

A close-up, side-profile photograph of a person's face wearing clear safety glasses. The person's eye is visible through the lens. The background is a soft, out-of-focus bokeh of light and warm tones.

# Annual Report 2014

## PERFORMANCE

Reporting solid results, Roche will propose an increase of the dividend for the 28<sup>th</sup> year running. Discover how the new Chairman, Christoph Franz, plans to build on this strong foundation.

**08**

## INNOVATION

From prevention to life-extending medicines, important pipeline breakthroughs in 2014 included an HPV test for cervical cancer and survival data of nearly 5 years for a Roche breast cancer medicine.

**52**

## ENGAGEMENT

More than 80% of employees are proud to work for Roche. Find out what the company is doing to create a great workplace where people feel engaged and inspired to do their best work.

**108**

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# Roche in 2014

*ROCHE IS A RESEARCH-BASED HEALTHCARE COMPANY founded in 1896 and headquartered in Basel, Switzerland. We focus on creating truly innovative medicines and diagnostic tests in areas of unmet medical need. Our business model drives our ambition to make a significant difference to patients, reaching as many people in need as possible whilst continuously reinvesting in innovation to develop diagnostic tests and breakthrough treatments.*

**47.5** billion Swiss francs  
**sales\***

**14.29** Swiss francs  
**core earnings per share**

**229** billion Swiss francs  
**market capitalisation**

**88,509** employees

## Pharmaceuticals



- Esbriet approved in idiopathic pulmonary fibrosis
- RoActemra approved in early rheumatoid arthritis
- Avastin approved in cervical cancer and platinum-resistant ovarian cancer
- Gazyvaro approved in chronic lymphocytic leukemia

## Diagnostics



- New molecular testing systems, the cobas 6800 and cobas 8800, launched
- HPV test for primary screening of cervical cancer approved
- New diagnostic test for syphilis launched
- Investment of 450 million Swiss francs over next three years in new diagnostic manufacturing facility in China

## Product pipeline



- Anti-PDL1 immunotherapy medicine in bladder cancer
- Lampalizumab in geographic atrophy of the eye
- Cobimetinib and Zelboraf in advanced melanoma
- ACE910, an innovative bispecific antibody, in hemophilia A

\* Unless otherwise stated, all growth rates in this report are at constant exchange rates (CER; average full year 2013).

# No.1 in biotech

# in oncology

# in *in vitro* diagnostics

# in hospital market

## Acquisitions



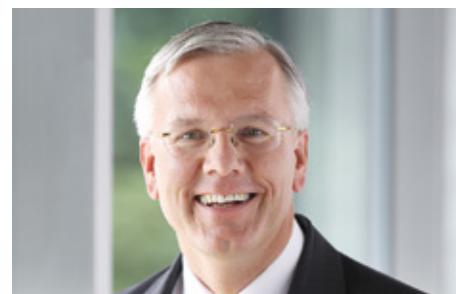
- InterMune in idiopathic pulmonary fibrosis
- Seragon Pharmaceuticals in hormone receptor-positive breast cancer
- Ariosa Diagnostics in non-invasive pre-natal testing
- Genia Technologies in next-generation gene sequencing
- IQum in molecular diagnostics

## Sustainability



- Dow Jones Sustainability Indices Group leader for sixth year running
- Global access programme to test viral loads in people with HIV infections launched
- 5.8 million people treated in 20 years through the Phelophepa train, a mobile health clinic in South Africa
- 71% fully engaged employees

## Group

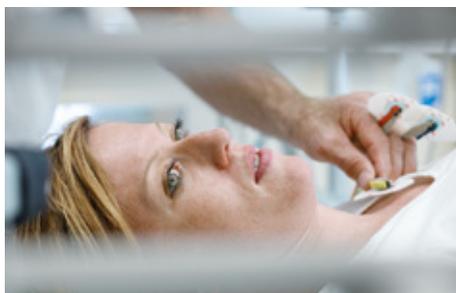


- Christoph Franz elected as Chairman of the Roche Board of Directors
- 4 billion Swiss francs of investments announced in state-of-the-art R&D, production facilities and infrastructure
- Increase in dividend proposed for the 28<sup>th</sup> consecutive year
- More than 100 new external partnerships

# Our business priorities

*WE HAVE A CLEAR SET of business priorities aimed at achieving sustainable growth and delivering value to all our stakeholders.*

## Focus on patients



We focus exclusively on developing innovative medicines and diagnostic tests that help patients live longer, better lives. Two thirds of all known diseases are either still not treated adequately or not treated at all. This medical need is an enormous challenge and better diagnostics and medicines can make a huge difference to the lives of millions of patients and their families.

## Excellence in science



We strive to address unmet medical needs through excellence in science. Breakthrough innovation in science and technology increasingly allow us to understand precisely what is malfunctioning in the body and develop drugs to counter the problem. We focus on oncology, immunology, infectious diseases, ophthalmology and neuroscience. However, we remain flexible and follow the science as new insights become available.

## Personalised healthcare



We combine our strengths in pharmaceuticals and diagnostics to better fit treatments to patients. When genetic differences can be identified, the efficacy and safety of medicines can be improved enormously. To this end we have a companion diagnostic strategy for every molecule we develop.

### *Performance in 2014*

19 million patients on a Roche top 25 selling medicine

More than 6 million women tested for HPV

More than 6.5 billion test strips for blood glucose monitoring sold

66 new molecular entities (NMEs) in the pipeline

11 pharmaceutical product approvals

>170 manuscripts published in top-tier journals

>350 personalised healthcare collaborations within Roche

>15 companion tests in development

41 NMEs with companion diagnostic programmes in pipeline

## Access to healthcare



We aim to bring our medicines and diagnostic tests to as many people in need as possible. Every healthcare system comes with different challenges and we customise solutions for individual markets. We work with many different local partners to reduce barriers to accessing healthcare and establish innovative, sustainable ways to bring effective and affordable healthcare to patients.

## Great workplace



We are committed to constantly maintaining and strengthening highly attractive workplaces where every person feels valued and respected and can grow to his or her full potential. Our people make our business. They discover, develop and manufacture our products and ensure they reach the patients who need them. We believe that the key to our success lies in our ability to attract, retain and motivate a highly skilled and diverse workforce.

## Sustainable value



We run our business in a way that is ethical and aims to create long-term value for shareholders and all our stakeholders. We want to create value through developing medical solutions and we aim for as many people to benefit from them as possible. We believe that our success lies in our ability to develop strategies where both industry and society benefit in a sustainable way.

### *Performance in 2014*

250,000 women screened for breast cancer in North Africa through a Roche mobile unit

1.3 million infants tested for HIV as part of Roche's AmpliCare programme

Global access programme for HIV viral load testing launched

81% of our employees are proud to work for Roche

71% fully engaged employees

48% of total workforce are women

11.5% improvement in eco-impact

28<sup>th</sup> consecutive year dividend increase proposed

6 times Group leader Dow Jones Sustainability Indices



# Supporting a strategy of lasting success

*2014 WAS ANOTHER SUCCESSFUL YEAR FOR ROCHE, with a solid business performance, highly promising medical advances and ground-breaking investments. The Board of Directors is once again proposing a dividend increase.*

Dear Shareholders

After my first year as Chairman of the Board of Directors, I am very pleased to present you with solid results. In 2014, despite challenging conditions in some of our markets, particularly Europe, we delivered strong sales growth across both divisions and reported a strong net income of 9.5 billion Swiss francs.

We also had some notable successes in research and development. Thanks to some of our medicines, we helped to improve the treatment of leukemia, pulmonary diseases and skin disorders. We also introduced a test for the detection of the virus causing cervical cancer. Once again, millions of people were treated with our medicines in 2014, and thanks to our diagnostic tests, even more received a reliable diagnosis for the basis of targeted, successful treatment.

*“Our main objective remains to offer patients a better quality of life and, where possible, to cure them or help them live longer.”*

At last year's Annual General Meeting, I made a commitment to continue the course Roche has set to ensure that the Group remains a driver of innovation in the healthcare sector. I am particularly impressed by the large number of projects in our pharmaceutical and diagnostic pipelines. We are tackling serious diseases with high unmet need, such as

bladder cancer, a devastating disease with limited treatment options. Our main goal will always be to use cutting-edge science to offer patients a better quality of life and, where possible, to cure them or help them live longer.

In 2014, Roche invested close to 9 billion Swiss francs in research and development. We are convinced of the enormous potential of modern biosciences and will continue to rigorously pursue our efforts and investments in this area. As the world's largest biotech company, we are in the best possible position to use our knowledge of disease biology to develop new treatments and tests that are better tailored for specific patient groups, making them safer and more effective. But, of course, it's always better to prevent than to treat – and as a global leader in healthcare diagnostics – Roche is playing a crucial role here. From early screening to personalised medicines, our products can help to overcome some of the major challenges healthcare systems are facing today.

Innovation is at the heart of what we do. For us, this means being open to good ideas, including ones generated outside of Roche. In fact, about one third of our pharmaceutical products were born out of a partnership, usually with a smaller biotech firm or university. We maintain an impressive global partnership network spanning over 240 alliances, underpinned by the targeted acquisition of technologies, active ingredients and expertise. In 2014, we entered into a number of important strategic partnerships. The acquisition of the biotech company InterMune, for example, significantly strengthened our portfolio in the area of respiratory disorders with Esbriet, a treatment for a fatal lung disease.

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*“Sustainable success demands long-term thinking.”*

---

Another important achievement for the Group in 2014 was certainly the selection by the Dow Jones Sustainability Indices as the world’s most sustainable company in the life sciences sector for the sixth year running. For me, it’s just another indicator that we’re on the right track. Sustainable success – and this is not only true for Roche – requires long-term thinking and commitment. When it comes to the implementation and development of our long-term strategy, Roche benefits from a tremendous advantage thanks to the guidance, support and trust provided by the Hoffmann and Oeri families. To me, this is one of the Group’s biggest strengths.

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*“Roche’s decentralised management style is a strength that we want to continue to foster.”*

---

In 2014, I visited many of our 150 sites around the world to meet our employees and also get to know the company’s key stakeholder groups. What really stood out for me were the vast differences from one national healthcare system to the

next, along with the unique challenges each system is facing. Our success hinges on giving our employees sufficient responsibility and latitude to adapt to their local situation. In this context, our decentralised management style is a core strength that we want to continue to foster.

Nonetheless, providing access to our innovative tests and medicines in economically weaker countries is a major challenge, particularly in oncology, where treatments are complex and the demands made on facilities, expertise and resources are high. We need to work with local partners, who best understand local barriers, to find ways to help patients and also improve preventive screening.

Whilst our primary focus is always on developing innovative treatments and tests, 2014 was also a year of site expansions. This is largely to provide more space for our growing workforce, additional research infrastructure, and increased production capacities. The biggest investment we announced was in our Basel headquarters, where we aim to invest 3 billion Swiss francs over the next decade, primarily in a new, modern research centre and in a second, state-of-the-art office building. In addition, we will spend 450 million Swiss francs on increasing our production capacity in China over a three-year period in order to meet the growing demand for our diagnostic tests. We are also investing in an IT hub at another site in Switzerland, in modern research laboratories in South San Francisco, and in expanding our research and production capacities in Germany.



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*“In light of our good performance, we propose a 3% dividend increase to 8.00 Swiss francs per share and non-voting equity security.”*

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Roche is a very successful company with excellent prospects. However, I know from personal experience that it requires just as much effort to keep a company at the top as it does to get it there. Roche is unique in that it is focused on science-driven innovation, cooperative despite a decentralised structure, rooted in Switzerland, but open to the world. We are deeply committed to sustaining this distinctive culture in the future.

Whilst I look forward to addressing you in person at the 97<sup>th</sup> Annual General Meeting (AGM) of Roche Holding Ltd on 3 March 2015, I would like to highlight two important items on the agenda.

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*“We are proposing two prominent figures, with a wealth of experience in the pharmaceutical sector, as new Board members.”*

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In light of our strong performance and solid outlook, the Board of Directors is proposing a 3% dividend increase to 8.00 Swiss francs per share and non-voting equity security. Subject to your approval, this will be the 28<sup>th</sup> consecutive dividend increase.

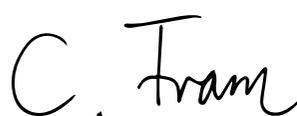
In addition to the re-election of existing members, the AGM will see some changes on the Board of Directors. Art Levinson decided to step down from the Roche Board of Directors to avoid potential conflicts of interest following his appointment as CEO of a research institution. Art has been a major contributor to Genentech's success over the years. Under his leadership, Genentech has become one of the most important biotech companies in the world. He joined the Board of Directors of Roche in 2010, following the integration of Genentech. On behalf of the Board, I would like to thank him sincerely for his invaluable contribution to the company's overall success.

I am delighted to propose Bernard Poussot and Professor Richard Lifton as new members of the Board of Directors. These two prominent figures would bring a wealth of experience in the pharmaceutical sector and basic biomedical research respectively. Bernard comes from Wyeth where he spent 23 years leading the company in positions including President, CEO, and Chairman. Director of the Yale Center for Genome Analysis, Richard is an award-winning scientist who provided valuable insights as a member of advisory boards of various leading pharmaceutical companies.

With its clear strategic focus on innovative medicines and diagnostics, Roche is well positioned to continue growing. The Board of Directors and Management are committed to ensuring that Roche remains one of the world's most successful research-based healthcare companies.

I would like to take this opportunity to extend sincere thanks – as does the entire Board of Directors – to our 88,509 employees, as well as to the Corporate Executive Committee, for their achievements.

I also wish to thank you, valued shareholders, for your confidence in our company.



Christoph Franz  
Chairman of the Board

# Board of Directors



**Prof. Sir John Irving Bell (1952)**  
B, E

**Dame DeAnne Julius (1949)**  
B\*, E

**Prof. Pius Baschera (1950)**  
A, E

**Dr Christoph Franz (1960)**  
C, D\*, E, Chairman

**André Hoffmann (1958)**  
Representative of the shareholder group with  
posted voting rights, A, C\*, D, E, Vice-Chairman

A Corporate Governance and Sustainability Committee  
 B Audit Committee  
 C Remuneration Committee  
 D Presidium/Nomination Committee

E Non-executive director  
 F Executive director  
 \* Committee chairperson

Roche Board of Directors  
 on 31 December 2014



**Paul Bulcke (1954)**  
 B, E

**Prof. Beatrice Weder di Mauro (1965)**  
 B, E

**Dr Severin Schwan (1967)**  
 F

**Dr Andreas Oeri (1949)**  
 Representative of the shareholder group with  
 posted voting rights, A\*, E

**Peter R. Voser (1958)**  
 C, E



# Building our capabilities for the future

*IT IS TESTAMENT to the strength of our portfolio and the commitment of our employees that we were able to achieve eleven pharmaceutical product approvals and launch fourteen new diagnostic instruments and tests.*

Dear Shareholders

Our innovation based strategy and our focus on excellence in science led us to a number of significant breakthroughs for patients in 2014. A highlight was the unprecedented clinical trial results for Perjeta, one of our medicines for a very aggressive type of advanced breast cancer, which showed that it could help patients live for as long as five years. Another was our new HPV test, which can detect the virus that can cause cervical cancer earlier and is now approved for primary screening in the United States. As we worked to deliver the next generation of medicines and tests, our financial performance remained solid.

Demand for our products was high in both divisions, with 4% growth in Pharmaceuticals and 6% in Diagnostics. I was very pleased to see a substantial contribution coming from our new products, particularly Perjeta and Kadcyla for HER2-positive breast cancer. Our oncology portfolio continues to grow strongly, as does our immunology portfolio, especially Actemra, our medicine for rheumatoid arthritis and Xolair for chronic hives and asthma.

Our net income in 2014 decreased by 10%. This was a result of costs relating to restructuring of part of our debt, as well as impairments and restructuring programmes. The underlying strength of our company was not affected and without these items, net income would have been 6% higher than in 2013. Core earnings per share were 14.29 Swiss francs, 5% higher at constant exchange rates. Excluding a one-time double charge relating to the US Branded Prescription Drug fee, core earnings per share were 7% higher.

We continue to make good progress with our product pipeline. In 2014 alone, three medicines were granted Breakthrough Therapy Designation from the FDA, reflecting the potential benefit these medicines could offer to patients: anti-PDL1, one of our immunotherapy medicines, showed encouraging results in advanced bladder cancer, a disease that has seen no advances in treatment in 30 years and affects 400,000 people worldwide. Lucentis, our eye medicine, which is already approved in a number of different indications, for use in diabetic retinopathy. And Esbriet, a medicine which we brought into the portfolio last year

**5%** increase in Group sales\*

**3** FDA Breakthrough Therapy Designations

**11** pharmaceutical product approvals

**14** diagnostic product launches

\* Unless otherwise stated, all growth rates in this report are at constant exchange rates (CER; average full year 2013).

through the acquisition of InterMune, was approved in the US for the treatment of lung fibrosis in October.

We also had positive data from the combination of the new compound cobimetinib and Zelboraf, which demonstrated remarkable improvements for patients with advanced melanoma, a deadly form of skin cancer.

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*“Innovation comes with an inherent risk of failure.”*

---

Developing highly innovative medicines comes with an equally high risk that a medicine in development may not work as we had hoped and in this regard, 2014 was no exception. Whilst the medicine Kadcyla has been shown to significantly help patients as a second-line therapy in HER2-positive breast cancer, last year’s trial results for patients with previously untreated (first-line) advanced breast cancer unfortunately did not show the improvements we were hoping for. Kadcyla is a ground-breaking innovation in the treatment of this aggressive disease and we will continue to study it in different settings and combinations.

We had some setbacks in neuroscience during the year. Bitopertin, a medicine that was being developed to treat the negative symptoms of schizophrenia, did not reach its

primary endpoints; and one of our clinical trials of gantenerumab for treating the early stages of Alzheimer’s disease was discontinued. Both results, however, have greatly helped advance our understanding of neurological and psychiatric disorders. Neuroscience is an area of rapidly evolving science and high unmet medical need, and with 15 new molecules in development, it will remain a focus area for Roche.

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*“1.5 million people have been treated with Avastin since it was first approved in 2004.”*

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It is very encouraging to see just how many of our existing medicines are being approved for additional indications. One of our cancer medicines, Avastin, was approved in two new indications in 2014, cervical cancer and platinum-resistant ovarian cancer. Avastin is now used to treat seven different cancers and is still at the forefront of a new generation of treatment. In September, we had positive preliminary data on Avastin in combination with the immunotherapy drug candidate, anti-PDL1, in renal cancer; as well as positive phase III results in combination with our chemotherapy medicine, Xeloda, in HER2-negative breast cancer.



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*“Diagnostic testing is critically important in treatment decisions.”*

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Modern diagnostics is an area with huge potential, not only in managing disease – from early diagnosis to monitoring – but in avoiding illness in the first place. In 2014, we launched a new test to assess fertility levels, as well as a test to predict the likelihood of preeclampsia, a serious condition affecting 1 in 20 pregnancies. We were also able to speed up development of a diagnostic test for the Ebola virus, which the FDA has approved for emergency use. Another very significant milestone for our Diagnostics business was the launch of our new fully integrated laboratory testing systems, the cobas 6800 and cobas 8800, which deliver faster and more accurate molecular test results.

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*“For millions of people, access to innovative medicines is a world away.”*

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Whilst science and medicine are progressing at an incredible rate, gaps in access to quality healthcare are growing. I believe that as a healthcare company, we can be an important part of the solution to improve access to quality medicines and diagnostic tests. But we cannot do this alone. The barriers to accessing healthcare provision are multiple and complex. We are working in partnerships all over the world to overcome these barriers, be they infrastructure, affordability, training, supply or awareness.

This year we strengthened our approach with a new framework to analyse the barriers to access to healthcare. With this, we can analyse the root causes in individual healthcare systems more systematically and identify the right partners to work with to support improvements. 2014 also saw the launch of a new strategy to bring more innovative medicines into sub-Saharan Africa, where access is very difficult. Another initiative that I am particularly proud of is the Global Access Programme for HIV viral load testing, which was also launched in 2014.

Our achievements come from the difference our employees make. We are committed to ensuring that our innovation culture thrives at Roche through the diverse perspectives that reflect our global business. We are continuing to invest in new facilities and infrastructure for our employees and our science and we aim to retain our industry-leading levels of employee engagement. I would like to thank each and every employee for the difference they have made and to thank you, our shareholders, for your continued confidence in Roche.

Looking ahead, for 2015, we expect low to mid-single digit Group sales growth at constant exchange rates. Core earnings per share are targeted to grow ahead of sales at constant exchange rates.\* We also expect to further increase our dividend.

I am convinced that our uncompromising focus on medical innovation will continue to drive our business success well into the future.



Severin Schwan  
Chief Executive Officer

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\* This outlook excludes the benefit of 428m Swiss francs related to the divestment of filgrastim rights in 2014.

# Corporate Executive Committee



**Roland Diggelmann (1967)**  
COO Division Roche Diagnostics

**Silvia Ayyoubi (1953)**  
Head Group Human Resources

**Dr Gottlieb A. Keller (1954)**  
General Counsel

**Dr Alan Hippe (1967)**  
Chief Financial and IT Officer

**Dr Stephan Feldhaus\* (1962)**  
Head Group Communications

\* Member of the Enlarged Corporate Executive Committee

<sup>1</sup> Dr Richard Scheller retired on 31 December 2014. Dr Michael D. Varney became Head of gRED and member of the Enlarged Corporate Executive Committee on 1 January 2015.

Roche Corporate Executive Committee on 31 December 2014



**Dr Richard Scheller\*<sup>1</sup> (1953)**

Head Genentech Research and Early Development (gRED)

**Dr Severin Schwan (1967)**

CEO of the Roche Group

**Osamu Nagayama\* (1947)**

Chairman and CEO Chugai

**Daniel O'Day (1964)**

COO Division Roche Pharmaceuticals

**Dr Sophie Kornowski-Bonnet\* (1963)**

Head Roche Partnering

**Prof. John C. Reed\* (1958)**

Head Roche Pharma Research and Early Development (pRED)

# Business review and market environment



**47.5** BILLION  
Swiss francs in **sales\***

**17,636** MILLION  
Swiss francs in **core operating profit**

**14.29** Swiss francs in  
**core earnings per share**

**Sales growth in all regions**

North America  
**+6%**

Europe  
**+3%**

Latin America  
**+10%**

Asia-Pacific  
**+8%**

Japan  
**+6%**

\* Unless otherwise stated, all growth rates in this report are at constant exchange rates (CER; average full year 2013).

## Solid growth in both divisions

*DEMAND REMAINED HIGH for our innovative medicines and diagnostic tests, in a year with significant medical breakthroughs and strategic acquisitions to build new capabilities.*

Group sales reached 47.5 billion Swiss francs in 2014. Growth in Pharmaceuticals was driven by medicines for HER2-positive breast cancer (+20%), as well as Avastin (+6%). New products, Perjeta and Kadcyla for HER2-positive breast cancer, made a significant contribution to growth, more than offsetting declining sales of Xeloda, a medicine that now faces generic competition. There was also strong demand for immunology medicines, notably Actemra (+23%) for rheumatoid arthritis and Xolair (+25%) for chronic hives and allergic asthma. Sales of Tamiflu (+54%) increased considerably late in the year, as a result of the US flu epidemic.

In Diagnostics, sales continued to be driven by the Professional Diagnostics business, which grew 8%, whilst Molecular Diagnostics was 6% higher. There was also positive early uptake for the new molecular laboratory testing systems, launched during the year, the cobas 6800 and the cobas 8800.

The Swiss franc rose against a number of currencies in 2014, mainly the Japanese yen, along with a number of Latin American currencies and the US dollar. Overall, this led to a negative impact on the results reported in Swiss francs.

We had positive news from the pipeline in 2014, with three Breakthrough Therapy Designations from the FDA. We also had very positive results from the clinical trial study of the combination of Perjeta, Herceptin and chemotherapy, which increased survival time for patients with advanced HER2-positive breast cancer to almost five years. In Diagnostics, the FDA, along with a number of other health authorities, approved our HPV test in primary screening for cervical cancer. Overall, these advances in science reflected the strength of both the Pharmaceuticals medicine pipeline and Diagnostics innovation. For more information, please see the Innovation chapter of this Annual Report on page 52.

### Key figures 2014

	In millions of CHF 2014	In millions of CHF 2013	% change CER*	% change CHF
Group sales	47,462	46,780	5	1
Pharmaceuticals Division	36,696	36,304	4	1
Diagnostics Division	10,766	10,476	6	3
Core operating profit	17,636	17,904	3	-1
Core net income	12,533	12,526	6	0
IFRS net income**	9,535	11,373	-10	-16
Core earnings per share (CHF)	14.29	14.27	5	0

\* CER: constant exchange rates average full year 2013.

\*\* IFRS: International Financial Reporting Standards.

