is continuously monitored by the Audit Committee and by the Corporate Governance and Sustainability Committee and consists of the following elements:
  - Report on operating and financial risks (risk management system)
    Roche has a system in place to identify and manage all type of risks potentially affecting its business. Roche's Risk Management Charter sets out the approach and accompanying responsibilities. The Pharmaceuticals and Diagnostics Divisions and global functions conduct a formal risk assessment process at least once a year and must develop risk plans for their most material risks. These are monitored and deviations reviewed in regular performance dialogues. The consolidated Group Risk Report including target risk profile is discussed by the Corporate Executive Committee and approved together with the Group Business Plan. It is also presented to the Audit Committee. The process is subject to regular reviews, with findings presented to the Audit Committee or the full Board.
    For details on risk management, including risk factors and the Risk Management Charter see 'Risk Management & Compliance' on our website.[9] Financial risk management is specifically described in the Finance Report.[10]
  - System of internal controls over financial reporting (see pages 137 and 140 of the Finance Report)
  - Internal audit
    Group Audit reports to the General Counsel, has direct access and gives regular briefings to the Audit Committee about ongoing activities and audit reports. The Chief Audit & Risk Advisory Executive attends the Audit Committee meetings, as do the external auditors.
    Group Audit is an independent appraisal function, which evaluates and reviews the Group's activities as a service to management. The annual audit plan with yearly defined focus areas (e.g. emerging markets, third-party management) is validated by Senior Management and presented to the Audit Committee. The Roche Group is committed to maintaining a high standard of internal control throughout its worldwide operations. Management is responsible for assessing the business risks in all aspects of its operation and for implementing effective and efficient processes and controls whilst ensuring compliance with internal and external rules and regulations.
    By conducting operational audits, Group Audit determines management's response to the risks surrounding business processes and systems, and evaluates the appropriateness, completeness and efficiency of the processes and controls. Action plans to implement necessary changes and enhancements are developed together with the business/auditee and are tracked to completion.
  - Statutory auditors, see page 129
  - Chief Compliance Officer and Compliance Officers in subsidiaries, see page 130
  - Safety, Health and Environmental Protection Department[11]
  - Corporate Sustainability Committee[12]
  - Science and Ethics Advisory Group (SEAG), for issues relating to genetics and genetic engineering (established in 1999)[13]
- The members of the Corporate Executive Committee are invited to attend meetings of the Board of Directors for, and report in person on, those agenda items concerning them. When the situation warrants, members of the Enlarged Corporate Executive Committee may also be invited to attend. The Board committees invite the Chairman of the Board and Corporate Executive Committee members to deliver reports at committee meetings and may elect to commission independent expert reports and call on the services of consultants.

9 http://www.roche.com/corporate_responsibility/business_ethics/risk_management_and_compliance.htm
10 Additional information is provided in the Finance Report, Note 31 to the Roche Group Consolidated Financial Statements, 'Risk management', page 123.
11 http://www.roche.com/corporate_responsibility/environment.htm
12 http://www.roche.com/corporate_responsibility.htm
13 http://www.roche.com/corporate_responsibility/csr_research_and_development/genetics_and_bioethics.htm

Board and Board committees attendance 2012

	Board	Presidium/ Nomination Committee	Remuneration Committee	Audit Committee	Corporate Governance and Sustainability Committee
Number of meetings	**6**	**4**	**3**	**4**	**2**
F.B. Humer	6	4	–	*	*
B. Gehrig	5	4	3	–	–
A. Hoffmann	6	4	2	–	1
P. Baschera	6	–	–	–	2
J.I. Bell	6	–	–	4	–
P. Bulcke	6	–	–	4	–
W.M. Burns	6	–	–	–	2
L.J.R. de Vink	6	–	–	4	–
Ch. Franz	5	–	1	–	–
D. Julius	6	–	–	4	–
A.D. Levinson	6	–	3	–	–
A. Oeri	6	–	–	–	2
P.R. Voser	5	–	3	–	–
B. Weder di Mauro	6	–	–	4	–

– Not a member of that committee.
* Franz B. Humer is invited as a guest to these Board committee meetings.

- Each year several black-out periods are imposed during which senior employees are prohibited from trading in company stock. The following black-out periods are in effect for 2013:
  26 December 2012 to 30 January 2013
  1 April to 11 April 2013
  26 June to 25 July 2013
  1 October to 17 October 2013
  Black-out periods can be changed by the Chairman of the Board of Directors if circumstances warrant.
- In 2012 the Board of Directors met for six meetings, generally each from 3 to 6 hours in length**; in addition once for a full-day meeting** and once for a three-day visit to a major subsidiary**. The Board committees met as follows in 2012:
  – Presidium of the Board of Directors/Nomination Committee: four meetings (approx. 2 hours each**)
  – Remuneration Committee: three meetings[14] (approx. 2 to 3 hours each**)
  – Audit Committee: four meetings (approx. 3 to 4 hours each**)
  – Corporate Governance and Sustainability Committee: two meetings (approx. 3 hours each**).

  The composition of the Board's committees has remained unchanged since 1 March 2011.
- The Board of Directors regularly conducts an assessment of its performance.
- Members of the Corporate Executive Committee have a maximum ordinary notice period of twelve months.
- There are no management contracts which fall within the scope of Subsection 4.3 (annex) of the SIX Directive on Information relating to Corporate Governance.

4 Remuneration, shareholdings and loans

All details regarding remuneration, shareholdings and loans are set forth in the separate Remuneration Report on pages 132 to 145 and in the Finance Report, Notes 27 and 32 to the Roche Group Consolidated Financial Statements ('Equity attributable to Roche shareholders' and 'Related parties', pages 117 and 131), and are listed in the Notes 6 and 7 to the Financial Statements of Roche Holding Ltd ('Board and Executive remuneration' and 'Board and Executive shareholdings', pages 159 and 162).

** These figures indicate the actual length of meetings and do not include the directors' extensive pre-meeting preparations and post-meeting follow-up activities.
14 Remuneration Committee members are not permitted to contribute to or attend Remuneration Committee meetings at which matters concerning them are deliberated or decided.

5 Participatory rights of shareholders

- The participatory rights of shareholders are defined in Roche's Articles of Incorporation.[15] As Roche shares are issued to bearer, there are no restrictions on admission to Annual General Meetings, with the exception that shares must be deposited within a specified period before the date of a meeting and an admittance card must be issued in the shareholder's name, as provided in §12 of the Articles of Incorporation. Any shareholder can elect to be represented by a third party at an Annual General Meeting. The Articles of Incorporation contain no restrictions on the exercise of voting rights, and the only quorum requirements are those stipulated in §16, in conformity with the Swiss Code of Obligations.
- Under §10.2 of the Articles of Incorporation, shareholders representing shares with a nominal value of at least 1 million Swiss francs can request the placement of items on the agenda of an Annual General Meeting. This must be done no later than 60 days before the date of the meeting.

6 Change of control and defensive measures

- The Articles of Incorporation contain no provisions on the mandatory bid rule. Swiss law applies.
- There are no change-of-control clauses. Those components of remuneration based on Roche NES would be terminated in the event of an acquisition, and vesting period restrictions on pre-existing awards would be removed, so that all such options could be exercised immediately.