**Building up capabilities with strategic acquisitions**

Roche made a number of acquisitions during the year, including InterMune, the developer of Esbriet, a medicine for idiopathic pulmonary lung fibrosis, and Seragon Pharmaceuticals, which is researching treatment for hormone receptor-positive breast cancer. In Diagnostics, acquisitions were made to expand into point-of-care molecular testing and add new technology in gene sequencing.

**Core operating profit and cash generation**

Core operating profit increased by 3%, reflecting a double charge of 202 million Swiss francs of the US Branded Prescription Drug fee,<sup>\*\*\*</sup> following final regulations issued by the Internal Revenue Service, which advanced the timing of recording the liability. Excluding this double charge, core operating profit was 5% higher.

Operating free cash flow was 15.8 billion Swiss francs. The strong cash generation of the underlying operations was offset by higher capital investments in manufacturing facilities and other site development projects, resulting in a 2% decrease at constant exchange rates. Free cash flow was 5.3 billion Swiss francs, 1% higher at constant exchange rates.

**Restructuring and impairments**

IFRS net income was negatively impacted by debt restructuring, impairments and restructuring costs in 2014. The Group restructured part of its debt in 2014 to take advantage of the low interest environment. Net of tax, this measure resulted in a one-time loss of 279 million Swiss

francs, but will lead to interest savings over the longer term. Intangible impairments increased by 1.1 billion Swiss francs, in particular in Tissue Diagnostics, following the reassessment of a product in late-stage development and cuts in US laboratory test reimbursement. Costs for restructuring increased by 252 million Swiss francs due to a non-recurring, one-time income effect in the 2013 IFRS results.

The performance of the underlying business remained strong, with core earnings per share 5% higher at constant exchange rates, and stable in Swiss francs. Excluding the one-time double charge of the US Branded Prescription Drug fee, core earnings per share were 7% higher. Based on the strong business results, the Board of Directors has recommended the 28<sup>th</sup> consecutive dividend increase, 3% to 8.00 Swiss francs per share.

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**14.29** SWISS  
FRANCS  
CORE EARNINGS PER SHARE

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**Outlook for 2015**

For 2015, we expect low to mid-single digit Group sales growth at constant exchange rates. Core earnings per share are targeted to grow ahead of sales at constant exchange rates.<sup>\*\*\*\*</sup> We also expect to further increase the dividend.

<sup>\*\*\*</sup> US Annual Fee on Branded Prescription Drug Manufacturers and Importers.

<sup>\*\*\*\*</sup> This outlook excludes the benefit of 428m Swiss francs related to the divestment of filgrastim rights in 2014.



## The big picture

*THE OUTLOOK for the healthcare industry remains positive, but there are significant challenges. The world's growing and ageing population is driving demand for healthcare services, whilst supply is coming under increasing pressure.*

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Increasing access to healthcare is an expensive business for governments and the healthcare sector. Life sciences companies are faced with the challenge of delivering innovation and value in an environment of cost containment and public budget restrictions.

In addition, the world has witnessed major gains in life expectancy in recent decades. Low-income countries have made the most progress, increasing average life expectancy by nine years. And with increased life expectancy comes increased healthcare costs. The proportion of people aged over 60 years is growing faster than any other age group, a trend that has the potential to transform societies globally and see millions of people living with chronic diseases.

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*Average life expectancy has increased by six years, to 73 years for women and 68 years for men since 1990.<sup>1</sup>*

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Declining fertility rates have also played a role in these changing demographics, with the proportion of elderly people continuing to increase. And medical breakthroughs have meant that many more people can live longer whilst being treated for chronic conditions. Chronic diseases, however, are still the leading cause of mortality worldwide. Illnesses such as heart disease, stroke, cancer, chronic respiratory diseases and diabetes cause 63% of all deaths.<sup>2</sup> These illnesses are amongst the most costly, but the good news is that they are often preventable.

The combined trends of ageing populations and an increase in chronic disease are expected to drive demand for healthcare services. Average annual worldwide spending on healthcare is forecast to rise by 5.3% over the next three years.<sup>2</sup>

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**CHRONIC DISEASES  
ALREADY  
ACCOUNT FOR 75%  
OF EUROPE'S € 700 BILLION HEALTHCARE BILL<sup>3</sup>**

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# Focusing on value

Most countries face a formidable challenge managing the rapidly increasing cost of healthcare, whilst simultaneously improving patient outcomes and access to care. The continuing pressure on healthcare budgets, combined with muted economic growth over the last few years, has led many countries to introduce cost-control measures, including prescription drug price cuts and evidence-based medicine. The shift from volume- to value-based healthcare rewards providers for improving care and lowering costs as a way to make health systems more sustainable.

*The cost of Alzheimer's care is expected to reach 1.2 trillion US dollars in the US alone by 2050.<sup>4</sup>*

For healthcare companies, this means closer scrutiny of new medicines or medical devices. More than ever, companies must clearly demonstrate evidence of better health outcomes at reasonable costs to an increasingly broad range of stakeholders. These include health technology assessment agencies, insurers and payers, patient advocacy groups and hospital administrators, amongst others, that are playing an increasingly important role in the selection and purchase of medical products. The primary effect of this trend has been to raise barriers to reimbursement for all but high-value, innovative drugs, especially cancer treatments.

All healthcare stakeholders, however, share the goal to define, measure and improve the value of care delivered to patients.

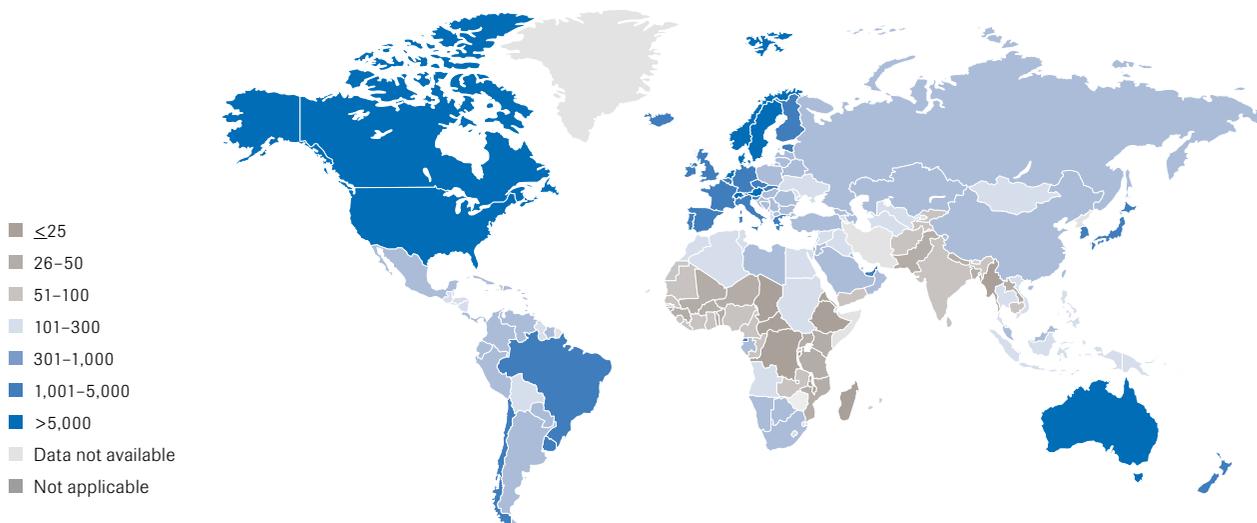
# Access to healthcare

Access to healthcare remains a global challenge. Healthcare varies significantly from one country to another and even within a region or a country. Life expectancy in Romania, for instance, is nine years less than in Spain.<sup>5</sup> In some countries, sophisticated medicines and tests are widely available, whilst in others there is little or no basic infrastructure. Even in established markets, medicines can take years to become available to patients.

Improving access to healthcare is an objective in many countries and central to many reform efforts, but finding affordable, effective solutions is an enormous task.

Governments face challenges on many fronts. In addition to the rising cost of healthcare, workforce shortages and poor healthcare infrastructure can also hamper efforts to improve care. Patients often live in remote or

## Healthcare spending worldwide varies dramatically<sup>6</sup>



1 WHO. World Health Statistics 2014. | 2 Deloitte. 2014 Global healthcare outlook: shared challenges, shared opportunities. | 3 EFPIA contribution on the Public Consultation of the European Commission's Green paper on mobile health 2014. | 4 Alzheimer's Association, 2014 Alzheimer's Disease Facts and Figures. Alzheimer's Dementia, Use and Costs of Healthcare, Long-Term Care and Hospice. | 5 EFPIA. Health & growth working together for a healthy Europe. A vision towards a life sciences strategy for Europe 2014. | 6 WHO. Health financing 2014. Per capita total expenditure on health at average exchange rate (USD).

difficult-to-reach regions, such as 80% of the population of India, which also makes access to healthcare difficult to improve.

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*The number of doctors for every 1,000 people worldwide is expected to remain virtually the same throughout 2015.<sup>2</sup>*

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The incidence of breast, lung, gastric and colorectal cancer in many countries is also rising rapidly, especially in urban areas in emerging markets. The adoption of Western diets and sedentary habits, cigarette smoking and environmental pollution have all contributed to the increase in cancer rates, but access to proper treatment is patchy at best. And whilst the number of cancer patients is increasing, the percentage of those getting access to treatment is not. An ageing population, increased unemployment and economic pressures further aggravate inequalities in access to healthcare.

Eighty countries, backed by a consortium of supra-national bodies including the World Health Organization, the World Bank and Save the Children, are taking steps

towards achieving universal health coverage. This is defined as everyone having access to quality health services without financial hardship. In practice, the aim is for healthcare costs to be shared amongst entire populations through pre-payment and risk-pooling, rather than shouldered by the sick. By 2030, the aim is for all populations, independent of household income, expenditure or wealth, place of residence or gender, to have at least 80% essential health services coverage; as well as 100% financial protection from out of pocket expenses.

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**100**  
**MILLION PEOPLE**  
**FALL INTO POVERTY**  
**EVERY YEAR TRYING TO**  
**ACCESS HEALTHCARE<sup>7</sup>**

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## Technological advances

Companies in the life sciences sector have long embraced technology. Today, rapid and accelerating technological advances are transforming imaging, genomics, proteomics, diagnostics and other disciplines. New technology, combined with medical breakthroughs, is also playing an important role in new approaches to improving patient outcomes and reducing costs with innovations such as personalised healthcare.

Even readily available and inexpensive technologies like text messaging and smartphone apps are helping to improve lives in developing countries. In the Middle East, Asia and Africa, for instance, wireless and mobile telecommunication has enabled patients living in isolated areas to gain access to healthcare and engage in their own care by monitoring medical conditions and promoting health.

Key is also data from clinical trials, which provides insight into the effectiveness of treatment, safety and disease management, and when combined with real-world data has considerable potential to benefit patients and healthcare

systems. This data helps payers and providers assess the value of treatment guidelines, patient pathways and specific interventions. Importantly, it can also help to identify patients at risk of developing specific diseases early by using algorithms of disease risk factors from patient data. The challenge for the pharmaceuticals industry, however, is to find ways to properly compare and use in-house and real-world data, which is subject to different interpretations and inconsistencies.

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*The biggest challenge is to generate meaningful conclusions from enormous volumes of data.*

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Overcoming these challenges requires new investment in technology and partnerships amongst healthcare stakeholders.

<sup>7</sup> WHO. Universal health coverage (UHC) 2014. | <sup>8</sup> The Economist Intelligence Unit. Healthcare 2015. | <sup>9</sup> IDF diabetes atlas. Sixth edition 2013.



## Growth of emerging markets

Healthcare spending as a percentage of gross domestic product (GDP) varies considerably around the world: from 16.5% of GDP in North America and 10.6% in Western Europe, to 7.6% in Latin America and around 6.5% in Asia/Australasia and 5.8% Middle East/Africa.<sup>8</sup>

*Spending on healthcare is growing significantly in many emerging markets.*

Although there are clear disparities between different markets, growing prosperity, better nutrition and shifting disease patterns are driving growth in emerging markets.

Diabetes, for example, is growing exponentially in emerging markets, and is expected to reach globally 590 million people living with diabetes by 2035.<sup>9</sup>

There are, however, significant challenges in emerging markets, ranging from lack of infrastructure and trained professionals, to affordability, and major differences between local private and public healthcare.

Market growth in the healthcare sector is closely connected to GDP growth, population growth, an ageing population, government spending and, in some regions, rising wealth. So despite its challenges, emerging markets are expected to represent a third of the global pharmaceutical market by 2016.

### The rise of emerging markets in healthcare spending (in billion US dollars)

2005		2010		2016	
Rank	Size	Rank	Size	Rank	Size
1. USA	249.2	1. USA	322.0	1. USA	350-380
2. Japan	84.9	2. Japan	111.2	2. China ▲ +1	155-165
3. France	33.3	3. China ▲ +6	66.7	3. Japan ▼ -1	105-135
4. Germany	33.1	4. Germany	45.0	4. Brazil ▲ +2	42-52
5. Italy	21.3	5. France ▼ -2	41.3	5. Germany ▼ -1	39-42
6. UK	16.4	6. Brazil ▲ +4	29.9	6. France ▼ -1	32-42
7. Spain	16.1	7. Italy ▼ -2	28.6	7. Italy	23-33
8. Canada	15.9	8. Spain ▼ -1	22.7	8. India ▲ +5	24-34
9. China	14.1	9. Canada ▼ -1	22.4	9. Russia ▲ +2	23-33
10. Brazil	11.8	10. UK ▼ -4	21.5	10. Canada ▼ -1	19-29

■ Emerging markets ▲ Placement movement

Source: IMS Health 2014.

# Diagnostics





**10.8** BILLION Swiss francs in sales  
**+6%\***

**450** MILLION Swiss francs  
**investment in China**

**8%** **sales growth**  
in Professional Diagnostics

**14** **diagnostic products launched**

\* Unless otherwise stated, all growth rates in this report are at constant exchange rates (CER; average full year 2013).

# Good sales growth in 2014

*THE DIAGNOSTICS DIVISION sales continued to increase strongly at 6% to 10.8 billion Swiss francs. Professional Diagnostics, with 8% sales growth, was the main growth contributor led by its immunodiagnosics business.*

Sales of Molecular Diagnostics increased by 6%, with 8% growth in the underlying molecular businesses. Sales were up 10% in Tissue Diagnostics and 1% in Diabetes Care.

Sales growth across the Diagnostics Division was driven by demand in the Asia–Pacific region (+15%), with a strong performance in China (+23%). Sales also increased in Europe, the Middle East and Africa (EMEA; +4%). Additional contributions came from North America (+4%) and Latin America (13%). In Japan, sales were flat.

### Professional Diagnostics

Outperforming the market in all regions, Professional Diagnostics demonstrated strong growth at 8%. Growth was primarily driven by the immunodiagnosics business (+13%), which now represents 26% of divisional sales. This was supported by the clinical chemistry business (+7%) and coagulation monitoring (+8%).

The Professional Diagnostics business was the major contributor to divisional performance in all regions, especially in Asia–Pacific (+18%), with continued strong sales in China.

In 2014, the cobas 6500, a new automated instrument for urine analysis, the Elecsys Syphilis and the Elecsys anti-Müllerian Hormone tests were launched. Also, new study results highlighted the value of the Elecsys preeclampsia tests in predicting preeclampsia in pregnant women. This test is already available in the EU and all countries accepting the CE mark, a market authorisation designation. The additional usage of these tests further broadens our portfolio for women's health and reconfirms our commitment to this area.

### Sales growth of the Diagnostics Division by region



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**Top-selling diagnostics** in millions of Swiss francs
 

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**cobas e602**  
Immunodiagnosics

**2,797** +13%



**Accu-Chek Aviva Nano**  
Blood glucose meters

**2,159** +1%



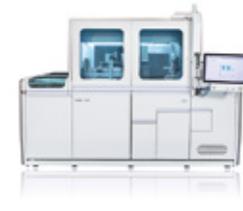
**cobas c502**  
Clinical chemistry

**1,626** +7%



**BenchMark Ultra**  
Tissue diagnostics

**716** +10%



**cobas 6800**  
Virology

**530** +7%

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### Molecular Diagnostics

Sales rose by 6% with strong growth in the underlying molecular businesses (+8%, excluding sequencing), with the major contributions coming from virology (+7%) and human papillomavirus (HPV) screening (+48%). All regions, except Japan, showed positive sales development, with the biggest growth contribution coming from North America as a result of strong performance in HPV, blood screening and hepatitis C virus monitoring.

In 2014, the fully automated cobas 6800 and 8800 systems and assays for blood screening as well as virology testing were launched in markets accepting the CE mark. The cobas HPV test was approved for primary screening for cervical cancer in Australia, Canada and the US. Three additional diagnostic tests (MRSA/SA, C-difficile, HSV), which expand the cobas 4800 menu, were launched in countries accepting the CE mark.

Roche also made several important acquisitions in this space including IQuum, Inc., Genia Technologies, Inc., and Ariosa Diagnostics, Inc. (completed in early 2015). IQuum provides Roche with access to the Liat™ (Laboratory-in-a-tube) system, which performs rapid point-of-care molecular diagnostic testing. The analyser and two initial assays, cobas Influenza A/B and cobas Strep A, are CE marked and FDA-cleared. Importantly, Genia brings Roche a single-molecule, semiconductor-based DNA sequencing platform using nanopore technology. Finally, Ariosa adds a highly targeted and accurate non-invasive prenatal testing service to Roche's portfolio. Ariosa's proprietary Harmony™ Prenatal Test is a blood test that is performed as early as ten weeks into pregnancy and designed to assess the risk of Down syndrome and other genetic abnormalities.

### Tissue Diagnostics

Sales rose 10%, driven by 9% growth in the advanced staining portfolio, which includes immunohistochemistry reagents (+10%). The CINtec franchise for cervical cancer diagnosis grew by 18%, showing continued good uptake. Regionally, growth was driven by EMEA, North America and Asia-Pacific. In North America, sales increased despite reimbursement reductions.

### Diabetes Care

Sales were up 1% despite continuing challenging market conditions for the blood glucose monitoring portfolio in major markets, including the US. Sales increased in EMEA, Asia-Pacific and Latin America, which strengthened the business unit's global market leadership position in blood glucose monitoring. In North America, however, sales were down 6% as a result of Medicare changes in the reimbursement of test strips in the US and changes in the number of reimbursed strips in Canada. In Japan, sales declined by 6% impacted by strong competition and the bi-annual price cut by the health authorities.

Sales of the premium product Accu-Chek Mobile grew 19%, while Accu-Chek Aviva/Performa grew 7%. The Accu-Chek Insight system, the new insulin delivery system combining insulin pump and a blood glucose metre, and the Accu-Chek Connect system, which connects a blood glucose metre to mobile applications via smartphones and web-based platforms for Diabetes Care self-management, were launched in the EU in 2014. Additionally, efficiencies were gained across this business area with the implementation of specific initiatives started in 2013, helping to streamline processes and decision-making.



## Setting new industry standards with our innovative instruments

### Fully automated instruments for molecular testing

Roche launched the cobas 6800 and cobas 8800 systems, two integrated and fully automated molecular testing systems, in Europe and markets accepting the CE mark.

The cobas 6800 system and cobas 8800 system represent a new class of molecular diagnostic instruments which were developed to meet the evolving needs of the medium and the high volume of molecular diagnostics laboratories. These systems are setting new industry standards with technical innovation for throughput, speed of results, automation and flexibility.

The portfolio launched includes the cobas 6800 system and 8800 system, and next generation tests for donor blood screening as well as multiple tests for viral load monitoring.

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*Setting new industry standards for throughput, speed of results, automation and flexibility.*

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Each system provides results for the first 96 tests in less than 3.5 hours, with the cobas 6800 system delivering up to 384 results in an eight-hour shift, and the cobas 8800 system generating up to 960 results in the same amount of time. Both systems also allow for simultaneous processing of multiple assays and are designed to enable up to eight hours (cobas 6800 system) and four hours (cobas 8800 system) of 'walk-away' time with minimal user interaction.

### Enhanced result reliability and staff safety

A new, fully automated urine testing system, the cobas 6500, consists of two modular analysers combining urine strip testing and digital urinary microscopy and allows tests for 23 parameters to help diagnose diseases such as urinary tract infection, kidney disease and diabetes. It offers the highest throughput on the market, ensures high-quality results and increases laboratory productivity significantly, whilst reducing manual steps and contamination risks for laboratory staff. The system is available worldwide except in the US, where the launch coincides with an FDA clearance of the cobas u 701 and cobas u 601 modules.

### Additional diagnostic tests for women's health

Cervical cancer is the third most common cancer in women, with approximately 270,000 women dying from this disease each year. The most common cause of cervical cancer is HPV infection.<sup>1</sup>

Approvals of the cobas HPV test for primary screening in Australia, Canada and the US in 2014 followed the CE mark designation in Europe. With this new indication, Roche's CINtec Histology test and the newly fully automated CINtec PLUS Cytology kit, we offer the most comprehensive cervical cancer screening portfolio in the industry, supporting physicians across the globe to screen, diagnose and treat women with pre-cancerous lesions before full-blown cancer develops.

If caught early, cervical cancer is one of the most preventable and curable cancers with a survival rate of more than 90%. In cases when the disease has advanced at the time of the diagnosis, the average five-year survival rate is only around

20%.<sup>2</sup> (See the spotlight on Catherine Behrens, who worked on the cobas HPV test, on page 68).

## The survival rate with cervical cancer is more than 90%, if caught early.<sup>2</sup>

### Assessment of ovarian reserve for pregnancy

Fertility issues affect one in ten couples, accounting for up to 80 million people globally and this number is on the rise. Roche launched the new Elecsys anti-Müllerian Hormone Fertility test which increases the accuracy of ovarian reserve assessment compared to conventional methods.

### Prognosing preeclampsia

Results of the PROGNOSIS study are helping to support the extended use of the Elecsys Preeclampsia test to predict the absence of preeclampsia in pregnant women for one week and the development of preeclampsia within the subsequent four weeks. The test results enable healthcare professionals to avoid unnecessary hospitalisations, optimise prenatal care and improve outcomes for mother and child.

### Prenatal testing

The acquisition of Ariosa Diagnostics, Inc., brought a highly targeted, accurate and non-invasive prenatal testing service to Roche's portfolio.

Ariosa's proprietary Harmony™ Prenatal Test is a blood test that is performed as early as ten weeks into pregnancy. By evaluating circulating fetal DNA found in maternal blood, the test is designed to assess the risk of Down syndrome and other genetic abnormalities.

From fertility and pregnancy testing to breast, cervical and ovarian cancer management to monitoring and management of chronic, age-related conditions like osteoporosis, these tests further strengthen our broad portfolio of tests for women's health, providing clarity to women at every stage of their lives.

### Identifying syphilis in routine samples and donated blood

Syphilis is a sexually transmitted infection caused by the bacterium *Treponema pallidum*. Some 36 million people are currently infected with syphilis worldwide, with 12 million new cases reported every year.<sup>3</sup> The Elecsys Syphilis immunoassay helps to detect patients infected with syphilis in routine clinical practice and to make sure donated blood is not infected with syphilis. This disease has re-emerged as a health concern in a number of developed nations over the past decade.

## Key launches 2014

Area	Product name	Description	Market
<b>Instruments/Devices</b>			
Laboratories	cobas 6800/8800	next generation molecular (PCR) systems	WW*
	cobas 6500	automated urinalysis work area platform	EU
	VENTANA Connect	middleware providing connectivity to laboratory information systems	WW
Diabetes Care	Accu-Chek Insight	next generation insulin pump and blood glucose monitoring system	EU
	Accu-Chek Connect	blood glucose meter with connectivity to mobile applications and cloud	EU
<b>Tests</b>			
Oncology	MPX	next generation blood screening test	US
	MPX (HIV, HCV, HBV), HEV, DPX**, WNV***	full NAT blood screening menu for cobas 6800/8800	WW*
	HIV, HBV, HCV, HBV	virology tests for cobas 6800 and cobas 8800	WW*
	HSV	<i>Herpes simplex virus</i> detection on cobas 4800	EU
	Syphilis	<i>Treponema pallidum</i> detection (immunoassay)	EU
Microbiology	MRSA/SA	next generation assay on cobas 4800	EU
	C-difficile	diagnosis of infections and associated diarrhea	EU
Women's Health	AMH	assessment of ovarian reserve for fertility	EU
	PE Prognosis	short-term prediction of preeclampsia in pregnancy (claim extension)	EU

\* Excluding the US. | \*\* Parvovirus B19 and hepatitis A virus. | \*\*\* West Nile virus.

1 WHO. Sexual and reproductive health: New guidance for the prevention and control of cervical cancer 2015. | 2 National Cancer Institute. SEER Stat Fact Sheets: Cervix Uteri Cancer. | 3 WHO. Global incidence and prevalence of selected curable sexually transmitted infections - 2008 (2012).