7 Relationship to statutory auditors

At the Annual General Meeting of Roche Holding Ltd on 6 March 2012, the shareholders voted to appoint KPMG AG (KPMG) as statutory auditors. Based on the existing legal requirements of the Swiss Code of Obligations (Article 730a) concerning the maximum term of office of seven years of the auditor in charge, Ian Starkey replaced his predecessor John Morris as auditor-in-charge starting with the business year 2011 (information on how long the auditors and auditor-in-charge have been serving in these capacities is provided on page 15). The statutory auditors participate in Audit Committee meetings. They prepare written and oral reports on the results of their audits. The Audit Committee oversees and assesses the auditors and makes recommendations to the Board (for information on the authorities and responsibilities of the Audit Committee, see Article 8.1 of the Bylaws[16]). The statutory auditors participated in three meetings of the Audit Committee in 2012.

The reports of statutory auditors on the Consolidated Financial Statements and on the Financial Statements can be found on pages 138 and 166, respectively, of this year's Finance Report.

KPMG received the following remuneration for their services as statutory auditors of Roche Holding Ltd and as the auditors of other Roche companies (including Chugai):

	2012	2011
	(millions of CHF)	
Auditing services	19.2	19.2
Audit-related services	2.1	1.3
(accounting services,	0.3	0.7
assurance services)	1.8	0.6
Tax consultancy services	1.4	1.6
Total	**22.7**	**22.1**

The statutory auditors are elected each year by the Annual General Meeting.

8 Information policy

- As provided by §33 of the Articles of Incorporation[17], corporate notices are published in the *Swiss Official Gazette of Commerce* and in other daily newspapers designated by the Board of Directors *(Basler Zeitung, Finanz und Wirtschaft, L'Agefi, Le Temps, Neue Zürcher Zeitung).*
- Roche reports its half-year and full-year results in business reports (published in print and online formats) and at media events. In addition, detailed first- and third-quarter sales figures are published each year in April and October. The most current list of publication dates is available in English and German on the Internet.[18]
- All relevant information and documents, including all media releases, investor updates[19] and presentations to analyst and investor conferences are available on the Internet. Further publications can be ordered by e-mail, fax or telephone:
  basel.webmaster@roche.com,
  tel. +41 (0)61 688 83 39,
  fax +41 (0)61 688 43 43.
- The contact address for Investor Relations is: F. Hoffmann-La Roche Ltd, Investor Relations, Group Finance, 4070 Basel, Switzerland;
  tel. +41 (0)61 688 88 80,
  fax +41 (0)61 691 00 14.

15 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm
16 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm
17 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm
18 http://www.roche.com/media.htm
19 http://www.roche.com/investors.htm

Additional information, including details on specific contact persons, is available on the Internet.[20]

9 Chief Compliance Officer and Compliance Officers network

The Chief Compliance Officer with his Compliance Officers network is committed to ensuring that the Roche Group Code of Conduct[21] is consistently complied with throughout the Roche Group. He also serves as a contact person for shareholders, employees, customers, suppliers and the general public on issues relating to the implementation of and compliance with this Code. Employees and other parties who become aware of violations of the Roche Group Code of Conduct can bring them to the attention of their managers or supervisors or report them to the Chief Compliance Officer (Urs Jaisli, direct phone number: +41 (0)61 688 40 18, e-mail: urs.jaisli@roche.com). Such disclosures will be treated confidentially. In addition, as of the end of 2009, employees may anonymously report irregularities or complaints in their mother tongue via a 'Speak-Up hotline'.

In addition Roche has established a Business Ethics Incident Reporting (BEIR) system which enables the Chief Compliance Officer to capture, track and monitor alleged violations, from initial reports by local Compliance Officers through to resolution. Business ethics incidents are recorded in the system when the local Compliance Officer receives specific and concrete information about a material alleged violation of the Roche Group Code of Conduct in one of certain pre-defined categories.[22] The Corporate Governance and Sustainability Committee and the Audit Committee of the Board of Directors are informed of substantial violations.

The Chief Compliance Officer reports to the General Counsel and also submits regular reports to the Corporate Governance and Sustainability Committee and to the Audit Committee of the Board of Directors.

10 Non-applicability/negative disclosure

It is expressly noted that any information not contained or mentioned herein is either non-applicable or its omission is to be construed as a negative declaration (as provided in the SIX Swiss Exchange Corporate Governance Directive and the Commentary thereto).

20 http://www.roche.com/investors/contacts.htm
21 http://www.roche.com/about_roche/corporate_governance/code_of_conduct.htm
22 http://www.roche.com/corporate_responsibility/business_ethics/risk_management_and_compliance.htm

Remuneration Report

1. Principles

Roche's success depends on the abilities and dedication of all its people. Recognition of this forms the basis of our performance-oriented remuneration policy and system.

At Roche we strive to create innovative medicines and diagnostic products of benefit to patients. This requires outstanding performance by all our employees. It takes continuous innovation to help patients, sustain revenues and create long-term value. Innovation enables us to pay competitive compensation to all our employees and distribute rising dividends to our stockholders (until 2012: dividend increase for the 25th year in a row). One of the primary aims of our remuneration policy is thus to encourage a long-term focus and align management's interests with the interests of Roche's shareholders and holders of Roche's non-voting equity securities (NES).

Each year the Remuneration Committee of Roche's Board of Directors meets at least twice and sets the remuneration of Board members and the members of the Group's Corporate Executive Committee (base pay, bonuses, Stock-settled Stock Appreciation Rights [S-SARs] and policy decisions on pension benefits). The terms of Performance Share Plan (PSP) awards are determined annually by the Board of Directors, acting upon recommendations from the Remuneration Committee.

The Remuneration Committee tracks market data on salaries at other leading global pharmaceuticals companies[1] and reports its findings to the full Board. The external consulting firm Towers Watson assists Roche in performing market comparisons. Information on the Remuneration Committee's remit, powers and procedures for making remuneration decisions can be found in the Bylaws of the Roche Board of Directors[2] and are also outlined in the sections below on the principles governing specific remuneration components.

2. Summary of main activities in 2012 and outlook for 2013

The following were the key developments and decisions in 2012:

- The Remuneration Committee (assisted by the consultancy Towers Watson) regularly tracked the base pay of Roche directors against market data on directors' pay at other leading global pharmaceuticals companies[1] and at other major Swiss companies[3]. The base remuneration of Roche directors has remained unchanged for 12 years.
- The base salaries (fixed) paid to Corporate Executive Committee (CEC) members remained unchanged in 2012 except in the case of Daniel O'Day. Daniel O'Day's base salary increased following his promotion to COO Division Roche Pharmaceuticals.
- The bonus (variable) paid to CEC members for 2012 will consist entirely of cash payments (except in the case of Severin Schwan) and is reflecting the sales growth, the strong growth of Earnings per Share and non-voting equity security, and the development of the rich and further developed pipeline.
- Stock-settled Stock Appreciation Rights (S-SARs) (variable): As of 2012 S-SARs granted to CEC members all vest together after three years and then have to be exercised within seven years of the grant date. Unexercised S-SARs lapse without compensation. Since 2012, the fair value of S-SARs has been calculated at the grant date using the trinomial model for American options (for details see page 138 and 139).
- S-SARs granted from 2006 to 2008 have strike prices above the NES price on 31 December 2012 and for the time being have no value for the recipients. This can change if Roche's NES price improves.
- Performance Share Plan (PSP) awards (variable): As in the case of the PSP 2007–2009, PSP 2008–2010 and PSP 2009–2011 cycles, there will be no pay-out or award of targeted NES for the PSP 2010–2012 cycle. The plan's key performance metric, Total Shareholder Return (TSR), is calculated as a three-month moving average at constant CHF exchange rates.
- In 2012 the Remuneration Committee decided that the Chief Executive Officer (CEO) and other CEC members must acquire Roche shares and/or NES equivalent to two annual base salaries (CEO) and one annual base salary (other CEC

1 Peer set for 2012: Abbott Laboratories, Amgen, Astellas, AstraZeneca, Bayer, Becton Dickinson, Bristol-Myers Squibb, Eli Lilly, GlaxoSmith-Kline, Johnson & Johnson, Merck & Co., Novartis, Pfizer, Sanofi-Aventis, Takeda.