# How we are adding value in healthcare

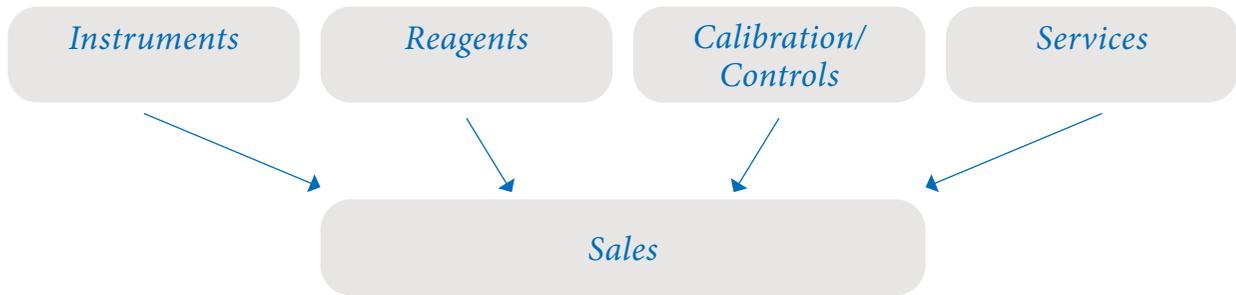
The huge potential of modern diagnostics in keeping people healthy by preventing diseases or guiding treatment decisions is often overlooked. The value of diagnostics lies in knowing. Tests performed on patients' tissue samples, blood or other fluids provide crucial answers about a disease. Whether it is the risk for a disease or a patient's response to treatment, a sample of blood gives physicians and caretakers critical knowledge, enabling them to intervene early and to actively manage health conditions.

Today, diagnostics is no longer just a stepping stone to treatment. It is about intervention. It is about better disease management and better patient care. It is about preventing

a disease from getting worse – or even – before it starts. Modern diagnostics reduce costs by diminishing health problems, decreasing hospitalisation and avoiding unnecessary treatment. The future of sustainable healthcare depends on diagnostics. In 2014, approximately three billion tests were conducted with Roche tests (excluding Diabetes Care), supporting physicians in their decision-making.

*Three billion test results – three billion decision points supporting optimal patient care.*

## Our business model



Our customers' needs for instruments, tests and services depend on their specific focus and the way they organise their business. This in turn results in a diversity of commercial models that Roche offers to meet this demand. Overall, our sales are generated predominantly by the reagents business. Additional contributions come from sales of instruments, fees for calibration, controls, as well as from services provided to the laboratories. As the market leader in *in vitro* diagnostics, Roche operates a large number of instruments in laboratories worldwide, with more than 55,000 instruments for immunodiagnosics and clinical chemistry alone. Beyond that, we also offer systems for

polymerase chain reaction-based molecular diagnostic testing or tissue analysis.

Running a broad portfolio of tests on this installed base allows economies of scale for our customers since it helps the laboratories to optimise their operations by ensuring efficient usage of their resources, including people and space. Upon regulatory approval, our new tests can be run without delay on the existing instrumentation to rapidly benefit patients worldwide. The high number of Roche instruments placed in laboratories for immunodiagnosics and clinical chemistry and our broad test menu for these systems are the key contributor for the continued strong growth the Division has reported for many years now.

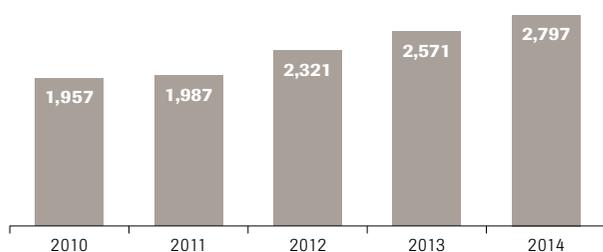
### Sales generated predominantly by reagents



### Business environment

In recent years, the *in vitro* (IVD) diagnostic market has grown 3%–5% annually to 48 billion Swiss francs in 2013 and is expected to reach more than 60 billion Swiss francs by 2018. Future growth prospects continue to be positive on the basis of further technological and scientific advances and a growing global patient population.

### Sales of immunodiagnostic tests, in Swiss francs



The market is characterised by differing testing technologies and continued innovation. The competitive landscape is fragmented despite consolidation driven by mergers and acquisitions, with new entrants coming in from various industries. Emerging markets provide the largest opportunities, with healthcare access and infrastructure developments driving growth.

The classic blood testing market (immunodiagnostics and clinical chemistry) continues to exhibit robust growth with the opportunity for more efficient and expanded testing. The molecular diagnosis market (including sequencing) is considered as the highest growth (8%–10%) segment in IVD. Tissue diagnostics will benefit from further market penetration globally and point-of-care diagnosis will increase in importance as technologies advance and decentralised diagnosis expands.

Meanwhile, diabetes self-testing will continue to face reimbursement and economic challenges while the fundamental need for blood glucose monitoring will further increase.

### *The diagnostics market continues to be financially attractive.*

Regulatory requirements are becoming more fragmented, with many countries expanding their guidelines. At the same time, regulations in China, the EU and the US are becoming increasingly stringent. Whilst these dynamics create headwinds for the overall market, they tend to favour companies such as Roche with extensive regulatory expertise and experience.

#### **New opportunities triggered by new knowledge**

The constantly expanding knowledge of molecular causes of diseases and an increasing availability of targeted medicines require complementary diagnostics capabilities. These developments support physicians' approaches in treatment decision-making.

Additionally, companion tests support payer decisions, allowing the reimbursement of targeted medicines for only those patients with a high likelihood to benefit. Roche is the only company with both Diagnostics and Pharmaceuticals Divisions, and this combination continues to position Roche at the forefront of personalised healthcare.

Beyond this, the re-emergence of infectious disease-causing micro-organisms (e.g. bacteria, viruses or fungi), including tuberculosis and multi-drug-resistant strains of these micro-organisms, is increasing the need for fast and reliable testing.

*EONE's new diagnostic laboratory with Roche leading-edge technology in Incheon, South Korea (see page 36).*





“Passion and  
teamwork were the  
keys to success.”

*EunOck Kim*

*EunOck's first task as a project manager was a huge challenge: construct Roche's most advanced diagnostics system for South Korea's largest commercial laboratory – and complete it in record time.*

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# A race against time to install leading-edge technology

*THE FIRST large-scale use of cobas connection modules means faster and more reliable test results for thousands of patients.*

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After completing a Master's degree in bio-engineering at Kyung Hee University, Seoul, Korea, I began working at Roche Diagnostics Korea in 2010 as a sales representative. In 2012, I was transferred to the Workflow & IT team and chosen to lead a project for our top customer, EONE, as a project consultant.

EONE is South Korea's largest commercial laboratory, serving dozens of hospitals and clinics. The lab screens 300,000 blood samples and performs 2.5 million other types of diagnostic tests every month. Physicians and patients depend on EONE for accurate and timely results.

With the demand for testing rising 10% every year, EONE's existing diagnostic platforms were reaching their capacity limits. In the summer of 2012, staff members approached Roche about constructing a new laboratory in Incheon, about one hour away from their existing lab in Seoul.

EONE's requirements included nine of our most advanced analytical diagnostic platforms, the cobas 8000, as well as six p 612 pre-analytical platforms and our latest innovation, the cobas connection modules (CCM). The CCMs transport test samples automatically in closed tubes between multiple analytical and pre-analytical systems – speeding up the screening process and reducing the chance for human error.

At that time, no one at Roche Diagnostics Korea had ever installed cobas connection modules on this scale. In addition, EONE needed to complete the laboratory by the end of the Lunar New Year holiday on 12 February 2013, when millions of Koreans returned to work. That meant we had only eight months to complete a job that normally takes from one to two years.

My task was to bring together all the teams directly involved – installation, workflow and information technology, customer service – into one smoothly functioning operating unit and bridge any gaps to EONE's needs. We also received invaluable support from Services, Finance, Logistics, Sales and Marketing, Communications and other colleagues throughout Roche Diagnostics Korea.

To mobilise everyone to meet these tough deadlines, I drew on the people and communication skills I had learned as a sales representative. I relied on checklists and project management software to stay on top of thousands of details and track progress, as well as on the continuous commitment of everybody on the team. Our motto was 'palli, palli', a phrase used in Korea to mean 'hurry, hurry'.

In Germany, Roche Diagnostics manufacturing teams were under pressure to deliver all of this high-tech equipment in record time. Our Chief Operating Officer, Roland Diggelmann, ensured that the project was a top priority. By December 2012, the equipment had arrived, so we were able to assemble and test the new systems.

That was the most intense phase of the project because we only had a little more than two months to finish one of our largest projects ever. This task required presence on site

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PROJECT COMPLETED IN  
**8 MONTHS**  
INSTEAD OF 12-24 MONTHS

---

**CAPACITY**  
FOR TESTING INCREASED BY  
**19%**

around the clock for many of us. Complications ensued when the customer suddenly asked for additional capabilities, such as separating the data read-outs for screening tests based on immunology from those based on chemistry. Our information technology team worked at top speed on the new requests.

I was at the Incheon site to coordinate the work. Because the biological samples we used to test the diagnostics systems arrived at 22:00, midnight and 02:00, we relied on energy drinks and coffee to get through the night. All of us were driven by the passion to succeed.

*“That commitment and the total support of all functions at Roche Diagnostics Korea helped us achieve this nearly impossible task.”*

We finished the project on time. And after the go-live date, we needed only two weeks to stabilise the system and eliminate remaining bugs – the older system had taken six months to stabilise.

EONE was extremely pleased with the results. “Now we understand why Roche is the leader in this field,” they told us. With the new laboratory up and running, the staff could see an immediate difference. Capacity for testing increased by 19% and overall throughput speed rose by over 11%.

News about EONE’s new laboratory spread fast, and representatives from other labs wanted to see it in action, particularly the cobas connection modules. I arranged schedules for visitors from Australia, China, India, Portugal, Poland and Egypt.

The visitors from Poland and Egypt returned home and convinced their colleagues to acquire similar diagnostics systems. It makes me proud that Roche Diagnostics Korea can share best practices with other countries.

**THROUGHPUT**  
INCREASED BY OVER  
**11%**

Another leading laboratory in Korea, Seoul Clinical Laboratories, wants to partner with Roche in constructing a new diagnostics centre. We signed the contract in August 2014 and our customer needs the lab completed by the end of the Lunar New Year holiday in February 2015.

*“This was the largest laboratory Roche Diagnostics Korea ever installed.”*

I am leading this project as well. The experience gained from EONE should help us, but once again we have a large number of complex tasks to complete in a very short timeframe.



**Regular operation after only two weeks:** the customer was very pleased by the rapid stabilisation of the processes, increased capacity and throughput of the new laboratory.



# Pharmaceuticals

**36.7** BILLION Swiss francs in sales  
**+4%\***

**5%** growth **in oncology**

**13%** growth **in immunology**

**23%** contribution from **personalised healthcare**



\* Unless otherwise stated, all growth rates in this report are at constant exchange rates (CER; average full year 2013).

## Solid performance in 2014

**SALES INCREASED 4%** in the Pharmaceuticals Division, with strong growth coming from the oncology and immunology portfolios.

Sales increased 4% in the Pharmaceuticals Division, with the oncology portfolio performing very strongly, particularly medicines for HER2-positive breast cancer (+20%). Sales of new cancer products made a significant contribution, as did sales of Avastin, which were 6% higher. In immunology, sales also grew strongly in treatment of rheumatoid arthritis, with Actemra/RoActemra up 23% and MabThera/Rituxan up 12% in this indication. Sales of Xolair for chronic hives and asthma were also higher, up 25%. These increases more than offset lower sales of oral chemotherapy drug Xeloda, which now has generic competition in key markets; and hepatitis medicine Pegasys, which faced competition from a new generation of treatment. Tamiflu (+54%) also grew very strongly towards the end of the year as a result of the flu epidemic in the US.

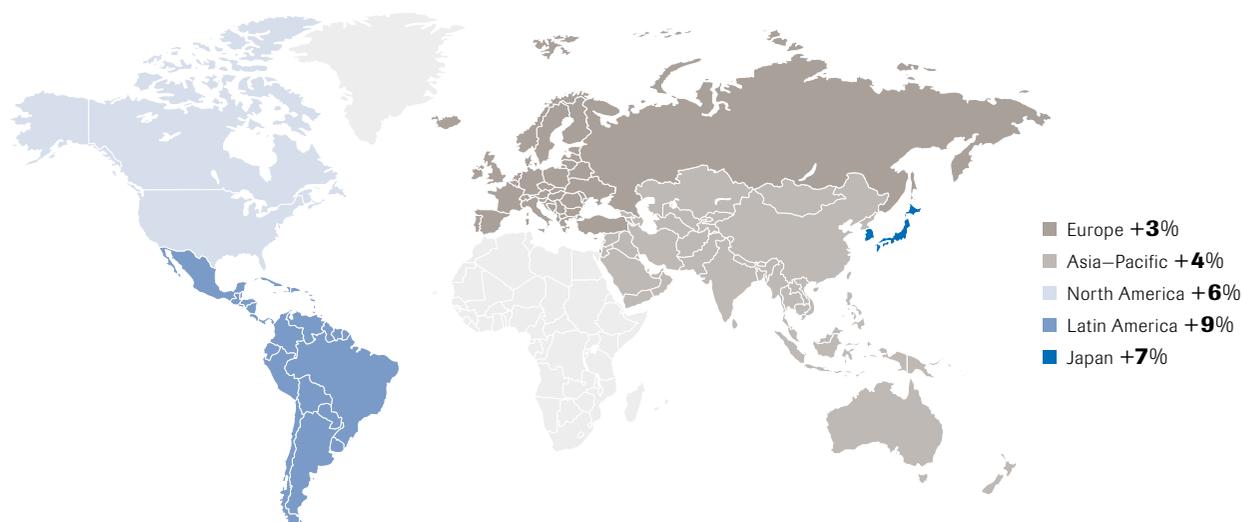
In the US, sales were 6% higher, with medicines for HER2-positive breast cancer driving growth, along with Tamiflu (+62%). Xolair and Avastin also grew significantly, up 25% and 6% respectively. Xolair was FDA-approved to treat a new indication, a form of chronic hives, in 2014. Early uptake of Esbriet, our newly acquired medicine for lung fibrosis was

very positive. Sales did not, however, reflect demand as patients in the US are currently transitioning from a patient assistance programme to normal commercial supply.

In Europe, 3% higher sales were driven by solid growth in Germany and the UK, particularly in sales of HER2-positive breast cancer medicines. In the UK there was also some stockpiling of Tamiflu. Ongoing pricing pressure had an impact on sales in a number of markets, however demand remained high.

Sales in the International region were 2% higher, with strong growth in Latin America, in particular Venezuela, Argentina and Brazil, as well as in Algeria. In Russia, sales declined significantly, as a result of local economic conditions, whilst sales in the Middle East were impacted by a change in distributor. In China, sales were 4% higher, with demand increasing in the fourth quarter, and continued strong growth for key products such as Herceptin, MabThera/Rituxan and Actemra/RoActemra. Growth was negatively impacted by the base effect of strong Tamiflu sales in 2013, as well as competition for Tarceva.

### Sales growth of the Pharmaceuticals Division by region



## Growth-driving products 2014 in millions of Swiss francs



**Avastin**  
Oncology

**6,417** +6%



**Herceptin**  
Oncology

**6,275** +7%



**Actemra/RoActemra**  
Immunology

**1,224** +23%



**Perjeta**  
Oncology

**918**



**Kadcyla**  
Oncology

**536**

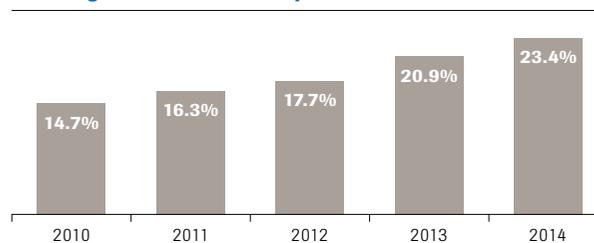
In Japan, 7% higher sales were driven by strong demand for HER2-positive breast cancer medicines, as well as Avastin and Actemra. In the osteoporosis segment, there was solid sales growth for Ediol, as well as Bonviva. Early uptake was very strong for the newly approved Alecensa (alectinib), in ALK-positive lung cancer.

## Pharmaceuticals Division – sales by therapeutic area

Therapeutic area	2014 (mCHF)	2013 (mCHF)	% change (CER)
Oncology	22,797	22,553	5
Immunology	5,087	4,628	13
Infectious diseases	3,194	3,180	4
Ophthalmology	1,701	1,689	2
Neuroscience	726	810	-6
Other therapeutic areas	3,191	3,444	-3
<b>Total sales</b>	<b>36,696</b>	<b>36,304</b>	<b>4</b>

The 2014 performance also reflected the continued increased contribution from personalised healthcare, a key focus for Roche. Not all patients respond the same way to a medicine, however, using specific diagnostic tests, it is possible to predict how well a patient responds to treatment for some diseases or conditions. Sales of products with a companion diagnostic test on label now represent 23% of Pharmaceuticals Division sales.

## A strong contribution from personalised healthcare



## Key products performing well

**Avastin** (+6%), for advanced colorectal, breast, lung, kidney, cervical and ovarian cancer, and glioblastoma (a type of brain tumour). Sales in the US (+6%) were driven by growing demand in colorectal, cervical and ovarian cancer, whilst in Europe growth of 3% stemmed from increased demand in treatment of ovarian cancer and strong demand across other indications. In Japan, sales were 9% up, with higher sales in breast cancer, as well as ovarian cancer and malignant glioma. In the International region, growth of 12% was driven by launches in a number of markets for ovarian cancer treatment, as well as in colorectal cancer.

**Herceptin, Perjeta, Kadcyla** (+20%), for HER2-positive breast cancer and Herceptin for HER2-positive metastatic (advanced) gastric cancer. Herceptin sales were particularly strong in the US (+12%), as demand increased with use in combination with Perjeta in treating HER2-positive breast cancer. In Europe, where the subcutaneous formulation is now available in many markets, sales increased 3%. Sales in Japan were 1% higher, with use with Perjeta. In the International region (+8%), sales growth was strong in Latin America, with high demand in the public sector; as well as in Asia, where growth came particularly in China from the patient assistance programme. Perjeta sales (918 million Swiss francs) grew in all regions, with strong uptake in the US, Germany and France. Kadcyla sales (536 million Swiss francs) continued to grow well in Europe and the US, and in Japan, where Kadcyla was approved in 2014 and early uptake has been very positive.

**MabThera/Rituxan** (+2%), for common forms of blood cancers, non-Hodgkin's lymphoma, follicular lymphoma and chronic lymphocytic leukemia; as well as for rheumatoid arthritis and certain types of ANCA-associated vasculitis. Sales were up 6% in Europe, where demand increased in the treatment of follicular lymphoma, as well as for chronic lymphocytic leukemia. In the US, sales were 1% higher and reflected a base effect from the release of sales reserves in 2013 (from the 340B programme). Excluding this effect, sales in the US in 2014 were 5% higher. In the International region (-1%), sales were impacted by economic conditions in Russia. Sales remained strong in Latin America, where demand increased in key markets.

**Lucentis** (+2%, US only), for eye conditions, wet age-related macular degeneration, macular edema following retinal vein occlusion and diabetic macular edema. Growth was driven largely by increased adoption of Lucentis in treating diabetic macular edema. Lucentis has been granted Priority Review and Breakthrough Therapy Designation by the FDA for treatment in diabetic retinopathy.

**Actemra/RoActemra** (+23%), for rheumatoid arthritis, systemic juvenile idiopathic arthritis and polyarticular juvenile idiopathic arthritis. Demand was strong in all regions, particularly the US (+31%), Europe (+22%) and Japan (+19%), driven by increased use in monotherapy and earlier use in treatment for rheumatoid arthritis, with significant uptake of the new subcutaneous formulation. In the International region, sales were 14% higher driven by strong launches in China and Turkey and continued fast uptake in Australia and Argentina. RoActemra was approved to treat early-stage rheumatoid arthritis in the EU in 2014.

**Zelboraf** (-12%), for BRAF V600 mutation-positive metastatic melanoma. As the standard of care is now moving to combination targeted therapy in advanced melanoma, Zelboraf has been under intense competitive pressure, as expected, particularly in the US. In Europe sales were stable, and in the International region (+41%), there was strong growth in a number of markets including Argentina and Brazil. Clinical trial data for Zelboraf in combination with cobimetinib have shown very positive results and the data was filed with the FDA and EMA in 2014. Zelboraf was approved in Japan in 2014.

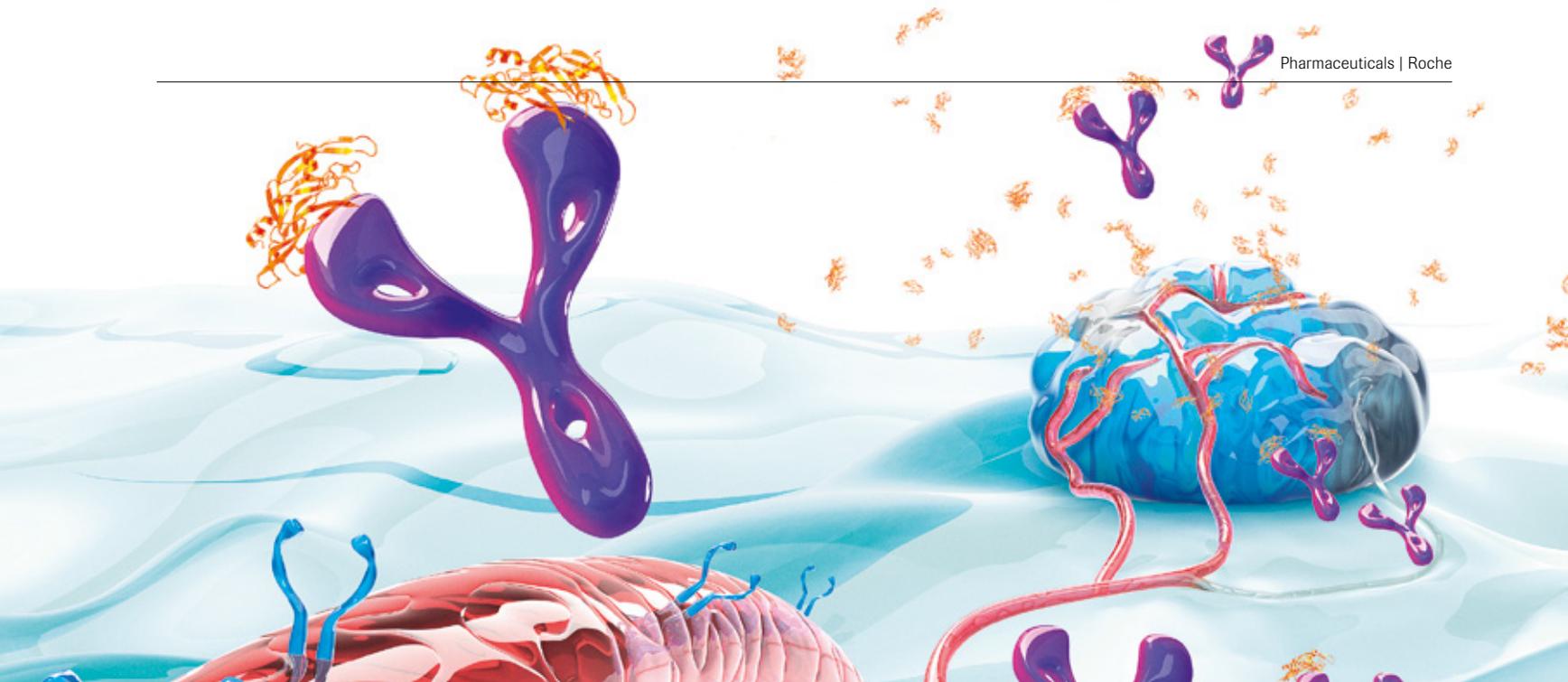
**Gazyva/Gazyvaro** (49 million Swiss francs), for treatment of chronic lymphocytic leukemia. Initial uptake in Europe has been positive, whilst limited use of chlorambucil (the chemotherapy medicine approved with Gazyva), as well as competition have impacted uptake in the US. In late December 2014, the FDA approved a supplemental biologics licence application expanding Gazyva's label to include data which showed significant improvements for Gazyva plus chlorambucil over MabThera/Rituxan plus chlorambucil. As of January 2015, Gazyva has been approved in 40 different countries worldwide.