2 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm

3 ABB, Credit Suisse, Holcim, Nestlé, Swiss Re, UBS, Zurich Insurance Group, Actelion, Nobel Biocare, Sonova, Straumann, Synthes.

members), respectively, by the end of 2016 and retain these holdings for as long as they serve on the CEC.
- In addition to applicable statutory provisions, Roche's long-term incentive plans include the option to partially reclaim distributed compensation as a result of special circumstances (clawback) (for details see page 143).

Starting in 2013, Restricted Stock Units (RSUs) — non-voting equity securities with a vesting period of three years — will be introduced as a new remuneration component partially replacing S-SARs and options. This will result in a better alignment of Roche long-term incentives. The value of S-SARs awards will be reduced to 65% and the 35% balance will be awarded in the form of RSUs. The company will incur no additional costs as a result of this change. The aim is to further strengthen the alignment of management's interests with the interests of Roche's shareholders for the Group's long-term success.

As in previous years, this Remuneration Report will be submitted separately for an advisory vote at the 2013 Annual General Meeting.

For all further details please refer to the following sections of this Remuneration Report[4].

3. Remuneration policy

Roche regularly reviews its policy and principles on remuneration. They are part of a framework of employee policies aimed at motivating and retaining current employees, attracting talented new ones and helping all Roche employees to perform at consistently high levels. Our remuneration policy is designed to foster value creation and reinforce a culture of performance and innovation. It applies both to non-managerial employees and to managers.

The S-SARs and PSP (and [starting in 2013] Restricted Stock Units [RSUs]) remuneration components are intended to align management's interests with those of shareholders and holders of non-voting equity securities and to give participating managers an additional incentive to achieve continued value growth in the form of long-term total shareholder returns. By creating value for Roche investors, management benefits as well. When no added value is created for investors, management is 'penalised' by receiving less.

The key principles underpinning this policy are:
- Focus on value creation
- Pay for performance
- Enabling employees to share in the company's success
- Fairness and transparency in remuneration decisions
- A balanced mix of long- and short-term remuneration components
- Market competitiveness

4 See also in the Finance Report, Note 32 to the Roche Group Consolidated Financial Statements ('Related parties', page 131) and Notes 6 and 7 to the Financial Statements of Roche Holding Ltd ('Board and Executive remuneration' and 'Board and Executive shareholdings', pages 159 and 162).

4. Remuneration components

Base pay, bonuses, blocked non-voting equity securities (NES), awards of Stock-settled Stock Appreciation Rights (S-SARs), a Performance Share Plan (PSP) and (starting in 2013) Restricted Stock Units (RSUs) support the fundamental aims of Roche's remuneration policy. These remuneration components are linked to our company's financial performance and commercial success and thus align the interests of Roche employees with those of shareholders.

After explaining the principles that govern the various remuneration components, this report details the amounts paid to each member of the Board of Directors, the components of the Chairman of the Board's remuneration and the amount of each remuneration component paid to each member of the Corporate Executive Committee for 2012.

A. Base pay

Base pay (cash payment) is determined for each position based on salary market data on other leading global pharmaceuticals companies[1] and reflects individuals' abilities, experience and performance over time. Pay increases are likewise linked to individual performance and take into account prevailing market conditions[1] and the company's overall financial situation.

The Remuneration Committee makes and reviews the final decision on the base pay and pay increases paid to the Chairman of the Board of Directors and members of the Corporate Executive Committee and on the remuneration of the other members of the Board.

B. Bonuses

Bonuses are awarded for individual contributions to value creation that go beyond normal job expectations and are meant to be an incentive to strive for outstanding results and to create new business opportunities. Bonus amounts are linked to Group and divisional profits, sales growth, Operating Profit After Capital Charge (OPAC), Earnings per Share and NES growth, pipeline and to the achievement of measurable and qualitative individual or functional performance objectives. For competitive reasons, Roche does not disclose the individual performance objectives of members of its Corporate Executive Committee.

Each December the Remuneration Committee determines the bonuses payable to the Chairman of the Board and the members of the Corporate Executive Committee in respect of the current reporting year, based on performance against the aforementioned objectives. At the same time the Remuneration Committee also decides in what form bonuses will be awarded (cash payments and/or blocked non-voting equity securities).

C. Stock-settled Stock Appreciation Rights (S-SARs)

A Stock-settled Stock Appreciation Rights (S-SARs) plan was introduced on 1 January 2005 establishing a uniform system of remuneration throughout Roche. S-SARs entitle holders to benefit financially from any increase in the value of Roche's non-voting equity securities between the grant date and the exercise date.

S-SAR awards are allocated individually at the Remuneration Committee's discretion.

D. Restricted Stock Units (RSUs)

Starting in 2013, Restricted Stock Units (RSUs) — non-voting equity securities with a vesting period of three years — will be introduced as a new remuneration component partially replacing S-SARs and options. This will result in a better alignment of Roche long-term incentives. The value of S-SAR awards will be reduced to 65% and the 35% balance will be awarded in the form of RSUs.

E. Performance Share Plan

The members of the Corporate Executive Committee and other members of senior management (currently some 140 individuals worldwide) participate in the Performance Share Plan. The PSP was established in 2002 for periods of three years each and is based on a three-year comparison of the Total Shareholder Return (TSR) with 15 peer companies[1]. In 2012 there were three overlapping performance cycles (PSP 2010–2012, PSP 2011–2013 and PSP 2012–2014), of which PSP 2010–2012 closed on 31 December 2012.

The terms of the Performance Share Plan are conclusively determined by the Board of Directors on an annual basis, acting upon recommendations from the Remuneration Committee.