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# 20% INCREASE IN SALES

## OF MEDICINES FOR HER2-POSITIVE BREAST CANCER

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*Avastin is the first medicine to target and inhibit VEGF activity thereby inhibiting angiogenesis – a critical process in tumour development.*

## Significant breakthroughs in 2014

2014 had some very positive clinical trial results. In HER2-positive metastatic breast cancer, a particularly aggressive form of the disease, we saw unprecedented data on Perjeta, which, when combined with chemotherapy and Herceptin, increased survival time for patients to almost five years. In advanced melanoma, we also had very good clinical trial results for the combination of cobimetinib and Zelboraf, which halved the risk of the disease worsening. Roche now has over 30 different combination therapies in its oncology pipeline.

### *Cancer immunotherapy is a key focus area for Roche.*

We are making important advances in immunotherapy, which uses the body's own immune system to fight cancer. We have 7 investigational medicines in 5 types of cancer currently in development. Our most advanced investigational medicine in this area, anti-PDL1, was granted FDA Breakthrough Therapy Designation for the treatment of bladder cancer. It also showed promising early results in combination with Avastin in renal cell carcinoma and other solid tumours. There was also positive news from two phase III studies of Avastin in HER2-negative breast cancer. Avastin was approved in platinum-resistant ovarian cancer and cervical cancer during the year, and is now used to treat seven different cancers.

In hemophilia A, early data on ACE910, an innovative bispecific antibody, showed an encouraging reduction in bleeding rates for all patients on the trial. Lampalizumab, the first potential treatment for geographic atrophy, initiated phase III clinical trials in September.

There were some important approvals during the year, including Gazyvaro for chronic lymphocytic leukemia in Europe; Esbriet to treat idiopathic pulmonary fibrosis in the US. Esbriet was developed by InterMune, a company we acquired during the year; and Alecensa (alectinib), which was approved in Japan in 2014, to treat ALK-positive lung cancer. Further global studies of this medicine are ongoing.

With innovation, there is of course an inherent risk of failure and unfortunately we had some disappointing clinical trial results during the year. Bitopertin, for the negative symptoms of schizophrenia, which did not meet its primary endpoints; and one of our gantenerumab studies in early-stage Alzheimer's disease, which was discontinued after a futility analysis.

There was also a study of our antibody–drug conjugate, Kadcyla, both alone, and in combination with Perjeta, in first-line treatment of HER2-positive advanced breast cancer. The results did not show the hoped for superiority to Herceptin with chemotherapy, however, these results do not impact existing use of Perjeta or Kadcyla, both of which have been shown to extend survival in this type of breast cancer.

Further information about our pipeline can be found in the Innovation chapter of this Annual Report on page 78.

# 11 PRODUCT APPROVALS

## Pharmaceuticals Division approvals in 2014

	Product	Description
<b>US approval</b>	Xolair	chronic idiopathic urticaria (hives)
	Avastin	cervical cancer
	Avastin	platinum-resistant ovarian cancer
	Esbriet	idiopathic pulmonary fibrosis
<b>EU approval</b>	MabThera (subcutaneous formulation)	non-Hodgkin's lymphoma
	RoActemra (subcutaneous formulation)	rheumatoid arthritis
	Gazyvaro	chronic lymphocytic leukemia
	RoActemra	early rheumatoid arthritis
	Avastin	platinum-resistant ovarian cancer
<b>Japanese approval</b>	Alectinib	ALK-positive non-small cell lung cancer
	Zelboraf	BRAF-positive metastatic melanoma

# Making innovation accessible

As populations age and life expectancy increases, demands on healthcare systems are growing exponentially. Healthcare costs are rising and innovative medicines are expensive to develop.

*Our aim is for our medicines to be available to anyone who needs them.*

We are working closely with healthcare authorities and other healthcare stakeholders to develop solutions to bring our medicines to more patients.

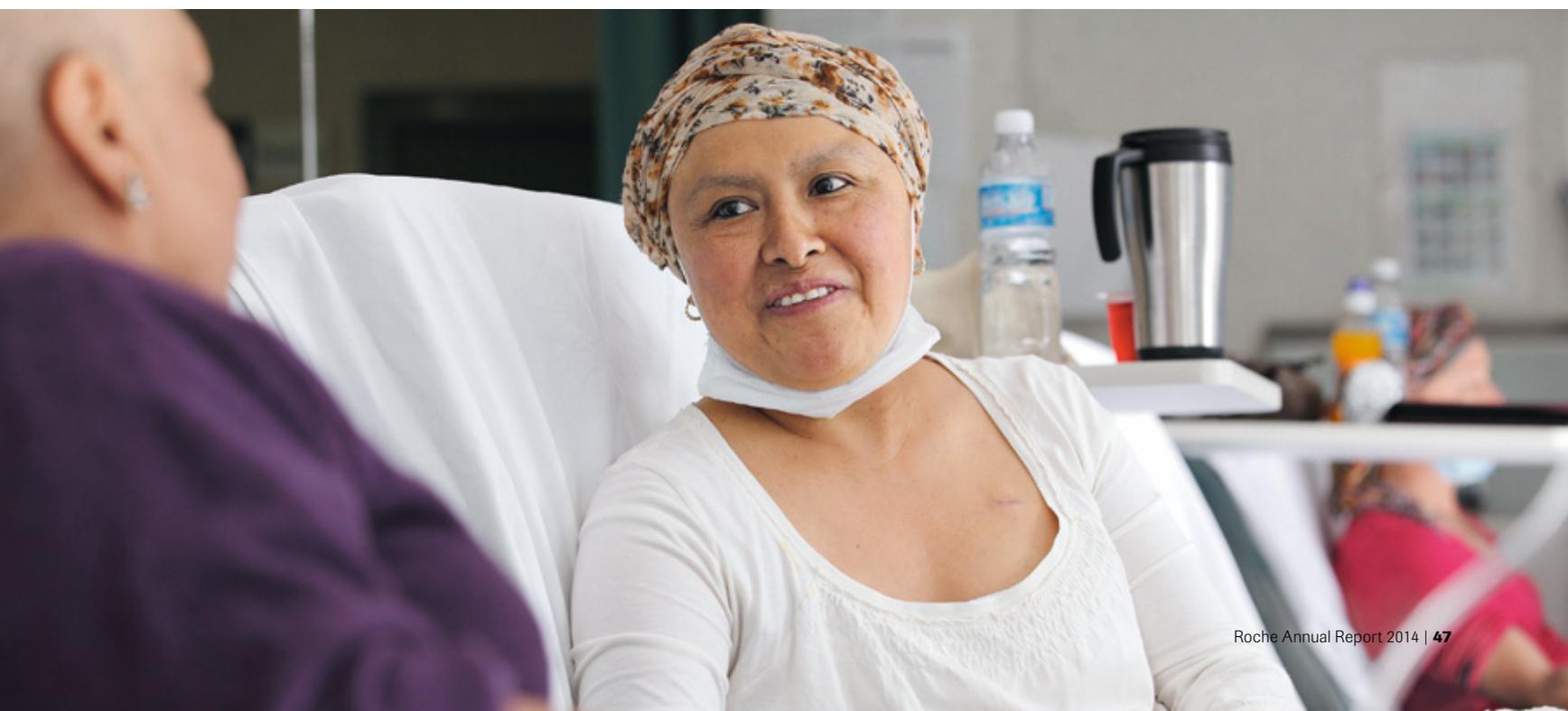
The barriers to accessing healthcare are multiple and complex, ranging from a lack of trained medical professionals and the necessary infrastructure to supply medicines safely, to low levels of awareness and affordability issues.

Our initiatives range from medical training to education, screening programmes, patient assistance programmes and funding solutions. We are also developing innovative pricing models, which better reflect the benefits the medicine brings in different indications.

*We have initiatives all over the world to help patients in need access our medicines.*

In 2014, we took some significant steps in improving access to our medicines. We launched a new framework to systematically analyse barriers to healthcare in different markets, supporting our affiliates to identify the root causes and find new solutions. We also launched a strategy to improve access to women's cancer and hepatitis medicines in sub-Saharan Africa, an area where access to innovative medicines is a particularly difficult challenge.

Further information can be found in the Access to Healthcare chapter of this Annual Report on page 80.





“To understand  
biology, you need to  
be able to measure it.”

*Michael Cannarile*

*Michael and his colleagues discovered biomarkers that helped to identify the optimal dose for a new cancer drug. The use of these biomarkers for similar therapeutic molecules is gaining acceptance at Roche.*

# A biomarker model that is almost 100% predictive

*USING BIOMARKERS for a cancer receptor antibody at an early stage accelerated dose selection to maximise therapeutic benefit for patients.*

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As a scientist, it is incredibly exciting to receive confirmation that an experimental molecule actually works in humans the way you hypothesised. That is especially true when the molecule was designed to fight a life-threatening disease like cancer.

I became interested in science as a teenager. I could not understand why there was no available cure for cancer and people had to die. I was determined to understand the biological basis of this disease. That is why I ultimately went into pharmaceutical research and joined Roche in 2009.

I work as Biomarker and Experimental Medicine Leader for Roche Pharma Research and Early Development in Penzberg, Germany. My focus is on developing biomarker strategies to explain and predict responses in patients treated with drug candidates. In simple terms, a biomarker is any biological parameter used as an indicator of disease process or drug response.

At Roche, biomarker teams play a vital supporting role that links Pharmaceuticals and Diagnostics. In the early stages of discovery, these biomarkers can provide us with insights on the disease biology and the mode of action of a therapeutic molecule.

Our Diagnostics colleagues are involved in the early phases of a project – a collaboration that is quite unique to Roche. Their ultimate goal is to develop a reliable biomarker-based test, known as a companion diagnostic, which will help us predict which patients will respond to our targeted therapies. This is central to our concept of personalised healthcare.

ROCHE OFFERS  
**SIX MEDICINES**  
REQUIRING A COMPANION  
TEST. THESE CONTRIBUTE  
**23%**  
TO THE SALES OF ROCHE'S  
PHARMACEUTICALS DIVISION

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**50%**  
OF ROCHE'S PIPELINE  
IS DEVELOPED WITHIN  
**PERSONALISED  
HEALTHCARE**

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In 2010, we were nearing the end of preclinical testing of a promising new cancer therapy with our anti-CSF-1 receptor antibody. This receptor is overexpressed on the surface of some tumour cells. The same receptor is also present on specific types of macrophages, white blood cells that are normally a beneficial part of the body's immune system. These macrophages are present in many tumour types.

Tumours sometimes hijack these macrophages and use them to stimulate tumour growth and prevent other cells from attacking the tumour efficiently. Therefore, colleagues in Drug Discovery developed an antibody that binds to and eliminates CSF-1 receptor-expressing cells.

Up to that point, experiments with the CSF-1R antibody had only been performed in laboratory pre-clinical tests. We still did not have data with the clinical version of the antibody targeting human macrophages.

The next step in the clinical development of the antibody, per regulatory requirements, was to test its safety profile. Here is where we saw an opportunity. Beyond safety parameters, we wanted to know whether our biomarker hypothesis and assays were accurate and whether there was a dose-dependent response to the therapy. Another goal was to develop a mathematical model correlating the drug exposure to the biochemical and physiological response of the body.

Amending the standard toxicity testing protocol, however, presented some challenges. The implementation of biomarkers increased the complexity and the budget significantly. Furthermore, the additional data generation and interpretation represented a potential risk for the tight development timelines for phase I clinical testing. Hence, we needed to explain the expected benefits for the patient to our colleagues. In the end, with the help of colleagues from Discovery and Pharmaceutical Sciences, we successfully incorporated these markers into the study protocol.

The results were very encouraging. They supported our hypothesis on the mode of action of the antibody, validated our assays and provided a rationale for the appropriate dose to treat the first patient. That meant we did not need to expose study participants to insufficient or excessive doses of the therapy, and thus potential side effects. By shortening standard dose escalation procedures, we also accelerated the timelines of the phase I trial.

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ROCHE DIAGNOSTICS IS  
CURRENTLY DEVELOPING  
**MORE THAN 15**  
NEW COMPANION TESTS

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**Michael:** "Early and close collaboration between Roche Pharmaceuticals and Roche Diagnostics is crucial for the development of reliable biomarker-based tests."

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*"Using biomarkers early enabled us to avoid exposing study participants to excessive doses of the compound and related potential side effects."*

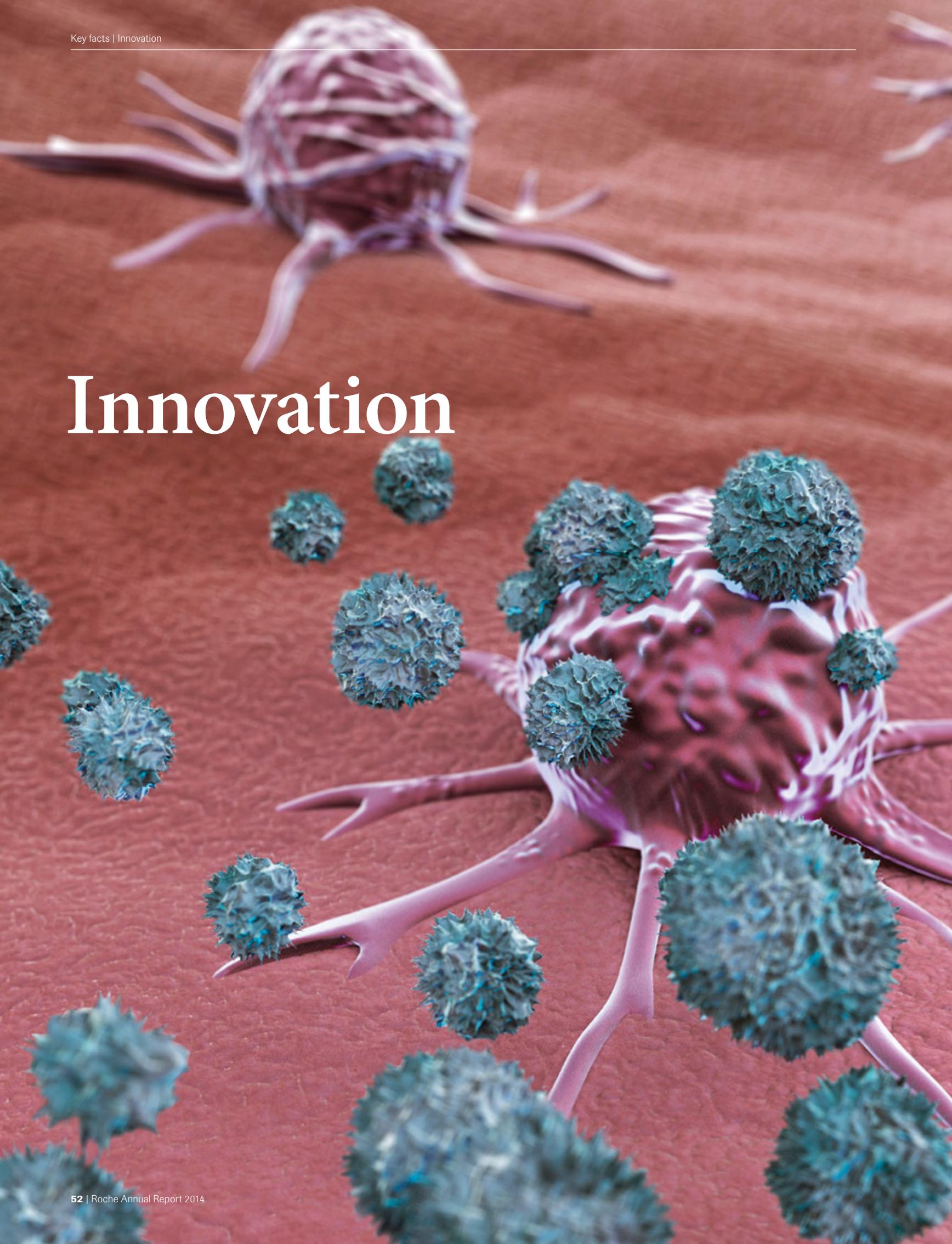
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Now that we have progressed in phase I monotherapy studies with this new cancer drug candidate, we can look back and see that our biomarker model generated in preclinical testing was almost 100% predictive of what happened later in humans.

As a result, the implementation of biomarkers for pharmacodynamics (biochemical and physiological responses) as well as mode of action in primate studies is gaining more acceptance at Roche for this new type of targeted therapy. Further clinical development of the anti-CSF-1R antibody will focus on identifying a predictive marker that enables physicians to select patients with the highest likelihood of response. The identification of a predictive marker will trigger the development of a companion test for the safe and effective use of the therapeutic drug.

To me, this is what personalised healthcare is all about – knowing which medicines will work for a specific group of patients. We're not there yet, but it is an important step in understanding cancer and how best to treat it.

# Innovation



**66** **new molecular entities** in clinical development

**>30** **cancer drug combinations** in clinical development



**11** **Pharmaceutical** product approvals



**14** **diagnostic** launches

# Diverse approaches to Research and Development

*SIGNIFICANT PROGRESS* has been made to find new medicines that transform the way we treat diseases. Today, there are answers for illnesses, such as metastatic melanoma, that only a few years ago had no effective therapies.

However, millions of people worldwide continue to suffer from debilitating conditions, that have limited treatment options and poor prognosis. At Roche, we invest in research and development (R&D) to transform science into medicines and diagnostic tests to address these patient needs.

We draw on expertise from within the company and partners throughout the world to maximise our productivity. Our diverse approach to research and early development is carried out by four organisations: Genentech Research and Early Development (gRED), Roche Pharma Research and Early Development (pRED), Chugai Pharmaceutical Co., Ltd., Japan, a member of the Roche Group, and our Diagnostics Division. Roche's partnering functions maintain close links to external research organisations and we currently have

partnerships and alliances with more than 240 external companies and institutes. Compounds successfully developed by gRED, pRED, Chugai and our partners progress into our global late-stage development organisation.

The know-how that our experts in the Pharmaceuticals and Diagnostics Divisions have in molecular and cellular biology as well as in biochemical and signalling pathways of diseases is the basis of developing innovative medicines that offer significant benefits to patients in need. This expertise also allows for the development of tests to screen for disease-causing factors in the body.

## Core Research and Development expenditure in 2014

<b>Roche Group</b>	<b>8,913</b> million Swiss francs	<b>+4%</b> (CER)* 18.8% of sales
<b>Pharmaceuticals</b>	<b>7,876</b> million Swiss francs	<b>+4%</b> (CER) 21.5% of sales
<b>Diagnostics</b>	<b>1,037</b> million Swiss francs	<b>+3%</b> (CER) 9.6% of sales

\* Unless otherwise stated, all growth rates in this report are at constant exchange rates (CER; average full year 2013).

# Innovative R&D: focus on targeted therapies

From basic research to late-stage development, innovative approaches are applied throughout the entire R&D process. These advances include the use of new and industry-leading technology platforms to discover targeted therapies, clinical trial modelling and innovative patient recruitment methods for clinical studies.

## The future of RNA therapeutics research

The majority of today's medicines are small molecules, which are manufactured through chemical synthesis and have well-defined chemical structures. Large molecules, including monoclonal antibodies, represent a class of medicines which is produced in animal and plant cells. But many disease targets are very challenging or even impossible to reach with small molecules or antibodies.

*Roche is a leader in highly sophisticated antibody engineering technologies.*

To overcome these limitations, Roche is developing so-called ribonucleic acid (RNA) targeted medicines as a new therapeutic modality. Representing an entirely new class of medicines, these RNA therapeutics are expected to broaden the range of 'drug-able' disease targets. In 2014, Roche acquired Santaris Pharma A/S, a Danish biopharmaceutical company, which pioneered locked nucleic acid (LNA)

technology, a leading proprietary platform to discover and develop new RNA-based therapies.

## Advancing antibody engineering technologies

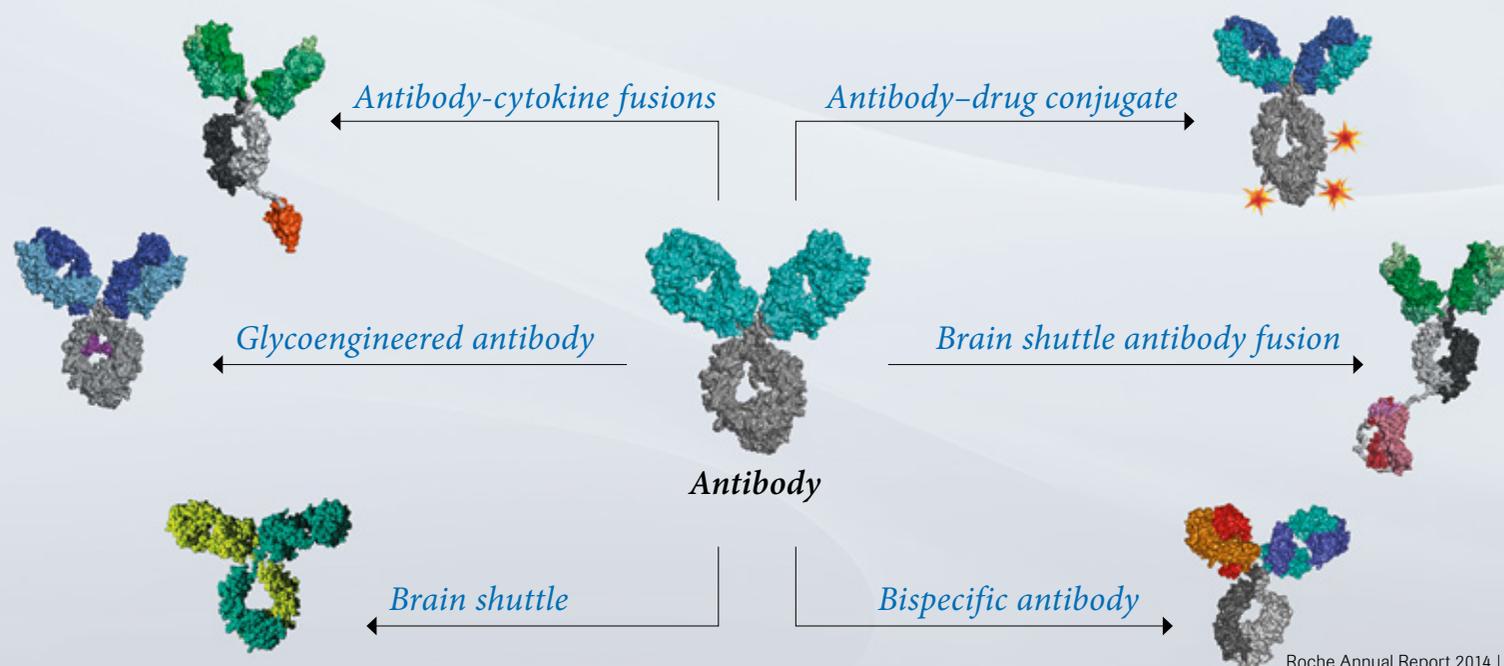
With its long history in antibody development and production, Roche is also a leader in highly sophisticated antibody engineering technologies including:

- Antibody–drug conjugates
- Glycoengineering
- Bispecific antibodies
- Brain shuttle technology

*Antibody–drug conjugates (ADCs)* are a new class of highly potent biologic medicines built by attaching a small molecule or other therapeutic agent to an antibody, with either a permanent or stable linker. The antibody targets a specific antigen only found on target cells. Once it binds to the cell, it triggers internalisation of the antibody, together with the medicine. This delivers medicine with a very high specificity to the target cells, maximising their efficacy and minimising systemic exposure and side effects. At Roche, we have several ADCs in clinical studies for different types of cancer, neurological disorders or infectious diseases.

*Glycoengineering* approaches generate new kinds of antibodies where the attachment of sugar molecules significantly enhances capacity to recruit immune cells, like natural killer (NK) cells, macrophages/monocytes and neutrophils. By designing and controlling the types of sugar molecules in a specific region of the antibody, the affinity

*Roche's leading capabilities in antibody engineering enabled the creation of new antibody variants to improve treatments of complex diseases such as cancer, viral infections and inflammatory diseases.*



of the antibody for immune effector cells is increased. This allows more effective antibody-dependent cellular cytotoxicity and improved targeting of cancerous cells.

*Bispecific antibodies* are a new generation of biologically engineered antibody medicines developed at Roche. Engineered bispecific antibodies combine the binding specificity of two antibodies in one molecule. Some of these antibodies were pioneered by applying the Roche invented CrossMAB technology, others by different in-house proprietary technologies. Bispecific antibodies are designed to bind two molecules simultaneously. The applications of bispecific antibodies are broad, including neutralising two different disease-causing proteins at the same time for conditions such as aberrant blood vessel growth (angiogenesis) or for physically bringing two types of cells into close proximity, such as cancer cells and immune cells. In addition to cancer drugs, candidates are also tested in ophthalmology, asthma and hemophilia.

Antibodies can be powerful therapeutic agents, but their use in treating brain disorders, such as Alzheimer’s disease, has been difficult because of the blood-brain barrier, which limits uptake of antibodies into the central nervous system (CNS). Different technologies have been developed within Roche’s early research and development organisations to overcome this natural barrier.

One approach is an innovative bispecific antibody platform, which greatly boosts antibody penetration into the brain by binding to the transferrin receptor, a molecule that normally transports another protein into the brain. One arm of the bispecific antibody is connected to the transferrin receptor while the other arm inhibits the activity of  $\beta$ -secretase, a molecule that is required for the production of the toxic  $\beta$ -amyloid peptide that is hypothesised to cause Alzheimer’s disease.

In a series of high-profile publications, the research team has reported key features of transferrin receptor-bispecific antibody design, including optimal affinity, *in vivo* safety, and molecular cellular mechanisms.<sup>1</sup> They have also recently shown that the transferrin receptor-bispecific platform works in non-human primates, setting the stage for testing in humans, and potentially opening the human brain to a wide range of antibody therapeutics.

The second approach, the so-called brain shuttle, also uses transferrin receptors to transfer investigational antibodies from the blood through the blood-brain barrier into the brain, but employing a different type of antibody design. In a preclinical mouse model of Alzheimer’s disease, Roche scientists showed that enhanced transport of antibodies through this barrier was associated with a marked improvement in amyloid reduction in the brain, increasing the target engagement in the brain by over 50-fold compared to the parent antibody.<sup>2</sup>

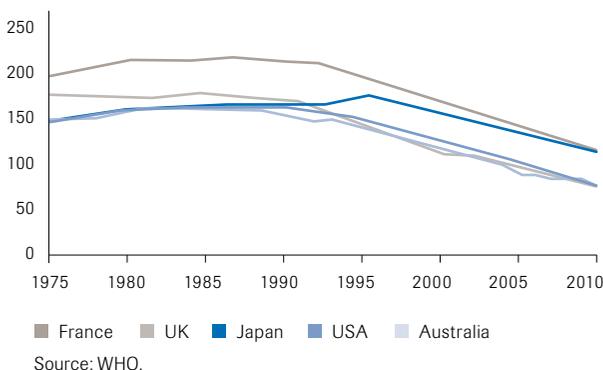
## Leading innovations from our pipeline

We take a focused approach to increase our chance of success in highly complex diseases. We focus on a select group of disease areas including oncology, hematology, neuroscience, immunology and inflammation, ophthalmology, infectious and rare diseases.

### Oncology

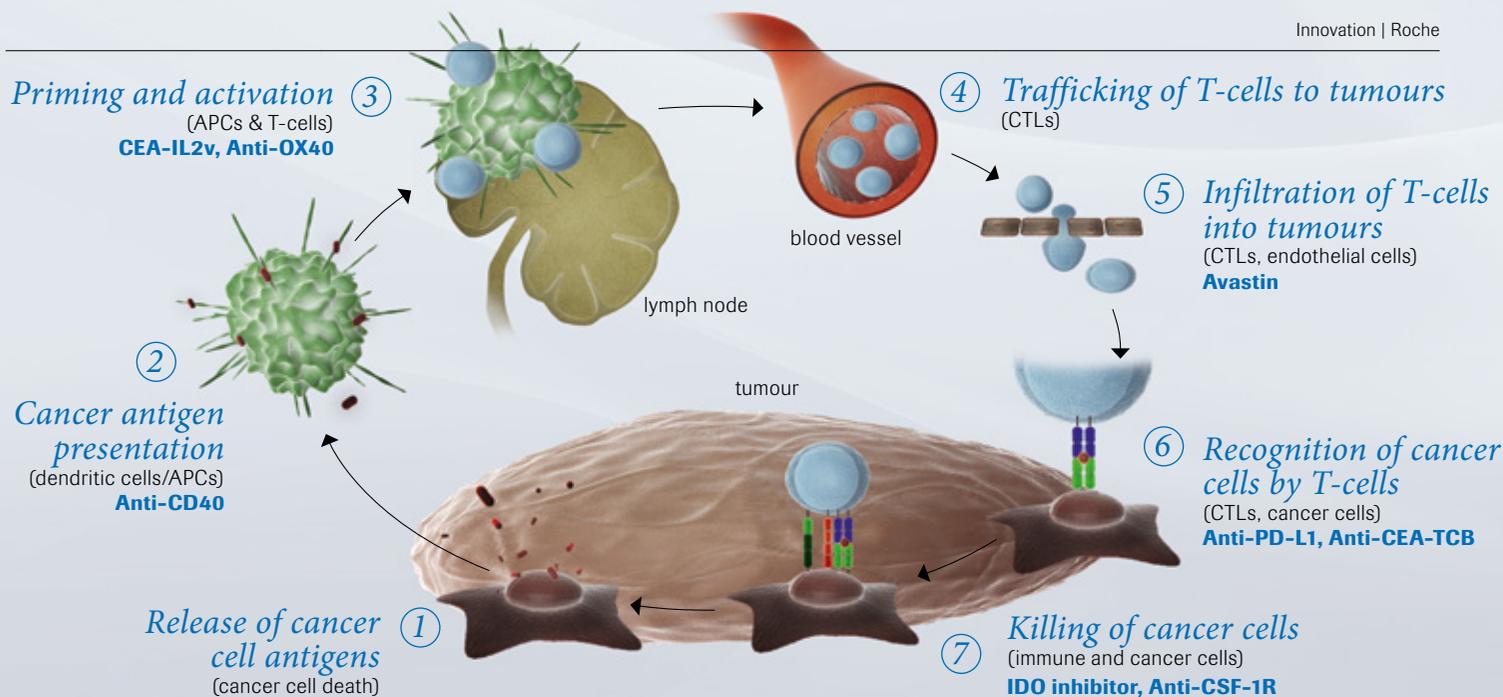
Roche has been at the forefront of cancer research for more than 50 years, discovering and developing cancer diagnostics and treatments with the aim of giving patients better options and constantly improving outcomes. Tremendous progress has been seen in the treatment of many forms of cancer, including breast, cervical, colorectal, lung and skin cancers, with especially good progress in some blood cancers.

**Decreases in cancer mortality, age-standardised rate per 100,000 men**



*Progress in cancer care has led to better patient outcomes, including decreased mortality rates.*

Nonetheless, cancer continues to be a major public health issue with incidence rates on the rise globally. According to the World Health Organization (WHO), 8.2 million people died of cancer in 2012, with more than 2.2 million patients



Source: Chen & Mellman, *Immunity* (2013); APC = Antigen Presenting Cells; CTL = Cytotoxic T-Lymphocytes.

dying from lung, breast, colorectal and cervical cancers alone. WHO expects that the absolute number of cancer cases will continue to grow and estimates that some 22 million people will be diagnosed with cancer within the next two decades.

By increasing our understanding of the underlying disease biology, we are confident that we will provide even better cancer medicines and tests in the years to come. The development of medicines which target and attack the specific way cancer cells work, grow and communicate has been our main focus in cancer research. This has led to the development of a number of targeted therapies. Now we are combining such targeted therapies to further block cell signalling that leads to cancer growth or initiate signalling that leads to cancer cell death, thus improving treatment outcomes. Our broad pipeline including our cancer immunotherapy portfolio allows for a range of early-stage combinations with our in-house drug candidates.

*Promising study results in the fight against solid tumours*  
Metastatic melanoma is the most aggressive and deadly form of skin cancer. In approximately half of all melanomas, there is a cancer-causing BRAF mutation. When melanoma is diagnosed early, it is generally a curable disease, but most people with advanced melanoma have a poor prognosis. More than 232,000 people worldwide are currently diagnosed with melanoma.<sup>3</sup>

Presented in September 2014, the results from the phase III coBRIM study demonstrated that people with previously untreated BRAF V600 mutation-positive, advanced melanoma who received Roche's investigational MEK

inhibitor cobimetinib plus Zelboraf (vemurafenib), a BRAF inhibitor, lived significantly longer without their disease worsening or death, as compared to Zelboraf alone. The combined therapy reduced the risk of disease worsening or death by half with a median progression-free survival of 9.9 months for cobimetinib plus Zelboraf compared to 6.2 months with Zelboraf alone. Phase III study results of the coBRIM study have been filed with EU and US authorities.

*Next-generation medicine against metastatic breast cancer*  
Every year, over 450,000 women die from breast cancer. Almost 60% of breast cancers depend on the hormone estrogen and the estrogen receptor to grow and spread; so-called hormone receptor-positive breast cancer.<sup>4</sup> Current treatment approaches have limited effect.

A next-generation class of selective estrogen receptor degraders has been designed to block estradiol action at the estrogen receptor and also eliminate the estrogen receptor from the cell altogether. The lead compound RG6046, an orally administered selective estrogen receptor antagonist and degrader, is currently in phase I clinical trials for patients who have hormone receptor-positive breast cancer and have failed current hormonal agents.

### Cancer immunotherapy

At Roche, we are investing heavily in cancer immunotherapies, which help a person's own immune system fight cancer. Our cancer immunotherapy R&D programme is comprised of more than 20 investigational candidates. Cancer immunotherapy has the potential to fundamentally change the treatment paradigm for people with cancer.

1 *Sci Transl Med* 2011 84ra44; *Sci Transl Med* 2013 183ra 57; *J Ex Med* 2014 Vol. 211 No. 2; *Sci Transl Med* 2014 261ra154. | 2 Niewoehner J. et al. *Neuron*. 81,49–60, 2014. | 3 WHO. *Globocan. Estimated cancer incidence and prevalence worldwide in 2012*. | 4 Boyle P. et al. *The State of Oncology* 2013.

One of our investigational monoclonal antibodies, RG7446 (anti-PDL1, MPDL3280A), is designed to interfere with a protein called PD-L1. It targets PD-L1 receptors expressed on tumour cells and tumour-infiltrating immune cells, preventing them from binding to corresponding receptors on the surface of T-cells, thus blocking the body's immune defence. By inhibiting PD-L1, RG7446 may enable the activation of T-cells, restoring their ability to effectively detect and attack tumour cells. The results from a phase I open-label study showed that RG7446 shrank tumours in 52% of people who were mostly pre-treated for metastatic urothelial bladder cancer (mUBC) and whose tumours were characterised as PD-L1-positive by a diagnostic test being developed by Roche. In the study, 86% of responding patients had ongoing responses at the time of data cut-off; the median duration of response was not reached. The FDA granted RG7446 Breakthrough Therapy Designation in mUBC.

Combination strategies are a central component of RG7446 development and we believe they will play an important role in future treatment options. We are currently studying multiple combinations with approved and investigational medicines in addition to immune doublets, both within and outside our own pipeline and across a broad range of tumours. The first combination data of the investigational cancer immunotherapy RG7446 and Avastin in untreated patients with metastatic renal cell carcinoma show that this combination is safe and well tolerated.

A new agonist antibody, RG7888 (MOX0916), is in development to inhibit OX40, a receptor on T-cells that promotes antigen-dependent effector T-cell activation and regulatory T-cell inhibition. Preclinical research shows durable tumour responses with the anti-OX40 agonism. The phase I clinical trial on RG7888 started enrolment in fall 2014.

## *Cancer immunotherapy – a potential paradigm shift in cancer treatment.*

In October 2014, Genentech Partnering entered into a strategic collaboration with NewLink Genetics Corporation for the discovery and development of small-molecule IDO (indoleamine 2,3-dioxygenase) pathway inhibitors for the treatment of cancer. We believe IDO is a compelling target for cancer immunotherapy and are very interested in combining RG6078 with investigational immunotherapies in our pipeline, such as RG7446 (anti-PDL1) and RG7888 (anti-OX40). The ability to leverage the molecules in our pipeline and evaluate biologically driven combinations gives us a competitive advantage in the cancer immunotherapy space.

### *Boosting the body's own defences*

For decades, scientists have strived to fuse anti-tumour antibodies with interleukin 2 (IL-2), an immune-stimulatory protein, with the goal of delivering IL-2 into tumours and thereby targeting the immune response where it is needed. When administered in an untargeted manner, IL-2 can be highly toxic, causing non-specific autoimmunity and inflammation. Roche scientists have worked to increase the affinity of IL-2 to target tumour antigen instead.

A leading example of Roche's highly sophisticated capabilities in antibody engineering is RG7813, our carcinoembryonic antigen-interleukin 2 variant antibody (CEA-IL2v). RG7813 represents a major advance in both taming and targeting IL-2 for improved cancer immunotherapy – avoiding the challenges related to autoimmune

*Molecular modelling: the computer-based three-dimensional representation of molecules is an ideal approach to visualise large molecules such as proteins or nucleic acids.*



side effects while delivering IL-2's anti-cancer potential where it is needed. This molecule combines an engineered version of IL-2 having a better safety profile, with an antibody against a protein expressed on several cancers, CEA. This new interleukin 2 variant is designed to reduce stimulation of immunosuppressive regulatory T-cells, and also shows reduced pulmonary toxicity. RG7813 is in phase I clinical studies.

#### *Targeting the colony-stimulating factor 1 receptor*

The humanised monoclonal immunoglobulin G1 antibody RG7155 specifically targets colony-stimulating factor 1 receptor (CSF-1R) by attacking a sub-set of immune cells known as macrophages. These macrophages contribute to tumour growth by suppressing the local immune system and promoting growth of cancer cells. RG7155 has been designed to target and deplete tumour-associated macrophages expressing CSF-1R in the tumour tissue. Thanks to innovative trial designs, Roche has been able to start early combination studies with chemotherapy in the treatment of breast and ovarian cancer while completing dose escalation studies as a single agent. Current data show that RG7155 is well tolerated and has a very broad applicability in combination therapy across various tumour types. Phase Ib combination studies are ongoing to establish if the depletion of tumour-associated macrophages supports the immune system in fighting tumours, leading to enhanced efficacy in malignancies.

### **Hematology**

For more than 20 years, Roche has been developing medicines that redefine treatment in hematology, or diseases of the blood. Roche's pipeline includes the small-molecule Bcl-2 inhibitor venetoclax, which is developed in collaboration with AbbVie, and the antibody-drug conjugate polatuzumab vedotin (anti-CD79b), a small-molecule antagonist of MDM2.

Venetoclax is designed to selectively block the function of Bcl-2 proteins with the goal of re-activating the 'self-destruct' mechanism in cancer cells called apoptosis. Bcl-2 plays a central role in suppressing cell death, encouraging tumour growth and causing resistance to chemotherapy. Bcl-2 becomes highly active in cancers such as non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL) and other B-cell neoplasms, as well as many solid tumours such as some types of breast, colon, lung and prostate cancer.

A phase Ib study of venetoclax tested in combination with Roche's anti-CD20 antibody MabThera/Rituxan showed remarkable clinical activity in patients with relapsed/refractory CLL. This clinical study also revealed strategies for improving the safety of this powerful drug combination, particularly starting with lower gentler doses of venetoclax to avoid potential toxicities caused by the very rapid killing of leukemia cells, so-called tumour lysis syndrome (TLS).

Dosing and scheduling modifications have been implemented to minimise risk of TLS going forward, and to date, no additional cases have been reported under the modified protocol.

In late 2014, early-stage data for venetoclax as well as for our MDM2 antagonist RG7388 were presented in acute myeloid leukemia (AML), the most common acute leukemia in adults. MDM2 is a protein that blocks the tumour-suppressing activity of p53, leading to the survival and proliferation of cancer cells. RG7388 is designed to disrupt the interaction between p53 and MDM2, to help restore activity that stops tumour growth and promotes apoptosis

A representative of Roche's highly innovative antibody-drug conjugates, polatuzumab vedotin, consists of an anti-CD79b monoclonal antibody that is linked to a potent microtubule-disrupting agent. By combining a highly selective antibody with a potent chemotherapy drug, polatuzumab vedotin can deliver the cell-killing payload directly to the cancer cells while sparing normal tissues. This compound is now in phase II clinical studies in NHL, a form of blood cancer that kills more than 200,000 people per year worldwide.

#### *A new approach in hemophilia*

Outside of blood cancers, Roche is also developing medicines for other blood disorders with high unmet need. Hemophilia A, the most common type of hemophilia, is a genetic disorder that results in reduced levels or lack of clotting factor VIII. The worldwide incidence is estimated at more than 400,000 people. Approximately 75% of people with hemophilia around the world still receive inadequate treatment or have no access to treatment.<sup>5</sup> The current treatment approach for hemophilia A is intravenous infusion of replacement factor VIII concentrate to prevent or stop bleeds.

RG6013 a bi-specific antibody, mimics the function of factor VIII by simultaneously binding to factors IXa and X, and thus can promote blood clotting in patients lacking factor VIII and in those who have developed inhibitors against factor VIII. RG6013 is the first bispecific antibody developed in hemophilia. It was licensed from Chugai, Japan, in summer 2014. Orphan drug designation has been granted in Europe and the US in December 2013 and January 2014.

Data presented in December 2014 demonstrate that the anti-Factor IXa/X antibody when given subcutaneously is highly effective in hemophilia A patients – significantly reducing the number of bleeding episodes. It was also shown to be well-tolerated and safe; showing no evidence of thrombogenic events (excessive blood clotting).

### **Neuroscience**

Roche has been active in diseases affecting the central nervous system (CNS) since the 1960s and has introduced innovative medicines, including Madopar for the treatment

<sup>5</sup> National Hemophilia Foundation. About bleeding disorders.

of Parkinson's disease. Today, Roche has one of the industry's largest and most diversified pipelines of investigational medicines for neurological disorders with the goal to develop more effective treatment options for people with chronic and potentially devastating diseases.

*Developing better treatments for Alzheimer's disease*  
 Today, 44 million people worldwide have dementia, and Alzheimer's disease (AD) represents up to 80% of those cases. The number of diagnoses is expected to quadruple by 2050 – making AD one of the most serious health issues of the 21<sup>st</sup> century.<sup>6</sup> Current AD treatments focus on alleviating symptoms, but are unable to stop the disease from destroying memory and thinking skills, leading to the inevitable stage when patients are no longer able to care for themselves.

*By 2050, the incidence of dementia is expected to quadruple.<sup>6</sup>*

Roche has a broad AD R&D pipeline that focuses on several proteins and pathways believed to play an important role in the disease.  $\beta$ -amyloid is a protein that accumulates in the brains of people with AD and is hypothesised to play a central role in disease development and progression. Roche is developing multiple molecules, including crenezumab and gantenerumab, to target this pathway.

Crenezumab is an investigational, fully humanised, monoclonal antibody designed to target all forms of  $\beta$ -amyloid. Two phase II studies (ABBY and BLAZE) evaluated whether crenezumab delayed cognitive and functional decline in people with mild-to-moderate AD. Although ABBY did not meet its co-primary endpoints in people with mild-to-moderate AD, it showed a positive trend in cognition observed with greater effect in people with mild disease who received a high dose of crenezumab intravenously. A similar treatment effect was observed in BLAZE, a smaller study that investigated primarily effects on disease biomarkers. Crenezumab is also being evaluated in a separate Alzheimer's Prevention Initiative (API) trial in

Colombia. The Banner Alzheimer's Institute and Genentech jointly lead this study in collaboration with the National Institutes of Health.

The investigational fully human, monoclonal antibody gantenerumab is designed to decrease levels of aggregated  $\beta$ -amyloid. In 2014, enrolment for a phase III study of gantenerumab in people with mild dementia due to AD (Marguerite RoAD) was initiated and recruitment is ongoing. Additionally, gantenerumab is included in the Washington University-sponsored Dominantly Inherited Alzheimer Network-Trials Unit (DIAN-TU) study. This worldwide clinical study is evaluating multiple investigational medicines in individuals at risk for, or with, a type of early onset AD caused by a genetic mutation.

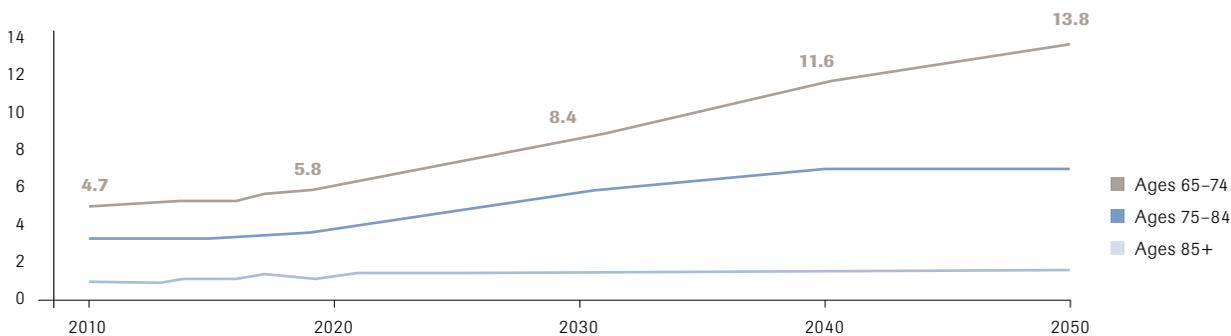
In December 2014, Roche announced the decision to discontinue the phase III SCarlet RoAD study of gantenerumab in prodromal (pre-dementia) AD, based on results of a pre-planned futility analysis.

Therapy with the investigational monoamine oxidase-B inhibitor RG1577 aims to reduce decline in cognition, function and to ameliorate the behavioural problems in mild-to-moderate AD. The phase IIb MAYflower RoAD study investigating 12 months of treatment with RG1577 as add-on to standard of care in AD will complete in 2015.

*Several programmes in multiple sclerosis*  
 Multiple sclerosis (MS) is an autoimmune-mediated disease of the CNS and is one of the leading causes of neurological disability in young adults. In MS, a malfunctioning immune system attacks healthy nerve tissue, which affects the transfer of electrical signals within the CNS and from the CNS to the body. Approximately 2.3 million people worldwide are affected by MS.<sup>7</sup>

Ocrelizumab is a recombinant humanised monoclonal antibody that selectively depletes CD20-expressing B-cells, while preserving the capacity of B-cell reconstitution and pre-existing humoral immunity. Innate immunity and total T-cell number are not affected. B-cells are believed to contribute to nerve cell and myelin damage in the brain

**Millions of people with Alzheimer's disease in the US**



Source: Alzheimer's Dementia: The Journal of the Alzheimer's Association 2014.



and the spinal cord of people with MS. In a phase II study, in patients with relapsing-remitting MS, ocrelizumab met its primary endpoint, significantly reducing signs of disease activity compared with placebo. Furthermore, in exploratory analyses, ocrelizumab significantly reduced signs of disease activity compared with interferon  $\beta$ -1a, a commonly prescribed MS treatment.

Ocrelizumab is currently being investigated in two phase III trials in people with the relapsing forms of the disease as well as in another phase III trial in people with primary progressive MS. Results from these trials are expected in 2015.

Roche also partnered with Inception Sciences and Versant Ventures in 2014 to explore groundbreaking new science to advance the treatment of MS. The objective of this collaboration is to develop novel therapies that promote remyelination of damaged nerve sheaths as a result of MS disease progression.

#### *Partnering for Parkinson's disease*

Roche has re-entered the Parkinson's disease (PD) field, an area where we have made significant progress in the past with the development of Madopar and Tasmar. In 2014, our partner Prothena initiated early development of a monoclonal antibody, RG7935 (PRX002), targeting  $\alpha$ -synuclein, a molecule that may be a cause for motor and cognitive functions in PD. A phase I study will evaluate the safety and tolerability of the compound in healthy volunteers.

#### *Upcoming data in neurodevelopment disorders*

Roche continues its commitment to finding new treatment options for patients with neurodevelopment disorders. We expect a phase II trial investigating the V1a receptor antagonist RG7314 in people with autism spectrum disorder to complete in 2016, where we will evaluate the safety of the

compound alongside improvements in social behaviour and communication.

In addition, in 2014 we started a phase II trial investigating a GABA-A  $\alpha$ 5 Negative Allosteric Modulator (RG1662) in people with Down syndrome. Preclinical data have shown that by selectively modulating GABA-A receptors in the brain, it may be possible to stimulate learning and memory pathways, leading to improvements in cognition and behaviour in Down syndrome. We expect the trial to report in 2016.

#### *Novel pain therapies*

Chronic pain is another area of significant unmet medical need impacting roughly 20% of the world's population. Of those individuals who experience moderate to severe pain, only 25% achieve adequate relief with currently available treatment options in part due to a combination of insufficient efficacy and dose-related side effects. For example, the opioid drug class is associated with poor tolerability (e.g., nausea, dizziness, respiratory depression and constipation) and the potential for addiction and abuse. As a result, there is a significant need for novel pain medicines with new mechanisms of action.

The voltage-gated sodium ( $\text{Na}^+$ ) channel, Nav1.7, expressed primarily in pain-sensing nerve fibres, has been identified as a potential target for novel pain therapies. Notably, humans with a rare genetic defect that results in defective function of this gene are unable to experience acute or inflammatory pain, suggesting that pharmacological inhibition of this channel could have effects on pain sensations. In collaboration with Xenon Pharmaceuticals, potent and isoform-selective inhibitors of the Nav1.7 channel with promising preclinical profiles have been discovered. A first Nav1.7 inhibitor, RG7893, is currently in phase I clinical trials.