F. Ratio of Corporate Executive Committee variable remuneration elements (bonuses, S-SARs and PSP) relative to fixed base pay

Criteria	Bonus	Until end of 2012: S-SARs; Starting in 2013: S-SARs/RSUs	PSP
Individual target value, assessed in consideration of the performance of competitors[1] and the macro-economic development (in % relation to value of base pay)	Max. 100%	Until end of 2012: 100% S-SARs Starting in 2013: 65% S-SARs 35% RSUs	33.33% (Based on annual base pay measured at 1 January of first year of cycle)
Minimum	0%	0%	0%
Maximum (in % relation to value of base pay)	200% (Cash payment/ blocked NES)	150% (Value development determined by performance of NES after grant)	66.66% (Value development determined by performance of NES after grant)
Performance criteria	Group objectives (Group and divisional business performance) and individual objectives considering profit, sales growth, OPAC (Operating Profit After Capital Charge), Earnings per Share and NES growth, pipeline	Individual contributions upon the Remuneration Committee's decision at its own discretion	Group performance of TSR in relation to TSR performance of peer set
Split in %			
a) Group objectives	70%	n.a.	100%
b) Individual objectives	30%	n.a.	–

5. Remuneration of the Board of Directors and the Corporate Executive Committee

Each year the Remuneration Committee of Roche's Board of Directors sets the remuneration of Board members and members of Roche's Corporate Executive Committee (base pay, bonuses, S-SARs and policy decisions on pension benefits). The terms of the Performance Share Plan are determined annually by the Board of Directors, acting upon recommendations from the Remuneration Committee. The Remuneration Committee tracks market data on salaries at other leading global pharmaceuticals companies[1] and reports its findings to the full Board. Information on the Committee's remit, powers and procedures for making remuneration decisions can be found in the Bylaws of the Roche Board of Directors[5] and are also outlined in the preceding sections of this report on the principles governing specific remuneration components.

The bonuses and salaries of the Chairman of the Board of Directors and members of the Corporate Executive Committee were set by the Remuneration Committee, taking into account revisions to Roche's remuneration policy, market comparisons with other leading pharmaceuticals companies[1] and management changes.

The remuneration of both Vice-Chairmen of the Board and all other Board members consists of fixed cash payments set by and at the discretion of the Remuneration Committee. The Remuneration Committee (assisted by the consultancy Towers Watson) tracked these cash payments of Roche directors against market data on directors' pay at other leading global pharmaceuticals companies[1] and other major Swiss companies[3].

The following pages provide detailed information on the remuneration paid to each member of the Board of Directors and each member of the Corporate Executive Committee for 2012 and includes comparisons with the remuneration paid in the previous years.

5 http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm

5.1 Remuneration of members of the Board of Directors. In 2012 the members of the Board of Directors[6] received the fixed remuneration in cash payments shown in the 'Remuneration of members of the Board of Directors' table below for their Board activities. The basic remuneration of the Board of Directors has remained unchanged since 2001 and remuneration of all members of the Board of Directors will again remain unchanged for 2013.

The members of the Board of Directors were not awarded any shares, non-voting equity securities or Stock-settled Stock Appreciation Rights (S-SARs) in 2012.

William M. Burns received honoraria amounting to a total of 25,000 US dollars (23,441 Swiss francs) for serving as a member of the Board of Directors of Chugai Pharmaceutical Co., Ltd.

Arthur D. Levinson received payments for his consulting work and for serving on the Board at Genentech amounting to 373,834 US dollars (350,514 Swiss francs).

6 For a list of members, their positions and their committee memberships and chairmanships see page 13.

A. Remuneration of members of the Board of Directors

	Remuneration 2012 (in CHF)	Additional compensation 2012 for committee members/chairs[7] (in CHF)	Additional special compensation 2012 (in CHF)
F.B. Humer	(see 'B. Highest total remuneration paid to a member of the Board of Directors')	(see 'B. Highest total remuneration paid to a member of the Board of Directors')	(see 'B. Highest total remuneration paid to a member of the Board of Directors')
B. Gehrig	400,000[8]	–	
A. Hoffmann	400,000[8]	–	
P. Baschera	300,000	30,000	
J.I. Bell	300,000	30,000	
P. Bulcke	300,000	30,000	
W.M. Burns	300,000	30,000	see above 23,441
L.J.R. de Vink	300,000	30,000	
Ch. Franz	300,000	30,000	
D. Julius	300,000	60,000	
A.D. Levinson	300,000	30,000	see above 350,514
A. Oeri	300,000	60,000	
P.R. Voser	300,000	30,000	
B. Weder di Mauro	300,000	30,000	
Total	**4,100,000**	**390,000**	

7 With the exception of members of the Presidium and the Vice-Chairmen, Board members receive CHF 30,000/year for each committee they serve on and CHF 60,000/year for each committee they chair.
8 Remuneration for serving as Vice-Chairman of the Board.

B. Highest total remuneration paid to a member of the Board of Directors

As Chairman, Franz B. Humer was the member of the Board with the highest total remuneration for 2012. The Chairman's remuneration consists of base salary and bonus awards. As Chairman of the Board since the handover of his executive function as CEO at the Annual General Meeting on 4 March 2008, he did not receive any additional S-SARs or NES from other programmes (PSP, RSU) and was no longer enrolled in any Roche S-SARs programme.

Highest total remuneration paid to a member of the Board of Directors

	2012 (in CHF)	2011[9] (in CHF)	2010[9] (in CHF)
Salary	4,000,000	4,000,000	4,507,500
Bonus			
— Cash payment	2,500,000	1,600,000	2,200,000
Total	6,500,000	5,600,000	6,707,500
Pension funds/MGB[10]	1,808,487	2,983,549	2,995,801
Roche Connect	75,000	75,000	75,000
Total (value)	**8,661,876[11]**	**8,884,687**	**10,033,431**

9 For detailed calculation of the remuneration for 2011 and 2010 see Annual Report 2011, page 133.
10 MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).
11 Includes annual expense allowance (CHF 50,000), payments for tax consulting services (CHF 68,168) and Chugai advisory mandate USD 170,880 (CHF 160,221), not including employer contribution to AHV/IV/ALV (CHF 291,045).

C. Stock-settled Stock Appreciation Rights (S-SARs)
On 31 December 2012 Franz B. Humer and William M. Burns (being the only members of the Board of Directors holding S-SARs due to their former positions) and the members of the Corporate Executive Committee held Stock-settled Stock Appreciation Rights (S-SARs) as shown in the 'S-SARs' table on page 145. Franz B. Humer's S-SARs are currently of no value.

D. Total remuneration paid to the Board of Directors
For 2012 the members of the Board of Directors received remuneration totalling 13,525,830 Swiss francs (2011: 13,784,080 Swiss francs).

In 2012 Horst Teltschik, a former member of the Board of Directors, received honoraria amounting to 19,635 euros (23,665 Swiss francs) for serving on the boards of several Roche subsidiaries in Germany.

No additional remuneration was paid.

5.2 Remuneration of members of the Corporate Executive Committee. The general provisions assigning authority for decisions on Corporate Executive Committee remuneration to the Remuneration Committee and to the Board of Directors are outlined on pages 132 to 135 of this Remuneration Report.

Remuneration of members of the Corporate Executive Committee

A. Base pay in CHF

	Annual salary 2012	Annual salary 2011	Annual salary 2010
S. Schwan	4,000,000	4,000,000	3,750,000
S. Ayyoubi	1,200,000	1,200,000	1,100,000
R. Diggelmann	647,750	*	*
A. Hippe	2,100,000***	1,200,000**	*
G.A. Keller	1,500,000	1,500,000	1,500,000
D. O'Day	1,575,000	1,225,000	1,000,000
Total	**11,022,750**		

* Not a member of the Corporate Executive Committee.
** Prorated remuneration for the period from April to December 2011.
*** Including CHF 500,000 for loss of pension rights granted by former employer (contractual agreement, each for 2012 to 2014).