### Immunology and inflammation

Roche's immunology medicines include rheumatoid arthritis treatments MabThera/Rituxan and Actemra/RoActemra, Xolair in asthma and Pulmozyme for cystic fibrosis. In addition to these immunology medicines, Roche's late-stage-pipeline projects include etrolizumab being studied in ulcerative colitis and lebrikizumab for severe asthma. Inflammatory bowel disease (IBD) is a chronic disease of the gastrointestinal tract. IBD commonly presents as either Crohn's disease or ulcerative colitis and is associated with significant morbidity, including surgical interventions, hospitalisations and increased risk of colon cancer. In the US alone, Crohn's disease may affect as many as 700,000 people.

Etrolizumab is a gut-selective antibody and targets beta7 resulting in a dual mechanism of action blocking a protein called alpha4beta7 to keep white blood cells from entering the gut, and also blocking another protein called alphaEbeta7. AlphaEbeta7 is thought to keep white blood cells lodged in the mucosa of the gut. This dual mode of action may not only make etrolizumab more effective, but it may also mean that the pre-treatment alphaEbeta7 level could be a biomarker for the disease. A companion test is being developed within Roche's personalised healthcare strategy. Etrolizumab is now in phase III development.

#### *Toward a new option in advanced asthma*

Over 300 million people suffer from asthma worldwide, and 250,000 die of asthma each year. Mild and moderate forms of the disease can be treated adequately with current medications, but around three million people in the US and Europe suffer from severe, uncontrolled asthma. We are currently developing lebrikizumab for the treatment of severe uncontrolled asthma. New data from the LUTE/VERSE phase IIb studies investigating lebrikizumab in patients with severe uncontrolled asthma showed that

asthma attacks were reduced by 60% in lebrikizumab-treated patients with a high level of the biomarker periostin, compared to only 5% in patients with a low level of periostin.<sup>8</sup> The data also showed that in patients with high periostin levels, lebrikizumab improved lung function.\* Results from the phase III clinical trials are expected in 2016. A companion test is being developed at Roche.

### Ophthalmology

Globally, age-related macular degeneration (AMD) ranks third as a cause of blindness after cataract and glaucoma. It is the primary cause of blindness in industrialised countries.<sup>9</sup> Phase III clinical studies have been initiated for lampalizumab, an investigational drug for geographic atrophy (GA), an advanced form of AMD, which can result in blindness. The phase III study programme with two trials called Chroma (GX29176) and Spectri (GX29185) are evaluating the safety and efficacy of lampalizumab and its potential to slow the progression of GA. The studies will also confirm if GA patients with a specific genetic biomarker, complement factor I, may benefit more from lampalizumab treatment.

Diabetic retinopathy is the most common diabetic eye disease. In the US, it impacts nearly 7.7 million people and is the leading cause of new cases of blindness. Due to the emerging diabetes epidemic, diabetic retinopathy is an increasing global health issue. In December 2014, Lucentis (ranibizumab injection) was granted Breakthrough Therapy Designation status for diabetic retinopathy by the FDA. If approved, diabetic retinopathy will be the fourth indication for Lucentis.

Roche is also pioneering the development of the highly innovative bispecific monoclonal antibody RG7716, targeting two angiogenic growth factors – anti VEGF and Ang2. This novel approach will be explored for diseases of the eye

*Age-related macular degeneration negatively impacts vision and is the third-leading cause of blindness.*



including wet AMD and diabetic macular edema. The compound RG7716 is currently in a phase I trial.

### Infectious diseases

The WHO recently highlighted that bacterial resistance to common antibiotics has reached alarming levels in many parts of the world and that in some settings few treatment options remain effective for common infections.<sup>10</sup>

Global public health authorities have come together to declare that, without urgent, co-ordinated action, the world is heading toward a post-antibiotic era, in which common infections, which have been treatable for decades, could kill once again. In the US, at least two million people become infected with antibiotic-resistant bacteria and at least 23,000 people die each year as a result of these infections and 25,000 people die in the EU according to the WHO report on antimicrobial resistance.<sup>11</sup>

Roche has a long and impactful history in the development of antibiotics, including Rocephin and Bactrim, and is committed to the research and development of medicines for the treatment of drug-resistant infections. Our lead compound, RG7929, is a new class of antibiotic designed to treat severe hospital-acquired bacterial infections caused by *Pseudomonas aeruginosa*, a bacteria that accounts for one in every ten hospital-acquired infections in the US and is listed as one of the six most dangerous drug-resistant microbes.

In partnership with Polyphor, a Swiss-based company, RG7929 is currently in phase II trials. In 2014, the compound was designated as a qualified infectious disease product (QIDP) for the treatment of *Pseudomonas aeruginosa* infections. A QIDP designation provides certain incentives for the development of new antibiotics, including priority review, eligibility of fast-track status, and a five-year extension of market exclusivity if the product is approved in the US.

### A wider net in influenza treatment

Seasonal influenza or the flu is an acute viral infection which circulates each year. A serious public health concern, it can cause severe illness and death in high-risk populations such as the very young, elderly or chronically ill. It is estimated that seasonal influenza causes three to five million cases of severe illness each year worldwide, resulting in 250,000 to 500,000 deaths. A vaccination against influenza is seen as the most effective way to prevent infection. Separately, antivirals such as Tamiflu are valuable treatments in reducing symptoms and complications in patients with influenza, although they need to be given within 48 hours of onset of symptoms to be most effective.

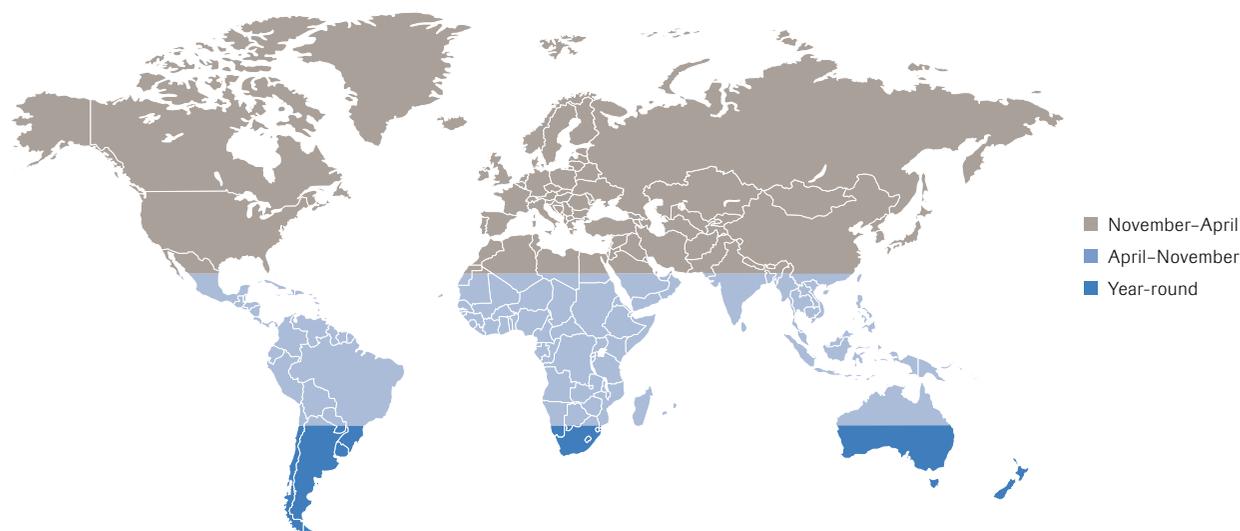
Roche is developing an antibody (RG7745), which targets all seasonal strains of influenza A by binding to a conserved part of the hemagglutinin protein on the surface of the virus that does not change from season to season. The antibody inhibits hemagglutinin-mediated fusion of viral and hosts cell membranes and prevents replication of the virus by blocking entry of viral RNA to the cell nucleus.

Preclinical survival data indicate that RG7745 may be effective as a single agent and additive benefit may be provided by combination with other anti-influenza drugs such as Tamiflu, which inhibits the release of new virus from the infected cell. This molecule has successfully completed a phase IIa clinical study demonstrating significant anti-viral activity and improved clinical symptoms. A global phase IIb clinical study for patients hospitalised with influenza A infection was initiated for the 2014/2015 flu season.

### Hepatitis – a remaining challenge

Hepatitis B continues to be a major global health problem despite the availability of a hepatitis B vaccine (since 1982) that is 95% effective in preventing infection. The disease results in approximately 780,000 deaths every year due to

### Seasonal risk areas for influenza



8 Corren J. et al. Lebrikizumab treatment in adults with asthma. *The new journal of medicine* 2011. | 9 WHO. Prevention of blindness and visual impairment: Priority eye diseases. | 10 WHO Europe. New report: antibiotic resistance, a global health threat. | 11 WHO. Antimicrobial resistance: Global report on surveillance 2014. | \* Maximum amount of air that can be forcibly exhaled in one second.

the acute or chronic consequences of the infection.<sup>12</sup> Pegasys has been one of the mainstays of chronic hepatitis B treatment in adults, and we are continuing our legacy in this area with the composition of one of the most advanced early development pipelines in the industry.

#### *Extending our commitment to virology in China*

The Roche Innovation Center Shanghai, China, is a key hub for the research and development of treatments for infectious diseases and celebrated its 10<sup>th</sup> anniversary this year. While infectious diseases remain the major causes of morbidity and mortality in China, there has been substantial progress in their control, which has led to significant knowledge and expertise in China.

With our commitment to the fight against infectious diseases, Roche will invest 136 million Swiss francs in the development of a state-of-the-art research centre in Shanghai. The centre will be the focal point for all R&D efforts in Shanghai and will facilitate collaboration in scientific excellence, both internally and with the Chinese scientific community. The building is expected to be completed in 2018.

#### **Rare diseases**

Roche is building up a portfolio of investigational medicines for rare diseases. In spinal muscular atrophy (SMA), Roche is developing a SMN2 RNA-splicing modifier in its unique collaboration with a biotech (PTC Therapeutics) and a patient organisation (SMA Foundation). Subsequent to a single-dose study in healthy volunteers, the phase Ib MOONFISH multiple-dose study has now been initiated to evaluate the safety and tolerability of the compound in adults and children with SMA.

#### **Projects that missed key milestones**

The research and development of innovative medicines in areas of unmet medical need is a high-risk venture. In 2014, read-outs of several key studies led us to discontinue or re-evaluate related development programmes.

The bitopertin schizophrenia programme was discontinued after a review of the totality of data from the phase III studies which did not show consistent evidence of clinical efficacy to support further development at this time. We continue to evaluate bitopertin in a phase II trial as an add-on treatment to selective serotonin re-uptake inhibitors for the treatment of obsessive compulsive disorder.

Roche discontinued its Fragile X development programme for basimglurant (RG7090) due to lack of efficacy. However, the primary indication for this molecule continues to be treatment-resistant major depressive disorder and a recent phase II trial produced encouraging results, in which basimglurant was added on top of standard-of-care anti-depressant therapy for patients who had previously failed to respond to conventional medicines.

The phase III METLung study failed to show clinical efficacy of onartuzumab in combination with Tarceva in non-small cell lung cancer and was stopped. Evaluating the implications of these study results, as well as those from some of our phase II studies, across the onartuzumab clinical programme led to the decision to discontinue the development of this compound in 2014.

In Alzheimer's disease (AD), the phase III SCarlet RoAD study of gantenerumab in prodromal AD (pre-dementia) was discontinued in late 2014. The decision was based on results of a pre-planned futility analysis. However, Roche continues a broad research programme targeting different mechanisms of Alzheimer's disease progression. This includes the phase III Marguerite RoAD study of gantenerumab in people with mild dementia due to AD.

In advanced breast cancer (aBC), the phase III MARIANNE study evaluated three HER2-targeted regimens – Kadcyla plus Perjeta, Kadcyla alone, and Herceptin plus taxane chemotherapy – in previously untreated patients with HER2-positive aBC. The study showed the three regimens helped people live without their disease worsening (PFS) for a similar amount of time, meeting its non-inferiority endpoint. However, neither Kadcyla-containing treatment arms significantly improved PFS compared to Herceptin and chemotherapy. In their approved indications Perjeta and Kadcyla help people with HER2-positive aBC live longer.

<sup>12</sup> WHO. Global alert and response (GAR): Hepatitis B 2014.



EMMA's compelling data visualisations and analytics deliver real-time insights into patient enrolment and management.

## Innovative approaches in design and recruitment for clinical studies

Multiple methods are used to design the clinical trials needed to show safety and efficacy of new drugs. Further, many alternatives exist to establish dosing regimen, patient profile, sample size, trial duration, measures of drug effect and drug combinations. At Roche, we are constantly asking how we can optimise our clinical trial methodologies to bring medicines and diagnostic solutions to patients faster.

### Computer modelling in clinical trial design

One key challenge in trial design is evaluating the performance of all possible designs at the outset. Our Clinical Trial Simulation (CTS) tool uses computer simulations to predict the outcomes of different possible clinical trials and helps select the most informative.

Within Roche, the clinical pharmacology function is developing new CTS capabilities to redefine the way we develop drugs and optimise the dose of these drugs. Clinical pharmacologists have long been experts in pharmacokinetic and pharmacodynamic modelling that is used to study the link between doses of drugs and their respective effects, to help optimise the choice of dose. Such modelling informs us of the possible effects of the drug we are studying, and when combined with modelling of the disease it provides the capability to simulate potential clinical trial scenarios.

Implementing CTS requires new software tools, and Roche has collaborated with external partners to develop Simulo, an innovative, cloud-based drug trial simulator, that provides the ability to simulate and analyse virtually limitless numbers of clinical studies.

### Imaging for precision medicine

Our scientists are working at the cutting edge of imaging science to develop and deploy new tools to visualise the effect of new medicines in patients. The data gathered helps to inform drug development decisions and treatment options for patients, ultimately leading to improved outcomes.

Imaging scientists at Roche are working in collaboration with Roche Diagnostics and academic groups to develop innovative new ways of assessing the efficacy of this new class of treatments.

### A data-driven, clinical operations environment

Our focus on innovation has also helped to drive better, data-driven clinical trial management, which is helping accelerate the transition of new molecules from early- to late-stage product development. Several approaches are investigated, including a new programme called Navigate. Launched in 2013, this multi-year initiative is integrating process and the latest information technology, to empower and transform how study teams use data. The Enrolment Measurement and Management Application (EMMA) is one of the first automated clinical trial tools created from Navigate and is enabling study teams to more accurately plan, track and manage patient screening and enrolment.

As a best-in-industry tool, EMMA collects large quantities of operational data in real time, synthesises and makes the information immediately available to study teams in the form of graphic visualisations and user-defined tables. The ability to see a trial's performance from multiple perspectives helps shorten the clinical development lifecycle.



## Reliable supply to patients

Roche Pharma Global Technical Operations is tasked with ensuring the availability of Roche medicines worldwide. We are engaged in activities ranging from the scale-up of production processes to all aspects of manufacturing, from drug substance to packaging and ultimately to delivery of medicines to more than 190 countries globally. Executing these responsibilities in a dynamic and complex business and regulatory environment requires constant vigilance and innovation.

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*Ensuring reliable supplies to patients worldwide from clinical studies to newly approved products.*

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Roche's current pipeline of 66 New Medical Entities (NMEs) is one of the strongest in the industry. Scaling up production, meeting the increasing stringent regulatory requirements, preparing for the launch of multiple new products and providing medicines to patients upon their approval is an extraordinary challenge for our technical operations. To ensure that Technical Operations can deliver Roche's robust pipeline including compounds which have received FDA Breakthrough Therapy Designation, we have implemented several innovative processes and methods. These include establishing seamless handover processes and streamlined product launch sourcing decisions as well as increasing the organisation's capacity and capability.

### **Biologics capacity expansion**

With some of the world's most sophisticated biopharmaceutical production plants, the Roche

manufacturing network hosts approximately 25% of total global biologic production capacity, making Roche the largest manufacturer in the biotech sector.

Activities to re-open the previously idled drug substance production unit in Vacaville, California, are on track and will further increase Roche's biologic manufacturing capacity significantly. The company will invest about 250 million Swiss francs and will offer work places for an additional 200 highly skilled people. The additional Vacaville capacity is expected to be operational in the first quarter of 2016.

At the Oceanside site in California, Roche is investing approximately 120 million Swiss francs into a second purification line to further increase its manufacturing flexibility. This will enable the site to process two products simultaneously. Oceanside plans to add approximately 50 highly skilled positions and is expected to be operational by the first quarter 2016.

At our manufacturing site in Penzberg, Germany, Roche will also expand its biologics capabilities. The company will be investing a total of 400 million Swiss francs over the coming four years. This expansion project will be operational in 2018.

### **New production facilities**

In Basel, Switzerland, Roche has begun the construction of a production centre for antibody-drug conjugates (ADCs). The new ADC facility will support the manufacturing of Kadcyla, a first-of-its-kind medicine used for the treatment of breast cancer, as well as future antibody-drug conjugates. This new centre will cost approximately 190 million Swiss francs and is planned to be operational in August 2016.

The Roche pipeline of small molecules requires special facilities for highly potent drugs. In May 2014, the construction of a launch facility in Basel for high-potent active pharmaceutical ingredients was approved. This new state-of-the-art facility will support the commercial launch and early market supply of important products. The co-location of this launch facility with the technical development team will enable effective and efficient knowledge transfer and thus help simplify registration processes with the authorities.

#### **End-to-end product management**

In order to manage our supply chain more effectively on an end-to-end basis, an enhanced technical product management approach was implemented and significant

progress was made in 2014. This includes clearer governance for sourcing decisions and better defined strategic supply plans over the product lifecycle.

#### **Supplier relationship centre in South San Francisco**

Roche has established a dedicated Supplier Relationship Centre (SRC) in order to work more closely with key suppliers on innovation. In 2014, Roche increased the scope of the SRC to form an Innovation Centre of Excellence to include more external partners and drive innovative strategies. We introduced a new fast-track process to deliver more ideas and value in shorter time. To date, 45 innovative business cases have been approved and 32 are in progress or have been implemented.

## Health IT: interpreting Big Data

Whilst data-driven business models have been employed in other industries for quite some time, the complexity of the healthcare environment represents major challenges for data mining and usage of 'Big Data'.

Within our own clinical studies, huge volumes of data are being generated, for example, in oncology with the sequencing of cancer tissues to identify cancer-driving mutations. Cross-analysis of large patient cohorts, follow-up of patients over time and studies combining several drug candidates generate enormous volumes of data that need to be understood and interpreted. Combining this in-house information with external real-world data poses challenges in terms of comparability of information since a large part of real-world data is unstructured or prone to subjective interpretation. Thus, generating meaningful conclusions that benefit patients and the healthcare systems is extremely challenging.

Nevertheless, several areas demonstrate the potential for such activities:

- Identifying patients who are at risk of developing specific diseases early, by using algorithms that combine different disease-related risk factors using patient data
- Supporting physicians' decision-making in complex diseases, such as cancer. The intrinsic complexity of cancer with its many subgroups, the multiple disease drivers combined with the increasing number of targeted medicines require new approaches in medical data interpretation and long-term patient care
- Analysing real-world patient data in collaborating with healthcare providers, patient registries and other related sources to understand the benefits and risks and cost-effectiveness of our treatments in real-world settings.

Prior to drawing conclusions about potential strategic opportunities resulting from Health IT and Big Data regulatory aspects, data ownership and confidentiality, need to be addressed.

Several initiatives are ongoing to enhance real-world data (RWD) and real-world evidence (RWE) capabilities at Roche. RWD/RWE provide information on the benefits and risks of our medicines in real-world settings. This helps us make informed decisions on development strategy, to improve medical practice and to make our medicines accessible to the right patient at the right time. Many countries are already using RWD/RWE for informed reimbursement decisions on medicines and this is expected to grow in the future. These activities are setting the initial foundation and enhance the infrastructure and capabilities for leveraging RWD/RWE.

A new function, 'Real World Data Science' (RWD-S), was created in Product Development in 2014. The purpose of RWD-S is to translate RWD into evidence and insights to enable better decisions for our medicines to improve patient care. RWD-S can influence global teams to appropriately incorporate RWD options to meet global and affiliate needs. RWD-S focuses on building RWD capabilities at Roche and fostering partnerships that shape the RWD environment. As a strategic partner with the research, development and commercial organisations, RWD-S aspires to be an effective connector across the organisation. With the understanding of evidence needs for our medicines, having knowledge of available data sources and analytical expertise and capacity, our RWD-S will be well equipped to generate RWD/RWE that benefit the various organisations at Roche as well as people in need of our differentiated products.



“My dream  
was always to have a  
direct impact on  
women’s health.”

*Catherine Behrens*

*Catherine, a trained gynecologist, led a team effort to get FDA approval for a new indication using the human papilloma virus (HPV) test as the primary screen for cervical cancer. This diagnostic tool has the potential to reduce the incidence of cervical cancer in women.*

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# New options to detect a virus that causes cancer

*CATHERINE ventured far from her comfort zone in testifying before an FDA Advisory Panel to obtain approval for the cobas HPV test in primary screening.*

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After getting my PhD in molecular endocrinology at the University of California at San Francisco, I went to medical school at Stanford, and also completed a residency programme there in obstetrics and gynecology. I became very committed to patient care, which postponed my plans to return to research. Sometimes, though, I wondered how much impact I was having on the 15–20 women I saw each day and how much more I would have in research.

An issue that troubled me was the screening procedure for cervical cancer. The standard of care for detecting cervical pre-cancer using cytology, known as the Pap smear, had reduced the incidence of cervical cancer by an impressive 75%. The test, however, involved looking at tissue samples under a microscope, which means a chance of human error. There were also many borderline Pap smears that did not provide us physicians with a clear basis for making decisions. On the other hand, we began to think that HPV, the principal cause of cervical cancers, would be a better target for screening.

In 2009, I began working with Roche as a consultant on a clinical trial for a new DNA-based HPV test. I was asked to join the company six months later as the Clinical Leader for the study, known as ATHENA. For me as a gynecologist, it was my dream to have a direct impact on women's health.

ATHENA was unprecedented in its scope and complexity. Over 47,000 American women at 61 sites in 23 states were screened using Roche's DNA-based cobas HPV test. I cannot tell you how many extra hours my colleagues and I put into this study.

What makes the cobas HPV test unique is the ability to detect, with a high rate of accuracy, the 14 highest risk subtypes or genotypes of HPV – including the strains HPV 16 and 18, which are responsible for about 70% of all cervical cancers.

In 2011, the FDA approved the cobas HPV test as an adjunct test to the Pap smear. It was an exciting moment for the team, of course, but the work was not over.

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IN MORE THAN  
**99%**  
CERVICAL CANCER  
IS CAUSED BY HPV INFECTIONS<sup>13</sup>

EVERY YEAR, CERVICAL CANCER  
KILLS MORE THAN  
**270,000**  
WOMEN<sup>14</sup>

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In 2013, we submitted new data to the FDA for the purpose of getting the cobas HPV test approved as the first-line primary screening test for cervical cancer.

Since evaluating a new primary screening tool for HPV was uncharted territory for the FDA, they appointed an Advisory Panel comprising leading experts in the field. As the Clinical Leader for ATHENA, I was expected to present the trial data and answer questions before this panel which convened outside of Washington, D.C.

I had never done anything like this before. It meant going well out of my comfort zone. I knew good preparation was key, so I worked closely with the HPV team and practised my presentation often with my colleagues. We tried to anticipate possible questions and prepared approximately 500 backup slides with additional data.

On 12 March 2014, we faced 13 members of the FDA Advisory Panel and an audience of over 200 people for nine hours. My testimony and the question-and-answer period were recorded on video and posted online as part of the public record.

At the conclusion of the hearing, there were three questions posed by FDA representatives to the Advisory Panel experts regarding the safety and effectiveness of the cobas HPV test as a primary screening tool. The panel voted unanimously in the affirmative to all three questions. My colleagues and I were really pleased!

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*“We faced the FDA Advisory Panel for nine hours of presentations and questions. They voted unanimously in favour of the cobas HPV test.”*

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Following the FDA approval, during a transition period, there will be co-testing, as many physicians continue screening with the Pap smear and add on the cobas HPV test. Outside the US, our test has been made available in the EU, and we are preparing filing or have filed in a number of countries to broaden the availability of this test to women around the world.

Both methods of testing work well together. As a primary screen, the cobas HPV test with its increased sensitivity casts a wide net to detect the presence of the virus. Those women who test positive for the most dangerous HPV strains, subtypes 16 and 18, should undergo further checking for pre-cancerous cells. Women who test positive

for the 12 other high-risk genotypes can be screened with Pap smear to see if further interventions are warranted.

The cobas HPV test could be important for women around the world – according to WHO about 270,000 deaths occur every year due to cervical cancer. In a number of countries, there is a lack of infrastructure and training to perform Pap smears. For them, it may make sense to leapfrog this technology, and go directly to the screening process using the cobas HPV test, which is largely automated.

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*“I feel truly privileged to be a part of a global team that could have an impact on the future of women’s healthcare.”*

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The cobas HPV test complements other products in the Roche portfolio. The CINtec and CINtec Plus tissue-based tests, approved in Europe, are helping to identify those HPV-positive women who would benefit most from treatment of the early disease (pre-cancer) stages.

Avastin, a cancer medicine from Roche, has been approved in the US in 2014 to treat metastatic cervical cancer.



**Catherine:** “The ATHENA study caused an enormous amount of extra hours for many of us, but it was enormously gratifying to work on developing a test which could help to save lives.”

13 WHO. Human papilloma virus (HBS). | 14 WHO. Sexual and reproductive health: New guidance for the prevention and control of cervical cancer 2015.

# The value of diagnostic test results

## Diagnosing heart attacks

A heart attack, or acute myocardial infarction (AMI), is a common cardiac event in which the blood supply to an area of the heart is interrupted, causing the cardiac muscle cells to die. There are over seven million fatalities from AMI worldwide annually. Fast and reliable diagnosis of heart attacks is critical for AMI patients as every delay between onset of symptoms and treatment increases the mortality risk.

The Roche-sponsored TRAPID-AMI clinical study showed that a novel approach to diagnose or exclude heart attacks in patients with acute chest pain reduces the typical observation time of three to six hours to just one hour. This accelerated one-hour approach is based on the Elecsys Cardiac Troponin T high sensitive test from Roche and will enable physicians to treat the patients much earlier. In case of heart attack, saving time avoids additional damage to the heart and is important to maximise the efficaciousness of treatment. Additionally, for cases where the diagnosis of heart attack is excluded, faster exclusion may reduce patient anxiety and help to alleviate emergency room workload.

## Improving prediction of preeclampsia

Preeclampsia affects about one in twenty pregnancies and is one of the leading causes of fetal and maternal morbidity and mortality. In the current guidelines, the diagnosis of preeclampsia is based on the clinical parameters of hypertension and proteinuria, but both are poor in predicting the clinical onset of the disease and disease progression.

Results of the PROGNOSIS study showed that the Elecsys immunoassay sFlt-1/PIGF ratio is useful for the short-term prediction of preeclampsia. It provides physicians with a reliable tool to identify women at high risk of developing preeclampsia and who require intensified monitoring. At the same time, the Elecsys immunoassay sFlt-1/PIGF test allows physicians to confidently release women with suspected

preeclampsia who are not going to develop the disease in the short term. From an economical perspective this may help save expenditures by healthcare systems on unnecessary hospital admissions or excessive medical treatment.

## Tumour characterisation and therapy monitoring

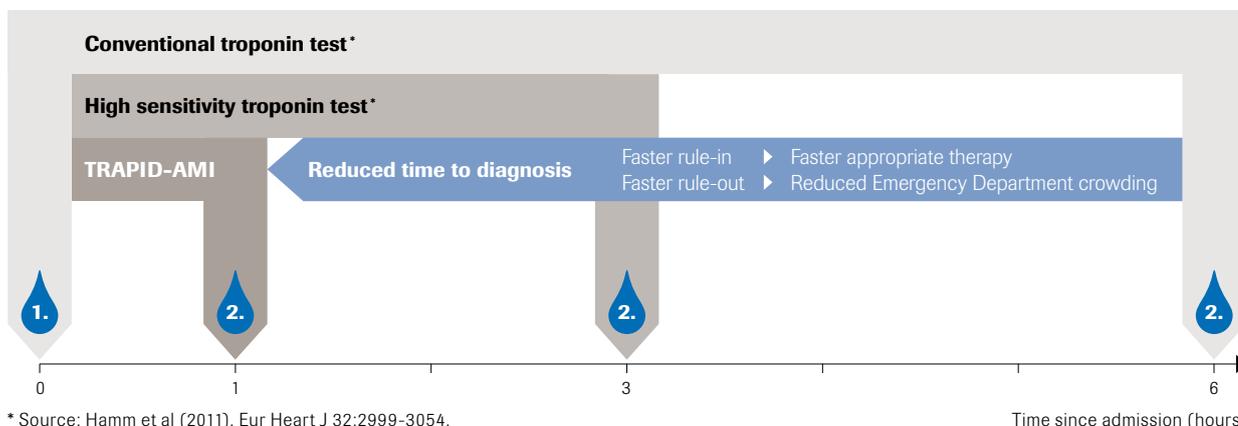
Liquid biopsy is an innovative, alternative method for assessing cancer genetic status based on blood drawn from the patient. Currently, patients with advanced cancer require an invasive tumour tissue biopsy for diagnosis; requiring the tissue to be sent to a laboratory for review and molecular testing. Clinicians rely on the identification of the correct molecular target to take the right treatment decisions, including targeted drug therapies. Occasionally, there is not enough tissue-based sample material available or a patient is not healthy enough to have the tissue biopsy procedure performed; in which case having an alternative solution is valuable. Studies have shown that tumours release proteins, nucleic acids and cancerous cells into the blood. Because blood samples can be easily obtained, the concept of a blood-based biopsy has long held promise as a non-invasive complement to traditional biopsy techniques.

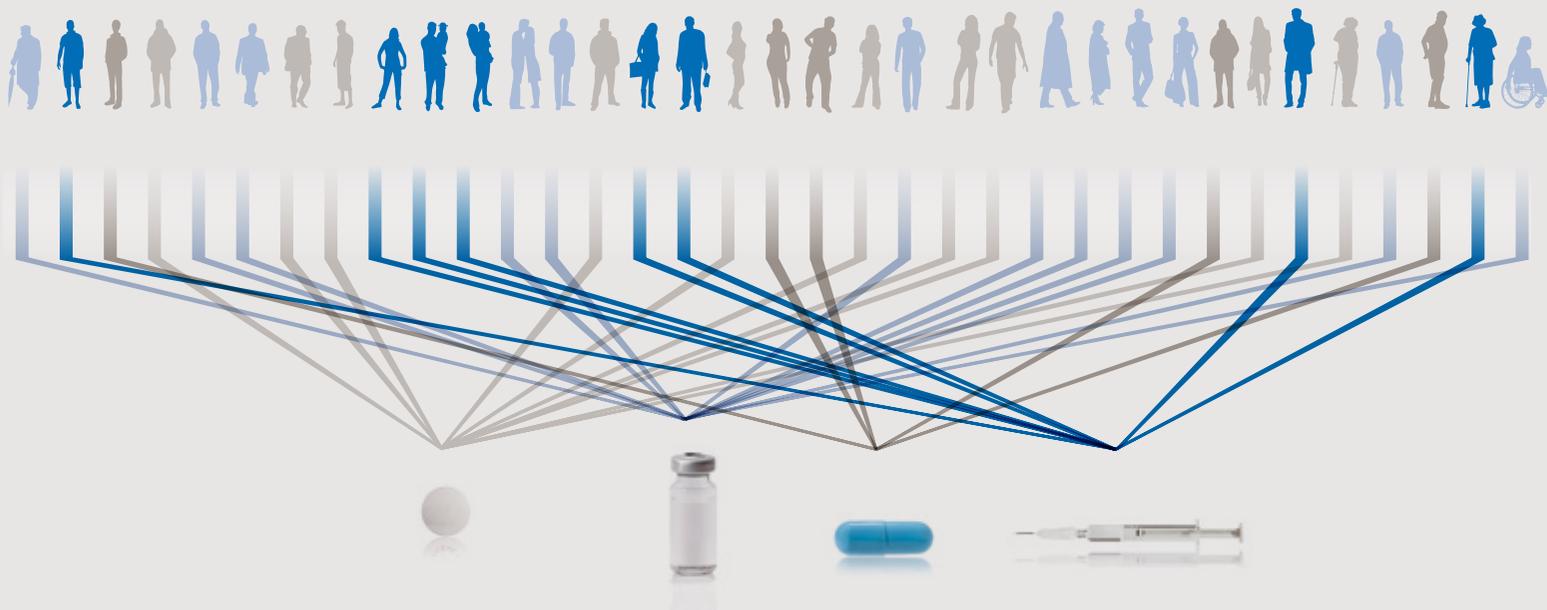
With a new molecular test for lung cancer patients in development, Roche will enable clinicians to evaluate the current health status of their patients, determine which biopsy to perform, tissue or liquid, and ultimately allow clinicians to bring the right treatment to the right patient and ensure that the therapy they have selected remains relevant.

## Next generation sequencing

Roche is developing an integrated genomics portfolio for next generation sequencing (NGS). Adding to internal potential breakthrough technologies we acquired Genia Technologies, Inc., Bina Technologies, Inc. and Ariosa Diagnostics, Inc. as well as technology of AbVitro and AvanSci. Collaboration agreements with Stratos Genomics,

### Fast and reliable diagnosis of heart attacks is critical for the initiation of specific medical care





Modern diagnostic tests allow the identification of specific cancer-causing genetic mutations, thus enabling physicians to apply targeted therapies.

The Garvan Institute, Cornell University and University of Washington complement these acquisitions.

Genia’s proprietary single-molecule electrical detection technology could reduce the cost of sequencing while increasing speed and sensitivity. A Roche expert team is actively working with Stratos and once their Xpandomer conversion chemistry has been developed, Roche will likely explore how to use it with Genia’s protein nanopore platform.

Our focus is to advance NGS in specific application areas. Ariosa is the first in a series of efforts to expand our menu in the NGS market. Ariosa’s Harmony™ Prenatal test for non-invasive prenatal diagnosis using circulating fetal DNA. Circulation DNA has the promise of providing non-invasive early testing in many segments including pregnancy, cancer and transplantation. The acquisition of Bina complements our existing technologies and enables the development of this end-to-end sequencing workflow solution.

**Diagnostics Division – key product launches planned for 2015**

Area	Product name	Description	Market
<b>Instruments/Devices</b>			
Laboratories	cobas c 513	dedicated HbA1C analyzer	EU
	cobas t 411	core laboratory coagulation analyzer	EU
	cobas 8100 V2	integrated pre- and post-analytical solution	WW
	cobas 6800/8800	medium- to high-volume automated real-time PCR	US
	VENTANA HE 600	automated H&E staining platform	WW
Diabetes Care	Accu-Chek Active no-code	next generation blood glucose meter, no coding of test strips	WW
	Accu-Chek Connect	blood glucose meter with connectivity to smartphones, mobile applications and cloud	US
Point of care	CoaguChek Pro II	professional system for PT and aPTT testing	EU
<b>Tests</b>			
Blood screening	MPX test	multiplex blood screening test for cobas 6800/8800 systems	US
Infectious diseases	Influenza A/B + RSV test	point-of-care detection on cobas LIAT	US
	HTLV test	human T-lymphotropic virus test	EU
Virology	HBV test	quantitative HBV viral load test for cobas 6800/8800	EU
	HIV-1 test	quantitative HIV-1 viral load test for cobas 4800	EU
	HCV test	quantitative HCV viral load test for cobas 4800	EU
	HBV test	quantitative HCV viral load test for cobas 4800	EU
Genomics and Oncology	EGFR test V2	detection of EGFR mutations in plasma	EU
Cardiology	cobas h 232 Troponin T test	point-of-care test version of Elecsys cTNT-hs	EU

WW – Worldwide. | PT – prothrombin time. | aPTT – activated partial thromboplastin time.



## Building partnerships with leading institutions around the world

Roche was one of the first healthcare companies to recognise the importance of external innovation and Genentech Partnering and Roche Partnering were established as organisational structures. The objective is to marry external scientific expertise and technology breakthroughs with Roche's internal drug discovery pipeline aligned with our overall R&D strategy. We focus on well-defined therapeutic areas and optimal synergies between external innovation and Roche's own R&D portfolio and development/manufacturing expertise. The resulting diversity of views, cultures and approaches, which is a hallmark of R&D at Roche, promotes creativity and innovation.

### Roche Partnering

Roche Partnering (RP) was founded over ten years ago to provide the company with an additional pillar of innovation. RP screens about 2,500 opportunities each year, from early development and platform technologies up to phase III molecules and merger and acquisition opportunities. As of 2014, RP is managing close to 190 external partnerships around the world. About 35% of Roche's R&D pipeline compounds are externally sourced, and Roche-partnered products contribute over a third of total Pharmaceuticals sales.

In 2014, RP signed 55 new agreements, including three acquisitions, four product transactions, 37 research and technology collaborations and 11 product out-licensing agreements. The RP team searches for novel compounds that address unmet medical needs and have the potential to become first-in-class, best-in-class or best-in-disease medicines. Committed to discovering truly cutting-edge

innovation, Roche maintains close contact with academia as well as biotechnology companies. A candidate compound will go through a series of checkpoints and studies driven jointly by the partner and Roche to increase the likelihood of success in clinical development, and ultimately provide new options to patients.

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*Externally sourced compounds contribute about one third of pipeline and Pharmaceuticals total sales.*

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Our mission is to follow the science, find true innovation and build strong, win-win alliances with our partners. This includes early-stage collaborations with leading academic centres to foster the development of novel targets, molecules, technologies and platforms.

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**MORE THAN**  
**100** **NEW**  
**EXTERNAL PARTNERSHIPS**  
**ACROSS THE ROCHE GROUP**

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RP is comprised of a multi-disciplinary workforce with strong expertise from therapeutic areas and business development with offices in Basel, New York, South San Francisco, Tokyo and Shanghai. RP works closely with internal partners in multiple functions, enabling in-depth expert assessments to select the most promising external projects. The overarching principle is seeking only the best of external innovation that will create the most fruitful synergies with Roche's in-house pipeline and expertise.

### **Innovative agreements beyond traditional partnerships**

Roche offers creative deal structures that go beyond the traditional partnership agreement to create win-win alliances tailored to the assets and partner companies. Roche's partners also benefit from Roche technologies, such as the brain shuttle technology. Partners can also take advantage from Roche's expertise in diagnostics, both to identify the most suitable patients for a treatment as well as to measure the effect of a drug.

A recent example of a new partnering approach is the 'build-to-buy' deal with Versant Ventures and Inception Sciences. The collaboration resulted in a new start-up company called Inception 5, which will research and develop novel small-molecule therapies that aim to promote re-myelination of nerve sheaths damaged as a result of disease progression in multiple sclerosis patients. Inception 5 builds on recent discoveries in the field and will use a proprietary screening platform developed by investigators at the University of California in San Francisco, pursuing multiple molecular targets for re-myelination. Versant provides equity financing to the company and Roche will fund the research based on a series of milestones. Roche retains an exclusive option to acquire Inception 5 upon a first lead compound reaching the filing stage of an investigational new drug application.

In the rare diseases area, Roche is collaborating with Canadian venture firm AmorChem to develop a new therapeutic approach for myotonic muscular dystrophy type 1, or Steinert disease. Currently, there is no approved treatment available to slow or stop disease progression. Based on research carried out at University of Montreal, the new approach aims to interfere with the splicing alteration caused by the genetic defect. Discovery will take place at AmorChem's medicinal chemistry contract research organisation, NuChem Therapeutics, and the University of Montreal laboratories. Roche will provide scientific support and will contribute R&D funding together with AmorChem.

To propel the discovery of RNA-targeting therapeutics, Roche acquired Santaris Pharma A/S, Denmark — now integrated in the R&D organisation as the Roche Innovation Center Copenhagen. RNA therapeutics research may produce a new modality, or a unique class of medicines,

to complement small- and large-molecule antibodies and protein therapeutics research.

An example of a Roche technology that supports a partner's R&D is the agreement developed between Roche and Prothena to tackle Parkinson's disease. It includes a programme to test and use the Roche brain shuttle technology to potentially increase the delivery of antibodies targeting  $\alpha$ -synuclein into the brain, to improve their potency for treatment of Parkinson's disease.

### **Genentech Partnering**

In 2014, Genentech Partnering and Genentech's Research Contracts group signed 55 new agreements including one acquisition, five product transactions, 11 research and technology collaborations, and 38 academic research collaborations.

In 2014, the acquisition of Seragon Pharmaceuticals, Inc., a privately held biotechnology company based in San Diego, California, was completed. The Roche Group obtained the rights to Seragon's portfolio of investigational next-generation oral selective estrogen receptor degraders (SERDs) for the potential treatment of hormone receptor-positive breast cancer. In 2014, breast cancer claimed the lives of nearly 40,000 women in the US, and up to half of these women had a disease driven by the estrogen receptor.<sup>15</sup> Although medicines have been approved for the treatment of hormone receptor-positive breast cancer for decades, more treatment options are needed. These investigational SERDs complement our existing R&D programmes, strengthen our pipeline, and could one day redefine the standard of care for hormone receptor-positive breast cancer.

In the neuroscience field, we entered into a second collaboration with our strategic partner Xenon for pain genetics, with the goal of discovering and validating new therapeutic targets and mechanisms for treating pain. The pursuit of targets with human genetic validation is core to our pain strategy, but developing drugs against such targets is highly competitive. This collaboration seeks to put Genentech in a first-in-class position for novel therapeutics to treat pain by leveraging Xenon's expertise in genetic validation of targets. Our aim is to discover highly validated targets that could yield novel non-opioid-based mechanisms to treat pain.

<sup>15</sup> Breastcancer.org. U.S. Breast cancer statistics 2014.

# Conducting responsible R&D

All of our R&D activities are conducted with the highest ethical standards. We have published several position papers on our 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.

## 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.

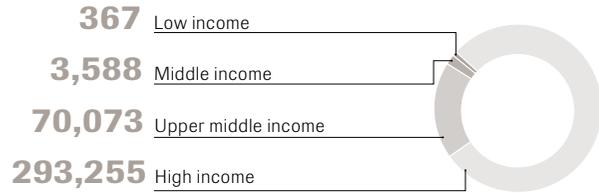
*In 2014, more than 360,000 patients were involved in our clinical trials.*

## Clinical trials

	2014
Number of clinical trials	1,809
Number of healthcare centres involved	32,750
Number of patients in phase I-IV clinical trials	367,283

## Roche clinical trial statistics 2014

Number of patients in clinical trials by World Bank country classification\*

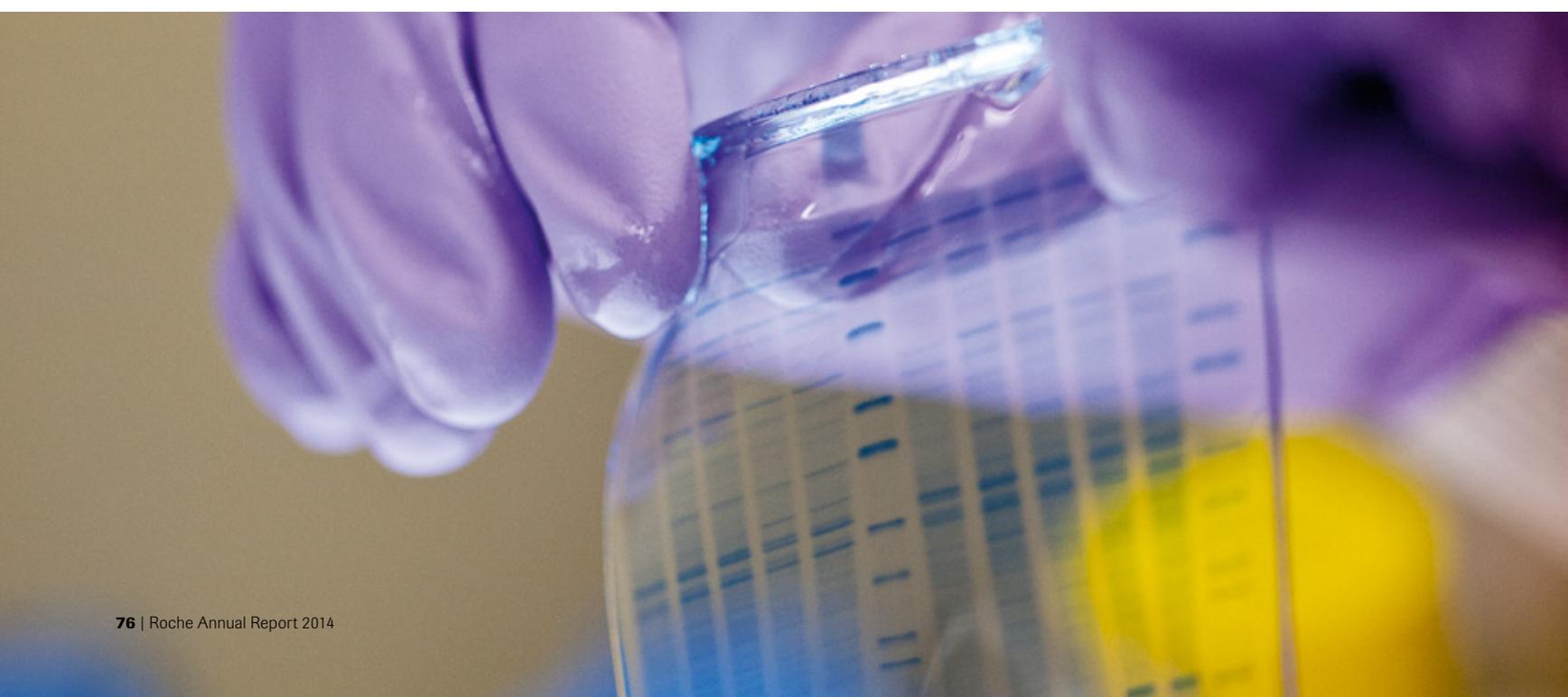


\* Source: World Bank, July 2014.

## Animal welfare

We continue to seek alternatives to the use of animals in studies, with technologies such as computer simulation or *in vitro* testing using differentiated cells or induced pluripotent stem cells. In Switzerland, we support the 3R Research Foundation which funds the development or improvement of methods based on the 3R strategy. This approach aims to use alternatives to animal testing whenever possible (Replace); improve existing methods so that fewer laboratory animals are required (Reduce) and improve existing methods so that animals experience as little discomfort and distress as possible (Refine).

In 2014, we used 328,655 animals in our internal research, a 7.8% decrease from 2013. The number of animals used by contract research organisations working on Roche's behalf decreased to 50,669 compared with 62,636 in 2013. Approximately 97.7% of the animals used were mice and rats.



All major research sites were awarded continued full re-accreditation status by the Association for Assessment and Accreditation of Laboratory Animal Care International, underscoring our commitment to ensuring animal welfare.

In October 2014, plans were announced to build a new *in vivo* research facility at the Basel site in Switzerland. The new state-of-the-art building, planned for completion in 2018, will meet the highest requirements of animal welfare and set a new standard in our industry for preclinical *in vivo* biology research.

### **Clinical-data sharing**

In January 2014, Roche announced its next step in sharing clinical trial data and providing access to analysable patient-level data to researchers.<sup>16</sup> Since June 2013, Roche has also provided access to Clinical Study Reports (CSRs) and other summary reports. This new approach provides a balance between our commitment to sharing data from our trials, while safeguarding patient confidentiality and the regulatory process. Both CSRs and analysable patient-level data are anonymised to respect the privacy of patients participating in our trials in accordance with relevant laws and regulations.

Overall, the policy goes beyond European and American industry guidelines, which came into effect 2 January 2014, and we are now at the forefront of the data-sharing movement identifying new ways to share clinical research with the scientific community.

For more details, please see [www.roche-trials.com/dataSharingPolicyInformation.action](http://www.roche-trials.com/dataSharingPolicyInformation.action)

<sup>16</sup> [www.clinicalstudydatarequest.com](http://www.clinicalstudydatarequest.com) | \* Based on Gross National Income per Capita in 2013: Low income: USD 1,045 or less, Lower middle income: USD 1,046 to USD 4,125, Upper middle income: USD 4,126 to USD 12,745, High income: USD 12,746 or more.

# Pharmaceuticals pipeline

*WE FOCUS* on a select group of disease areas including oncology, hematology, neuroscience, immunology, inflammation, ophthalmology, infectious and rare diseases.