B. Bonus

The Remuneration Committee of the Board of Directors determined the Corporate Executive Committee members' bonuses in December 2012 based on the performance 2012 against the agreed objectives.

Except in the case of Severin Schwan, all members of the Corporate Executive Committee will receive the bonus 2012 as a 100% cash payment which is due at the end of April 2013. Severin Schwan will receive the bonus 2012 in form of Roche non-voting equity securities which are blocked for ten years. The Roche non-voting equity securities will be granted at the end of April 2013.

Bonus

	Bonus for 2012 Total (in CHF)	Bonus for 2011 Total (in CHF)	Bonus for 2010 Total (in CHF)
S. Schwan			
Cash payment	–	1,500,000	3,000,000
Blocked non-voting equity securities	2,512,755***	837,585	–
Total bonus	2,512,755***	2,337,585	3,000,000
S. Ayyoubi			
Cash payment	1,700,000	500,000	1,000,000
Blocked non-voting equity securities	–	419,810	–
Total bonus	1,700,000	919,810	1,000,000
R. Diggelmann			
Cash payment	600,000	*	*
Blocked non-voting equity securities	–	*	*
Total bonus	600,000	*	*
A. Hippe			
Cash payment	2,200,000	600,000**	*
Blocked non-voting equity securities	–	335,034	*
Total bonus	2,200,000	935,034	*
G.A. Keller			
Cash payment	1,500,000	500,000	1,000,000
Blocked non-voting equity securities	–	279,195	–
Total bonus	1,500,000	779,195	1,000,000
D. O'Day			
Cash payment	2,300,000	650,000	1,300,000
Blocked non-voting equity securities	–	545,753	–
Total bonus	2,300,000	1,195,753	1,300,000
Total	**10,812,755**		

* Not a member of the Corporate Executive Committee.
** Prorated remuneration for the period from April to December 2011.
*** Calculation of value in consideration of reduction of value due to the blocking period of 10 years.

C. Stock-settled Stock Appreciation Rights (S-SARs)

The S-SARs shown in the 'S-SARs' table on page 145 were introduced by Roche on 1 January 2005 in place of stock options. S-SARs entitle holders to benefit financially from any increase in the value of Roche's non-voting equity securities (NES) between the grant date and the exercise date. The strike price for S-SARs under the terms of this multi-year plan was the closing price for Roche NES at grant date. All S-SARs vest three years after the grant date. Vested S-SARs can be exercised (converted into NES) within seven years of the grant date. Unexercised S-SARs lapse without compensation.

The fair value of the S-SARs is calculated at the grant date using the trinomial model for American options. The trinomial

model is an effective method for valuation of American call options, as it considers the possibility of exercising the option any time prior to maturity (called 'American' option, as compared to a 'European' option, which only allows exercise at their maturity date).[12]

12 For further information on the trinomial model for American options: Please refer to Boyle, Phelim P.: 'A lattice framework for options pricing with two state variables', *The Journal of Financial and Quantitative Analysis*, Volume 23, Issue 1 (Mar 1988), 1–12, www.roche.com/trinomial_model.pdf

The numbers of S-SARs, the strike prices, expiry dates and grant values for S-SARs are shown in the 'S-SARs' table on page 145. The numbers of S-SARs as calculated at the time of issue have been entered as values in the table below.

The S-SARs granted in 2006 until 2008 have strike prices above the NES price as at 31 December 2012 and currently have no value for the recipients. This could change if Roche's future NES price improves.[13]

13 See strike prices in table 'S-SARs', page 145.

Stock-settled Stock Appreciation Rights (S-SARs)

	S-SARs 2012 (value in CHF)	S-SARs 2011 (value in CHF)	S-SARs 2010 (value in CHF)
S. Schwan	4,000,000	3,560,209	3,559,911
S. Ayyoubi	1,200,000	1,068,095	1,068,022
R. Diggelmann	366,150	*	*
A. Hippe	1,600,000	178,086	*
G.A. Keller	1,500,000	1,335,107	1,335,010
D. O'Day	1,300,000	890,087	890,030
Total	**9,966,150**		

* Not a member of the Corporate Executive Committee.

D. Performance Share Plan (PSP)

The members of the Corporate Executive Committee and other members of senior management (currently some 140 individuals worldwide) participate in the Performance Share Plan (PSP).

In 2006 the PSP moved to overlapping three-year performance cycles, with a new cycle beginning each year. In 2012 there were thus three cycles in progress (PSP 2010–2012, PSP 2011–2013 and PSP 2012–2014). As in the previous years for PSP 2007–2009, PSP 2008–2010 and PSP 2009–2011, PSP 2010–2012 closed on 31 December 2012 without any awards of targeted NES.

Under the provisions of this plan, a number of non-voting equity securities (NES) have been reserved for the participants in each cycle. The number of securities actually awarded will depend on whether and to what extent an investment in Roche securities (shares and NES) outperforms the average return on an investment in securities issued by a peer set of comparator companies[14]. Comparisons are based on the securities' market prices and dividend yields, i.e. on Total Shareholder Return (TSR), which is calculated at CHF constant exchange rates. To reduce the effect of short-term market fluctuations, security prices are averaged over the three months (October to December) prior to the start of a performance cycle and over the three months (October to December) at the end of the cycle.

If Roche securities perform better than the average of the peer set and Roche's TSR increases at least 10% during a cycle, the Board of Directors can elect to increase the NES award. The maximum award is double the original level reserved (target number of NES according to the PSP plan) and requires that Roche securities perform as well as or better than those of 75% of the peer set. In the event that an investment in Roche securities underperforms the average return delivered by the peer companies, fewer or no NES will be awarded.

14 See footnote 1, page 132.

Performance Share Plan (PSP)

	Target number of NES for PSP 2012–2014	Target number of NES for PSP 2011–2013	No awards of targeted number of NES for PSP 2010–2012	2012[15] Total estimated value of PSP awards (2010–2012, 2011–2013 and 2012–2014) (value in CHF)	2012 No NES awarded in 2012 for PSP 2010–2012 (value in CHF)	2011 No NES awarded in 2011 for PSP 2009–2011 (value in CHF)	2010 No NES awarded in 2010 for PSP 2008–2010 (value in CHF)
S. Schwan	9,079	9,460	–	1,137,058	–	–	–
S. Ayyoubi	2,723	2,838	–	341,074	–	–	–
R. Diggelmann	1,038	1,040	–	127,450	–	–	–
A. Hippe	3,631	2,838	–	396,765	*	*	*
G.A. Keller	3,404	3,547	–	426,328	–	–	–
D. O'Day	2,950	2,365	–	325,986	–	–	–
Total	**22,825**	**22,088**	**–**	**2,754,661**	**–**	**–**	**–**

* Not a member of the Corporate Executive Committee.

15 Total estimated value for 2012: PSP 2010–2012: none of the originally targeted NES awarded. PSP 2011–2013 and 2012–2014: Estimated value calculated using the year-end price as at 31 December 2012, CHF 184.00 per non-voting equity security (NES), based on the number of NES originally targeted subject to changes in the number and value of NES awardable under the plan on 31 December 2013 and 31 December 2014, respectively, and spread over the relevant period of time, i.e. 1/3 for the year 2012. The Board of Directors will vote on the actual allocation of originally targeted NES on 31 December 2013 and 31 December 2014, respectively, according to the TSR achieved.

In 2012 NES were reserved under the plan for members of the Corporate Executive Committee as shown in the table above. The Board of Directors will decide on the actual level of NES or cash equivalent awards for the cycles 2011–2013 and 2012–2014 after the close of the 2013 and 2014 financial years, respectively. The aim of the PSP is to provide an incentive to participants to achieve steady value growth.

At the end of the PSP 2010–2012 cycle (based on a three-month moving average) with distributed dividends totalling 16.732 billion Swiss francs (2012: 5.865 billion Swiss francs; 2011: 5.692 billion Swiss francs; 2010: 5.175 billion Swiss francs), the TSR of the Roche securities (NES and shares) ranked 15th, compared with its peer set of companies operating in the same industry. Therefore, according to the terms of the plan, the participants received none of the originally targeted NES (see table above for details).

E. Indirect benefits

Employer contributions made in 2012 to social security schemes, pension plans and a Group-wide employee stock purchase plan (Roche Connect) in respect of members of the Corporate Executive Committee are shown in the 'Indirect benefits in 2012' table on page 141.

Roche Connect is a voluntary stock purchase plan offering employees the opportunity to buy Roche non-voting equity securities (NES) up to an amount equal to 10% of their annual salary at a 20% discount. NES purchased under this plan are subject to a holding period, which is four years in Switzerland.

Indirect benefits in 2012

	Pension funds/MGB[16]/ insurances (in CHF)	AHV/IV/ALV[17] (in CHF)	Roche Connect (in CHF)	Payments for tax consulting services (in CHF)
S. Schwan	747,229	674,968	100,008	10,335
S. Ayyoubi	479,823	174,023	3,000	2,305
R. Diggelmann	144,917	49,774	7,500	–
A. Hippe	389,553	163,550	39,996	21,148
G.A. Keller	570,867	219,846	37,500	–
D. O'Day	382,657	214,768	12,504	15,817
Total	**2,715,046**	**1,496,929**	**200,508**	**49,605**

16 MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).
17 AHV/IV/ALV: Swiss social security programmes providing retirement, disability and unemployment benefits.

F. Other remuneration, emoluments and loans

Members of the Corporate Executive Committee additionally receive annual expense allowances of 30,000 Swiss francs (Roland Diggelmann received a prorated amount of 10,000 Swiss francs), totalling 160,000 Swiss francs.

Silvia Ayyoubi and Daniel O'Day received a non-recurring special payment of 50,000 Swiss francs each for their 25 years' service with the company.

Due to contractual obligations, in 2012 Roche paid Daniel O'Day and Alan Hippe 45,071 Swiss francs and 37,950 Swiss francs, respectively, for their children's schooling costs.

Expenses totalling 347,051 Swiss francs were paid for Roland Diggelmann in his former position.

For 2012 Pascal Soriot, COO Division Roche Pharmaceuticals, who took on new responsibilities outside of the company starting 1 September 2012, received the following payments based on existing contractual obligations: salary (prorated) 1,500,000 Swiss francs, bonus (prorated) for 2012 (50% as a cash payment of 750,000 Swiss francs, payable in April 2013, and 50% in form of Roche non-voting equity securities blocked for three years, amounting to 750,000 Swiss francs [NES calculated based on the market value average over the last three months of 2012 and granted at the beginning of January 2013]), expense allowance (prorated) 22,500 Swiss francs, payments for tax consulting services 6,641 Swiss francs, employer contribution to pension funds etc. 234,653 Swiss francs and to AHV/IV/ALV 373,973 Swiss francs. These payments are already included in the Corporate Executive Committee members' total remuneration of 44,732,958 Swiss francs. All his unvested S-SARs and targeted PSP (NES) awards lapsed without compensation.

In 2012 pensions totalling 2,099,180 Swiss francs were paid to former Corporate Executive Committee members.

The maximum regular period of notice for members of the Corporate Executive Committee is 12 months. The contractually agreed severance payments (exceeding payments during the notice period) previously included in the employment contracts were eliminated or lapsed, respectively, in 2012. In future, therefore, severance payments are no longer agreed. There are no change of control clauses in the employment contracts. At the same time, provision was made for Severin Schwan and Alan Hippe to receive supplementary death and disability benefits and company-funded retirement benefits in the event of early retirement. These insurance benefits were fully funded with a single payment in 2012. This payment is included in the total remuneration of 44,732,958 Swiss francs paid to the Corporate Executive Committee (previous year 43,925,402 Swiss francs).

G. Highest total remuneration paid to a member of the Corporate Executive Committee

Severin Schwan as CEO was the member of the Corporate Executive Committee with the highest total remuneration for 2012:

Highest total remuneration paid to a member of the Corporate Executive Committee

	2012 (in CHF)	2011[18] (in CHF)	2010[18] (in CHF)
Salary	4,000,000	4,000,000	3,750,000
Bonus			
– Cash payment	–	1,500,000	3,000,000
– Blocked non-voting equity securities	2,512,755**	837,585**	–
Total	6,512,755	6,337,585	6,750,000
S-SARs (Grant value according to trinomial model for American call options[19])	4,000,000	3,560,209	3,559,911
Pension funds/MGB[20]/insurances	747,229	459,527	456,122
Roche Connect	100,008	100,008	89,588
Estimated value of targeted (not awarded) NES according to Performance Share Plan[21] (*2011–2013, 2012–2014, no awards/value of NES of 2010–2012)			
Total	1,137,058*	819,933	502,425
Total (value)	**12,537,385[22]**	**11,311,916**	**11,396,873**

** Calculation of value in consideration of reduction of value due to blocking period of 10 years (reduced market value: 55.839%).
18 For detailed calculation of the remuneration for 2011 and 2010 see Annual Report 2011, page 133.
19 Trinomial model for American call options value as described in 'Remuneration of members of the Corporate Executive Committee, C. Stock-settled Stock Appreciation Rights (S-SARs)', page 138 and 139.
20 MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).
21 Basic rules and detailed calculation see 'Remuneration of members of the Corporate Executive Committee, D. Performance Share Plan', page 140, footnote 15 respectively.
22 Includes an annual expense allowance (CHF 30,000), payments for tax consulting services (CHF 10,335), excluding employer contribution to AHV/IV/ALV payments.

H. Total remuneration paid to the members of the Corporate Executive Committee

For 2012 the members of the Corporate Executive Committee received remuneration totalling 44,732,958 Swiss francs (2011: 43,925,402 Swiss francs) including AHV/IV/ALV.

No additional remuneration other than the above mentioned payments was paid to current or former members of the Corporate Executive Committee.

6. Alignment of interests between managers and shareholders/holders of non-voting equity securities

The S-SARs and PSP remuneration components are intended to align management's interest with those of shareholders and holders of non-voting equity securities and to give participating managers an additional incentive to achieve continued value growth in the form of long-term total shareholder returns. By creating value for Roche investors, management benefits as well. When no added value is created for investors, management is 'penalised' by receiving less.

The table below shows the impact this has had on the effective remuneration of the current members of the Corporate Executive Committee over the past seven years.

Due to the movement in the price of the non-voting equity security, the strike prices of S-SARs granted in the years indicated in the table on page 143 are above the non-voting equity security price as at 31 December 2012 and are therefore currently worthless. The table shows the originally disclosed values of the currently out-of-the-money S-SARs that were added to the compensation paid to each member ot the Corporate Executive Committee.

As performance targets were not met, the PSP programmes for 2007–2009, 2008–2010, 2009–2011 and 2010–2012 ended with no allocation of targeted non-voting equity securities. The table on page 143 contains the remuneration equivalent of all non-voting equity securities not allocated under the PSP at the values originally credited to each member of the Corporate Executive Committee as published accordingly in the remuneration reports.

S-SARs out of the money as at 31 December 2012 and PSP participation programme remuneration not distributed

	S-SARs out of the money as at 31 December 2012, value granted for 2006–2008 Total (in CHF)	PSP* No disbursement/issuance PSP 2007–2009 PSP 2008–2010 PSP 2009–2011 PSP 2010–2012 Total (in CHF)	Total (in CHF)
S. Schwan	3,827,582	3,336,114	7,163,696
S. Ayyoubi	649,436	768,891	1,418,327
G.A. Keller	2,759,415	1,750,000	4,509,415
D. O'Day	999,367	333,333	1,332,700
P. Soriot	4,005,306	1,082,293	5,087,599
Total	**12,241,106**	**7,270,631**	**19,511,737**

* PSP value calculation based on $^1/_3$ of the corresponding base pay for 2007/2008/2009 and 2010.

Alan Hippe and Roland Diggelmann are not listed in the table since they were not yet Roche employees or Roche Corporate Executive Committee members during the periods in question.

7. Clawback

In addition to applicable statutory provisions, Roche's long-term incentive plans include the option to partially reclaim distributed compensation as a result of special circumstances (clawback).

If the employee voluntarily serves notice of termination of employment, S-SARs which are unvested at the date of termination of employment lapse immediately without any compensation.

Upon termination of employment as a result of serious misconduct all S-SARs granted and outstanding, whether vested or unvested, shall lapse immediately without any compensation. According to the S-SARs plan rules, serious misconduct by the participant may include (inter alia):

- activity leading to serious disciplinary action,
- repeated or willful failure to perform such duties as have been reasonably assigned by Roche,
- violation of any law or public regulation,
- commission of a crime,
- gross negligence or willful misconduct in employment,
- engaging in conduct bringing disgrace or disrepute to Roche and/or any of its subsidiaries,
- violation of any of Roche's directives and guidelines relating to business conduct.

According to the regulations of the PSP programme, the originally targeted but not awarded NES shall lapse without any compensation upon notice of termination of employment being given for any reason other than redundancy, disability or retirement.

8. Guidelines for security holdings

In 2012 the Board of Directors decided that the CEO and other CEC members must acquire shares and/or NES equivalent to two annual base salaries (CEO) and one annual base salary, respectively, by the end of 2016 and retain these holdings for as long as they serve on the CEC.

	Type of security	Equivalence
CEO	Shares and/or NES	2 x annual base salary
Members of the Corporate Executive Committee	Shares and/or NES	1 x annual base salary

9. Security holdings

Directors André Hoffmann and Andreas Oeri and members of the founders' families who are closely associated with them belong to a shareholder group with pooled voting rights. At the end of 2012 this group held 72,018,000 shares (45.01% of issued shares). Detailed information about this group can be found in the Finance Report, Note 32 to the Roche Group Consolidated Financial Statements ('Related parties', page 131) and in Note 4 to the Financial Statements of Roche Holding Ltd ('Significant shareholders', page 158). In addition, as at 31 December 2012 the members of the Board of Directors and persons closely associated with them and the members of the CEC and persons closely associated with them held shares and NES as shown in the table below.

Security holdings (as at 31 December 2012)

	Shares (number)	NES (number)	Close relatives' security holdings (number/type)	Others (number)
Board of Directors				
F.B. Humer	7,492	85,216	–	S-SARs see 10
B. Gehrig	50	300	–	–
A. Hoffmann	–*	200	–	250,000 UBS Long/Short Certificates linked to Roche Bearer Shares/ Roche Non-voting Equity Securities (Valor: 10 690 162, ISIN: CH0106901629) Expiry date: 28 March 2013
P. Baschera	1	4,600	–	–
J.I. Bell	300	1,647	–	–
P. Bulcke	–	1,350	–	–
W.M. Burns	3	83,990	–	S-SARs see 10
L.J.R. de Vink	–	–	–	31,600 American Depository Receipts (ADR), RHHBY, US ISIN: US7711951043
Ch. Franz	–	350	–	–
D. Julius	350	1,550	–	–
A.D. Levinson	–	–	–	–
A. Oeri	–*	187,793	–	250,000 UBS Long/Short Certificate linked to Roche Bearer Shares/ Roche Non-voting Equity Securities (Valor: 10 690 162, ISIN: CH0106901629) Expiry date: 28 March 2013
P.R. Voser	–	3,600	–	–
B. Weder di Mauro	200	800	–	–
Total	**8,396**	**371,396**	–	
Corporate Executive Committee				
S. Schwan	7,000	47,813	–	S-SARs see 10
S. Ayyoubi	3	15,832	–	S-SARs see 10
R. Diggelmann	–	802	–	S-SARs/Options see 10
A. Hippe	–	8,892	–	S-SARs see 10
G.A. Keller	2,153	25,783	1,100 shares	S-SARs see 10
D. O'Day	3	5,492	–	S-SARs see 10
Total	**9,159**	**104,614**	**1,100 shares**	

* Shares held by the shareholders group with pooled voting rights not listed.

10. S-SARs

Number of S-SARs held by current and former members of the Corporate Executive Committee on 31 December 2012

	2012	2011	2010	2009	2008	2007	2006	Total
Corporate Executive Committee								
S. Schwan	163,869	154,322	154,443	–	105,576	29,190	15,696	623,096
S. Ayyoubi	49,161	46,298	46,335	43,842	21,117	3,243	2,517	212,513
R. Diggelmann	15,000	12,732	6,489[23]	4,263[23]	*5,295*[23]	–	–	43,779
A. Hippe	65,547	*7,178*	–	–	–	–	–	72,725
G.A. Keller	61,452	57,872	57,918	–	63,345	24,327	15,696	280,610
D. O'Day	53,259	38,582	38,613	–	20,133	10,269	5,856	166,712
Total	**408,288**	**316,984**	**303,798**	**48,105**	**215,466**	**67,029**	**39,765**	**1,399,435**
Former Corporate Executive Committee members								
F.B. Humer	None[24]	None[24]	None[24]	None[24]	None[24]	48,651	52,317	100,968
W.M. Burns	None[25]	None[25]	None[25]	109,602	105,576	48,651	26,160	289,989
Strike price (CHF)	157.50	140.10 *140.30*	175.50	145.40	195.80 *188.90*	229.60	195.00	
Market price per NES on 31 December 2012 (CHF)	184.00							
Expiry date	8.3.2019	28.2.2018 *29.4.2018*	4.2.2017	5.2.2016	31.1.2015 *25.7.2015*	8.2.2014	2.2.2013	
Grant value per S-SAR (CHF) Since 1.1.2012: – Trinomial model for American call options	24.41	15.38* *16.54**	23.05*	20.30*	21.08* *23.61**	36.59*	34.02*	

* Values according to corresponding annual reports.

23 In his former position options held: All of the options shown in the table were issued by Roche as employee stock options. Each option entitles the holder to purchase one Roche non-voting equity security (NES). Under the terms of this multi-year option plan, the strike price for options shown was the closing price for Roche NES at grant date. All of the options shown are non-tradable. One-third of the options are subject to a vesting period of one year, one-third have a vesting period of two years, and one-third a vesting period of three years. Unvested options lapse without compensation if employment is terminated voluntarily (for reasons other than retirement), while vested options must be exercised within a limited period of time.

24 As of 2008 Franz B. Humer does not receive any additional S-SARs. Franz B. Humer received S-SARs as a member of the Corporate Executive Committee until 2007.

25 As of 2010 William M. Burns does not receive any additional S-SARs. William M. Burns received S-SARs as a member of the Corporate Executive Committee until 2009.

Independent Assurance Report

To the Corporate Governance and Sustainability Committee of Roche Holding AG, Basel ('Roche').

We have performed assurance procedures to provide limited assurance on the following aspects of the 2012 corporate responsibility reporting of Roche.

Subject matter

Data and information disclosed in the corporate responsibility reporting of Roche and its consolidated subsidiaries, excluding Chugai Pharmaceutical Co. Ltd., for the business year ended December 31, 2012 on the following aspects and with the indicated level of assurance:

- The management of reporting processes with respect to the corporate responsibility reporting and to the preparation of SHE, people and donations & sponsorships key figures as well as the control environment in relation to the data aggregation of these key figures with a limited assurance;
- The SHE key figures (including Scope 1 & 2 CO_2 Emissions and Business Travel) in the tables and graphs on pages 110 to 119 and some selected people key figures disclosed on pages 92 to 97 of the Roche Business Report 2012 with a limited assurance; and
- The consolidated data and information on the Roche Group level in relation to donations & sponsorships, excluding health care professionals (HCPs) related activities, with a limited assurance.

Criteria

- The Roche Group internal corporate responsibility reporting guidelines based on the Responsible Care Health, Safety and Environmental Protection reporting guidelines published by the European Chemical Industry Council CEFIC and the 'Sustainability Reporting Guidelines G3.1' published in 2011 by the Global Reporting Initiative (GRI);
- The Roche Group internal Corporate Reporting Manual, Version 2012 'Sustainability Reporting — Economic Performance Data'; and
- The defined guidelines by which SHE, people and donations & sponsorships key figures are gathered, collated and aggregated internally.

Responsibility and Methodology

The accuracy and completeness of corporate responsibility indicators are subject to inherent limitations given their nature and methods for determining, calculating and estimating such data. Our assurance report should therefore be read in connection with Roche's internal guidelines, definitions and procedures on the reporting of its corporate responsibility performance. Future orientated data and information were not part of our assurance scope. We do not provide assurance on statements out of our scope.

The Roche Corporate Governance and Sustainability Committee is responsible for both the preparation and the presentation of the selected subject matter in accordance with the reporting criteria. This responsibility comprises the arrangement, implementation and maintenance of adequate records and internal controls that are designed to support the sustainability reporting processes.

Our responsibility is to form an independent conclusion, based on our limited assurance procedures, on whether anything has come to our attention to indicate that the subject matter is not stated, in all material respects, in accordance with the reporting criteria, for the business year ended on December 31, 2012. We have conducted our engagement in accordance with the International Standard on Assurance Engagements (ISAE) 3000, as issued by the International Auditing and Assurance Standards Board.

Main Assurance Procedures

Our assurance procedures included the following work:

- **Evaluation of the application of Roche Group guidelines**
  Reviewing the application of the Roche Group internal corporate responsibility reporting and donations & sponsorships guidelines;
- **Site visits**
  Visiting selected sites of Roche's Pharma and Diagnostics Divisions in Germany, Morocco, South Africa, United Arab Emirates, Singapore and USA. The selection was based on quantitative and qualitative criteria; Interviewing personnel responsible for internal corporate responsibility reporting and data collection at the sites we visited and at the Roche Group level to determine the understanding and application of Roche internal corporate responsibility guidelines.
- **Assessment of the key figures**
  Performing tests on a sample basis of evidence supporting selected SHE, people and donations & sponsorships key figures (Roche accident rate, energy consumption, CO_2 emissions related to energy consumption, release of halogenated hydrocarbons, headcount/FTE data, staff statistics and labor practices information, contributions to philanthropic organizations, patient organizations, health institutions, public policy bodies) concerning completeness, accuracy, adequacy and consistency.
- **Review of the documentation and analysis of relevant policies and basic principles**
  Reviewing the relevant documentation on a sample basis, including Roche Group corporate responsibility policies, management of reporting structures and documentation; and
- **Assessment of the processes and data consolidation**
  Reviewing the appropriateness of the management of/and reporting processes for corporate responsibility key data; and
  Assessing the consolidation process of data at Roche Group level.

Conclusions

With reference to the identified subject matter information, and based on our work performed, nothing has come to our attention that causes us to believe that:

- the Roche Group internal corporate responsibility reporting guidelines based on the GRI G3.1 Sustainability Reporting Guidelines as well as the CEFIC Guidelines are not applied in all material respects, in accordance with the reporting criteria,
- the internal reporting processes to collect and aggregate SHE, people and donations & sponsorships data is not functioning as designed and does not provide an appropriate basis for its disclosure, in all material respects, in accordance with the reporting criteria, and
- the corporate responsibility information mentioned in the subject matter and disclosed with the corporate responsibility reporting in the Roche Business Report 2012 is not stated, in all material respects, in accordance with the reporting criteria.

Zurich, 25 January 2013

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Next Annual General Meeting:
5 March 2013

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This Annual Report contains certain forward-looking statements. These forward-looking statements may be identified by words such as 'believes', 'expects', 'anticipates', 'projects', 'intends', 'should', 'seeks', 'estimates', 'future' or similar expressions or by discussion of, among other things, strategy, goals, plans or intentions. Various factors may cause actual results to differ materially in the future from those reflected in forward-looking statements contained in this Annual Report, among others: (1) pricing and product initiatives of competitors; (2) legislative and regulatory developments and economic conditions; (3) delay or inability in obtaining regulatory approvals or bringing products to market; (4) fluctuations in currency exchange rates and general financial market conditions; (5) uncertainties in the discovery, development or marketing of new products or new uses of existing products, including without limitation negative results of clinical trials or research projects, unexpected side effects of pipeline or marketed products; (6) increased government pricing pressures; (7) interruptions in production; (8) loss of or inability to obtain adequate protection for intellectual property rights; (9) litigation; (10) loss of key executives or other employees; and (11) adverse publicity and news coverage.

The statement regarding earnings per share growth is not a profit forecast and should not be interpreted to mean that Roche's earnings or earnings per share for 2012 or any subsequent period will necessarily match or exceed the historical published earnings or earnings per share of Roche.

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