Project ID	Project/Product	Indication	Phase:	I	II	III	IV
<b>Oncology</b>							
RG7421	⊕ cobimetinib + Zelboraf	metastatic melanoma					
RG105	MabThera sc	CLL					
RG435 <sup>2</sup>	Avastin	recurrent cervical cancer					
RG1273 <sup>2</sup>	Perjeta	HER2+ BC neoadjuvant					
RG435 <sup>1</sup>	Avastin	glioblastoma 1 <sup>st</sup> line					
RG435 <sup>1</sup>	Avastin	ovarian cancer 1 <sup>st</sup> line					
RG435 <sup>1</sup>	Avastin	relapsed ovarian cancer, platinum-sensitive					
RG435	Avastin	NSCLC adjuvant					
RG1273	⊕ Perjeta	HER2+ mBC 2 <sup>nd</sup> line					
RG1273	⊕ Perjeta	HER2+ BC adjuvant					
RG1273	⊕ Perjeta	HER2+ gastric cancer 1 <sup>st</sup> line					
RG3502	⊕ Kadcyla	HER2+ gastric cancer 2 <sup>nd</sup> line					
RG3502	⊕ Kadcyla +/- Perjeta	HER2+ mBC 1 <sup>st</sup> line					
RG3502	⊕ Kadcyla	HER2+ BC adjuvant					
RG3502	⊕ Kadcyla + Perjeta	HER2+ BC adjuvant					
RG3502	⊕ Kadcyla + Perjeta	HER2+ BC neoadjuvant					
RG7159	Gazyva	DLBCL 1 <sup>st</sup> line					
RG7159	Gazyva	iNHL, rituximab refractory					
RG7159	Gazyva	follicular lymphoma 1 <sup>st</sup> line					
RG7204	⊕ Zelboraf	melanoma adjuvant					
RG7446	⊕ PD-L1 MAb	NSCLC 2 <sup>nd</sup> line					
RG7601	venetoclax (Bcl-2)	CLL relapsed/refractory					
RG7601	venetoclax + Gazyva	CLL 1 <sup>st</sup> line					
RG7853	⊕ alectinib (ALK inhibitor)	NSCLC					
RG435	Avastin + Tarceva	EGFR mut+ NSCLC					
RG3502	Kadcyla	HER2+ NSCLC					
RG6013	FIXa/FX bispecific MAb	hemophilia A					
RG6046	SERD	ER+ (HER2-neg) mBC					
RG7155	CSF-1R MAb	PVNS, solid tumours					
RG7221	⊕ Ang2-VEGF MAb	colorectal cancer					
RG7321	pictilisib	solid tumours					
RG7421	cobimetinib + paclitaxel	triple negative breast cancer					
RG7440	⊕ ipatasertib (AKT inhibitor)	solid tumours					
RG7446	⊕ PD-L1 MAb	NSCLC 2 <sup>nd</sup> /3 <sup>rd</sup> line					
RG7446	⊕ PD-L1 MAb + Avastin	renal cell carcinoma					
RG7446	⊕ PD-L1 MAb	bladder cancer					
RG7596	polatuzumab vedotin (CD79bADC)	hematologic tumours					
RG7599	⊕ ifastuzumab vedotin (NaPi2bADC)	platinum-resistant ovarian cancer					
RG7601	venetoclax (Bcl-2)	CLL relapsed/refractory 17p deletion					
RG7601	venetoclax (Bcl-2)	DLBCL					
RG7601	venetoclax (Bcl-2) + Rituxan	relapsed/refractory follicular lymphoma					
RG7604	⊕ taselisib (mutant selective)	solid tumours					
RG7686	⊕ glypican-3 MAb	liver cancer					
RG6016	⊕ LSD1 inhibitor	AML					
RG6046	⊕ SERD (2)	ER+ (HER2-neg) mBC					
RG6061	⊕ HIF1 alpha LNA	solid tumours					
RG6078	⊕ IDO inhibitor	solid tumours					
RG7116	⊕ HER3 MAb	solid tumours					
RG7155	⊕ CSF-1R + PD-L1 MAb	solid tumours					
RG7304	Raf & MEK dual inhibitor	solid tumours					
RG7388	⊕ MDM2 ant	solid & hematologic tumours					
RG7446	PD-L1 MAb + Tarceva	NSCLC EGFR+					
RG7446	PD-L1 MAb + Zelboraf +/- cobimetinib	metastatic melanoma					
RG7446	PD-L1 MAb + Avastin + chemo	solid tumours					
RG7446	PD-L1 MAb + cobimetinib	solid tumours					
RG7446	PD-L1 MAb + ipilimum./IFN	solid tumours					
RG7446	PD-L1 MAb	solid tumours					
RG7446	PD-L1 MAb + Gazyva	lymphoma					
RG7450	⊕ Steap 1 ADC	prostate cancer					
RG7597	⊕ HER3/EGFR DAF + cobimetinib	KRAS mut+					
RG7601	venetoclax (Bcl-2) + Gazyva	CLL					
RG7601	venetoclax (Bcl-2)	hematology indications					

Project ID	Project/Product	Indication	Phase:	I	II	III	IV	
<b>Oncology</b>								
RG7741	ChK1 inhibitor	solid tumours and lymphoma						
RG7775	⊙ MDM2 (4) IV prodrug	AML						
RG7787	⊙ MSLN PE cFP	oncology						
RG7802	⊙ CEA CD3 TCB	solid tumours						
RG7813	⊙ CEA IL2v	solid tumours						
RG7841	⊙ ADC	solid tumours						
RG7842	⊙ ERK inhibitor	solid tumours						
RG7876	⊙ CD40 iMAb + PD-L1 MAb	solid tumours						
RG7882	⊙ ADC	ovarian cancer						
RG7888	⊙ anti-OX40 MAb	solid tumours						
<b>Inflammation / Immunology</b>								
RG1569	Actemra	giant cell arteritis						
RG3637	⊙ lebrikizumab	severe asthma						
RG7413	⊙ etrolizumab	ulcerative colitis						
CHU	Actemra	large-vessel vasculitis						
CHU	Suvenyl	enthesopathy						
CHU	IL-6R MAb	neuromyelitis optica						
RG1569	Actemra	systemic sclerosis						
RG3637	⊙ lebrikizumab	idiopathic pulmonary fibrosis						
RG6062	Esbriet	SSc – interstitial lung disease						
CHU	IL-31R MAb	atopic dermatitis						
RG7625	NME	autoimmune diseases						
RG7880	NME	autoimmune diseases						
<b>Infectious Diseases</b>								
RG7227	⊙ danoprevir	HCV						1 US only:
RG7745	⊙ Flu A MAb	influenza						FDA submission decision pending
RG7790	setrobutvir	HCV						2 Approved in US, submitted in EU
RG7929	LptD antibiotic	bacterial infections						3 Submitted in US
RG6080	DBO β-lactamase inhibitor	bacterial infections						
RG7689	NME	infectious diseases						
RG7795	⊙ TLR7 agonist	HBV						⊙ Personalised Healthcare project
<b>Metabolic/Cardiovascular</b>								
CHU	URAT 1 inhibitor	gout						RG-No Roche Genentech managed
RG7697	GIP/GLP-1 dual ago	type 2 diabetes						CHU Chugai managed
RG7641	aldosterone synthesis inhibitor	metabolic diseases						RG105 MabThera is branded as Rituxan in US and Japan
<b>Neuroscience</b>								
RG1450	⊙ gantenerumab	Alzheimer's disease						RG1569 Actemra is branded as RoActemra in EU
RG1594	ocrelizumab	RMS						
RG1594	ocrelizumab	PPMS						
RG1577	⊙ MAO-B inhibitor	Alzheimer's						
RG1662	⊙ GABRA5 NAM	Down Syndrome						
RG1678	⊙ bitopertin	obsessive compulsive disorders						
RG7090	basimglurant (mGlu5 NAM)	treatment resistant depression						
RG7314	⊙ V1 receptor antagonist	autism						
RG7412	⊙ crenezumab	Alzheimer's disease						
RG7203	⊙ PDE10A inhibitor	schizophrenia						
RG7342	mGlu5 PAM	schizophrenia						
RG7345	TAUpS422 MAb	Alzheimer's disease						
RG7410	⊙ TAAR1 ago	schizophrenia						
RG7893	Nav1.7 inhibitor	pain						
RG7800	⊙ SMN2 splicer	spinal muscular atrophy						
RG7935	⊙ a-synuclein MAb	Parkinson's disease						
<b>Ophthalmology</b>								
RG3645 <sup>3</sup>	Lucentis	diabetic retinopathy						AML acute myeloid leukemia
RG7417	⊙ lampalizumab (factor D)	geographic atrophy						AMD age-related macular degeneration (wAMD = wet AMD)
RG3645	Lucentis sustained delivery	AMD/RVO/DME						BCC basal cell carcinoma
RG7716	⊙ VEGF-ANG2 MAb	wAMD						CLL chronic lymphocytic leukemia

1 US only:  
 FDA submission decision pending  
 2 Approved in US, submitted in EU  
 3 Submitted in US

⊙ Personalised Healthcare project  
 RG-No Roche Genentech managed  
 CHU Chugai managed  
 RG105 MabThera is branded as Rituxan in US and Japan  
 RG1569 Actemra is branded as RoActemra in EU

AML acute myeloid leukemia  
 AMD age-related macular degeneration (wAMD = wet AMD)  
 BCC basal cell carcinoma  
 CLL chronic lymphocytic leukemia  
 CMV cytomegalovirus  
 DLBCL diffuse large B cell lymphoma  
 DME diabetic macular edema  
 EGFR epidermal growth factor receptor  
 ER estrogen receptor  
 HBV hepatitis B virus  
 HCV hepatitis C virus  
 MAb monoclonal antibody  
 mBC metastatic breast cancer  
 iNHL non-Hodgkin's lymphoma  
 NSCLC non-small cell lung cancer  
 PPMS primary progressive multiple sclerosis  
 RA rheumatoid arthritis  
 RMS relapsing multiple sclerosis  
 RVO retinal vein occlusion  
 sc subcutaneous  
 SSc systemic sclerosis related interstitial lung disease

# Access to healthcare



**19** MILLION **patients** treated with a Roche top 25 selling product



**1.3** MILLION **infants** tested for HIV in sub-Saharan Africa

**11,446** **patients** treated with Herceptin in China on Roche patient assistance programme



**10,726** **pathologists, surgeons and technicians** trained through Roche SPHERE programme in Asia



## An enormous global challenge

*SIGNIFICANT BREAKTHROUGHS in diagnosing and treating serious diseases, as well as improvements in the delivery of healthcare, have steadily improved health outcomes and increased life expectancy in recent decades.*

Universal access to medical innovation and quality healthcare, however, remains a global challenge, particularly in emerging and developing countries. In many countries, there are severe shortages of equipment, medical professionals, medicine supplies and a lack of awareness of disease prevention. Added to this, with the adoption of more Western dietary habits and sedentary lifestyles, the incidence of cancer is rising in these countries and healthcare infrastructure is often inadequate. Innovative solutions are required to address these problems and make sure more patients in need have access to medicines and diagnostic testing.

In 2014, Roche developed a comprehensive strategy to improve this situation. We are systematically analysing the root cause of barriers in each individual market – in both developing, as well as established markets. We are also identifying the key healthcare stakeholders to partner with and support improvements in access. Through

developing innovative approaches in collaboration with international and local players, Roche strives to make a significant impact in addressing this disparity for many patients around the world, supporting the universal healthcare coverage goal, which aims for everyone to access quality healthcare services without financial hardship.

**1 BILLION**  
PEOPLE LACK ACCESS  
TO BASIC HEALTHCARE<sup>1</sup>



## Reaching more patients in need

**Improving affordability.** We are developing new pricing models that are tailored to the benefit the product delivers along with the ability of local payers to pay, rather than a uniform global price. We are also working on expanding reimbursement in the public market, along with private health insurance.

**Increasing availability of innovative products.** We are exploring ways to bring our innovative medicines and tests to the market faster, through supporting regulatory harmonisation, supply chain issues and other barriers.

**Strengthening infrastructure.** We have established programmes to strengthen local, national and regional capacities, including health systems. Building facilities, training healthcare professionals and transferring skills and expertise.

**Increasing awareness and patient support.** We support community partners to run screening, awareness, counselling and other support programmes that empower people with the knowledge to safeguard and manage their own health.

## Improving affordability

We recognise that despite improvements in healthcare infrastructure and funding, innovative medicines and diagnostics remain beyond the reach of many patients in need. People may have access to quality healthcare in the private sector, for example, where incomes are higher, but the public health system may not offer the same level of access.

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*Even in countries with advanced healthcare systems, treatment may not be fully reimbursed.*

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As a result, many patients are unable to either start treatment or continue a full treatment course. To ease these barriers, we have developed innovative pricing models, tailored to the needs of patients in different healthcare systems.

### **Personalised reimbursement models**

With our increased understanding of disease pathology, we have realised that similar mechanisms and pathways are relevant in different types of tumours. This progress in science has brought us medicines that improve patient outcomes in a variety of diseases, but the extent of the benefit for patients can differ between diseases. There are also an increasing number of combination therapies being developed, that require more than one medicine to achieve optimal outcomes for patients. This has led us to create

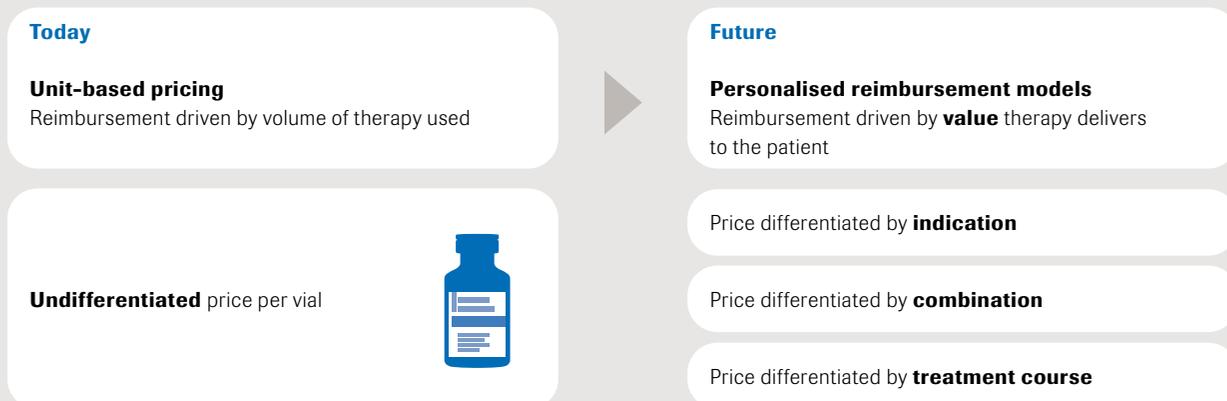
personalised reimbursement models that differentiate the price to reflect the benefit that the treatment delivers to patients.

Personalised reimbursement models have the potential to be of significant value to all stakeholders, speeding up patient access to innovative treatments and reducing the financial pressure on prescribing, by enabling the benefit of a medicine to be better reflected in its price. However, to implement this kind of model we need to be able to track the use of our medicines, which requires close collaboration between healthcare providers, as well as supporting infrastructure to share data easily without compromising patient confidentiality.

We have initiated a number of pilot projects in Europe over the last two years, to address these issues and work closely with the local healthcare stakeholders to bring the concept to fruition. In the UK, for example, we have now completed the pilot phase and are working with the National Health Service (NHS), which has a unique dataset on cancer medicine use. This Systemic Anti-Cancer Therapy dataset (SACT) has the potential to provide better intelligence about how cancer drugs are used and what benefits they bring patients. We have been able to demonstrate tangible benefits from the pilots about how this data can be the basis for more flexible commercial schemes, linking the price to the specific benefit to patients and the NHS. This also allows SACT data to be used to administer the necessary commercial schemes to ensure budget efficiencies for the NHS.

<sup>1</sup> WHO. Universal health coverage 2013.

## Reimbursement driven by the benefit of the therapy to the patient



Further pilot programmes demonstrating similar benefits are also underway throughout Europe, notably in Spain, where we have worked with the Government to have personalised reimbursement models included in new regulations. Over the last two years, Roche has been building awareness and understanding of the concept, as well as how best to implement supporting technologies. Several projects are now underway in different regions to build patient registries and records to determine the value of medicines in treatment. In Catalonia, which has a population database of 7.5 million people, infrastructure for personalised reimbursement will be available in 2015.

### Differential pricing

In countries with little private insurance or public reimbursement, people are often required to pay the majority of costs themselves. To address this disparity, we are piloting a number of differential pricing models, including local packaging or second brands of our products, in partnership with local manufacturers and government organisations.

The programmes include reduced prices to governments to facilitate reimbursement for medicines prescribed through public healthcare systems. We are establishing differential pricing programmes in a number of countries for some of our therapies, including Pegasys (hepatitis C and B), MabThera/Rituxan (non-Hodgkin's lymphoma and chronic lymphocytic leukemia) and Herceptin (HER2-positive breast and gastric cancer). As we learn from these programmes, we plan to expand differential pricing to our new innovative products.

### Second brands

In some emerging markets, we sell second brands of our products which are manufactured at the same sites and subject to the same quality control as the original Roche product. However, we package second brands under different names and may produce them in slightly different forms, such as in vials rather than syringes. This second brand programme was expanded into more countries in 2014

and now includes the Ukraine, Georgia, Ecuador, Egypt, Pakistan and India.

### Patient assistance programmes

We recognise that for many patients, including those living in developed countries, affordability can be a significant barrier to starting or continuing treatment. Even patients with insurance may not be able to pay for treatment if it is not fully covered by individual insurance plans. To reduce this barrier, we provide patient assistance programmes that help underinsured and uninsured patients to access our medicines.

In China, for example, Roche has entered into a partnership with the Cancer Foundation of China to increase access to the breast cancer treatment Herceptin, which is not fully covered in the public healthcare system. For a course of therapy, patients pay for the first six treatments and Roche provides the remaining eight free of charge via the Foundation. In addition, Roche China is working with regional governments to help them reimburse patients for part of their out-of-pocket expenses. As a result, more than 25,197 patients have been treated with Herceptin since the launch of the programme in 2011 – patients who otherwise would not have had access. In 2014 alone, 11,446 patients accessed Herceptin through our patient assistance programme.

Another way in which we are working to make sure medicines are affordable is in the Philippines, where there is limited public funding of healthcare. The government-owned Philippine Healthcare Insurance Corporation provides only basic national healthcare coverage, which excludes treatment with biologics, a relatively new class of drugs that includes Herceptin, our targeted therapy for HER2-positive breast cancer.

To improve access to Herceptin, and help patients adhere to the full treatment duration, we established the Roche Patient



Assistance Programme. Physicians refer financially constrained patients to the programme for an assessment by an independent third party of their ability to pay. Patients unable to pay the full price of Herceptin receive a discounted price based on their financial status.

#### **Helping establish health insurance**

Patients' access to innovative treatments, including cancer, depends on a number of factors of which funding is a key one. When public health systems cannot guarantee or pay for timely access to appropriate treatments, private insurance funds are often the only alternative.

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*Out-of-pocket payments can become financially catastrophic for individuals.*

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Private health insurance can play a key role here in providing coverage that offers access to treatment as well as protection from financial risks.

We have been working closely with insurance companies to help design products for their local markets. In Colombia, we are collaborating with Fasescolda, Colombia's association of private health insurers, to collect cancer-related data in the country. The data will be published and become publicly available, enabling insurers to create coverage that protects cancer patients from the financial impact of their disease and offers greater access to healthcare possibilities. We are developing similar programmes in other countries in Latin America, as well as in Asia and Africa. In countries where the public healthcare system fails to cover the costs of all treatments, private insurance is an invaluable way to bridge the gap and ensure that patients do not fall into poverty as a result of healthcare costs.

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*In many countries, insurance policies are difficult to design, with data on survival rates and treatment costs hard to find.*

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To improve the availability and usability of such information, Roche has made a concerted global effort to share data about cancer frequency and the cost of treatment. The aim is to enable insurers to better understand and predict the cost of cancer insurance.

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**31** MILLION  
INSURANCE  
POLICIES  
IN FOUR YEARS TO COVER  
CANCER CARE IN CHINA AS A  
RESULT OF A ROCHE INITIATIVE

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# Increasing availability of innovative products

Although inadequate infrastructure and a lack of trained medical professionals are often barriers stopping patients accessing medicines, slow and inconsistent regulatory processes, along with poor supply chain management can also present barriers. We are working at a local level to address some of these challenges and help reduce bureaucracy and inefficiencies in healthcare systems.

A common delay is the regulatory approval process. Many developing countries first require a Certificate of Pharmaceutical Product from the EMA and the FDA before starting their own approval process. However, in recent years, some emerging markets have become more autonomous, requiring not only European and US approvals for medicines, but their own approval as well. Roche is working closely with local authorities and global organisations to harmonise regulatory processes, allowing the approvals to happen in parallel, rather than sequentially. This enables companies to start the process much earlier and shave many months, or even years, off an approval.

Distribution of biologic medicines, which require constant cool temperatures, can also be a significant challenge. We work closely with governments, local manufacturers and distributors to provide training and develop locally appropriate supply chain capabilities to ensure safe, reliable delivery of high-quality medicines to patients. In Asia, Roche has been working with suppliers to develop and qualify a portable Medication Mobility Kit to enable patients to carry their cold medicines from the pharmacy to their home.

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*Access to innovative medicines is especially difficult in sub-Saharan Africa.*

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Africa is a continent which has the potential to be the next China. Economic growth in many countries is improving and healthcare spending is increasing, however, the development of healthcare systems varies considerably. Healthcare infrastructure is often poor, supply chains complex and expensive; and properly trained medical professionals are thin on the ground. In 2014, we launched a strategy to address this and improve access to innovative medicines in areas of Africa where they are not readily available. Our aim is to initially focus on key diseases where we believe we can make a difference: hepatitis, as well as breast, ovarian and cervical cancers. In December, Roche signed an agreement with the government of the Ivory Coast to develop a programme to increase access to viral hepatitis and breast cancer treatments.

Through partnerships with governments and other stakeholders, we aim to build disease solutions which support infrastructure development, support training and education and improve supply chain. We also plan to work with private insurers to create policies that cover treatment for cancer and that have regional, rather than a local risk pool. We also have plans to develop centres of excellence, as well as create a pan-African platform for healthcare professional education to train specialists. There is enormous scope to make a difference to patients in this part of the world.



# Strengthening infrastructure

Roche has established a number of programmes aimed at improving local, national and regional capabilities and infrastructure. These range from educating and training healthcare professionals; to helping establish clinics and laboratories; to strengthening local manufacturing capabilities and supply chains.

We believe that activities such as these are the most sustainable means of addressing local health needs and helping develop healthcare systems for the future.

## Improving testing capabilities

Timely and reliable diagnostic tests provide valuable information on a patient's health status, which not only improves patient care, but also helps control healthcare costs.

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*As populations age and the burden of chronic disease increases, so does the importance of diagnostics in achieving good health.*

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## Breast cancer testing

In Asia-Pacific we are helping improve awareness, testing and treatment of breast and gastric cancers with our SPHERE programme (Scientific Partnership for HER2 Testing Excellence). The aim is to integrate HER2 testing of patients at a single point of diagnosis to help patients receive accurate diagnosis of the disease and appropriate selection for treatment.

SPHERE now operates in 12 markets in Asia: Bangladesh, China, Hong Kong, India, Indonesia, Korea, Malaysia, Myanmar, the Philippines, Taiwan, Thailand and Vietnam.

## HIV viral load testing

We further expanded access to HIV viral load testing by joining with global and regional partners to launch a global access programme, a key action step in response to the Diagnostics Access Initiative launched during the International AIDS Conference in July 2014. Our partners include the Joint United Nations Programme on HIV/AIDS, the Clinton Health Access Initiative, the United States President's Emergency Plan For AIDS Relief and the Global Fund to Fight AIDS, Tuberculosis and Malaria.

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# 10,726

**PATHOLOGISTS, SURGEONS  
AND TECHNICIANS TRAINED  
THROUGH ROCHE SPHERE  
PROGRAMME IN ASIA IN 2014**

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The initiative calls for improving laboratory capacity to ensure that all people living with HIV can be linked to effective, high-quality HIV treatment services. To support the initiative, we have committed to expanding access to our HIV tests through a special pricing scheme for qualifying organisations in eligible countries.

## Socio-economic burden of illness

Illness not only has a profound impact on patients and their families, but it can also put a significant burden on society, especially in lower and middle income countries. In the ASEAN region, Roche is conducting a study in conjunction with the George Institute for Global Health to assess the broader burden of cancer in the region. The aim of the study is to support policy makers in making informed choices on cancer resource allocation and improve support for cancer prevention and testing, as well as treatment. It looks specifically at the economic impact of cancer on patients and their families, as well as the variation in management of hospital and non-hospital costs and the impact on quality of life. We hope that analysis such as this report will provide a strong basis for proper investment into cancer care.



## Increasing awareness and patient support

Healthcare education and awareness are as important to a patient's wellbeing as proper medical diagnosis and treatment. For this reason, we help local partners to run screening, awareness and counselling programmes, and seek to empower people worldwide with the knowledge to safeguard and manage their own health. We support a holistic approach to healthcare by producing newsletters, magazines and other publications aimed at helping people to make healthy choices and changing behaviours to prevent disease.

### Supporting patient organisations

We collaborate with patient organisations starting as early as the clinical trial phase. As the voice of patients and their families, these organisations help us learn more about what it is like to live with a disease and the role that drug therapies play in the management of the disease. We also support patient groups in their efforts to change public policy.

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*Our interactions with patient groups help us develop the right support tools for our products.*

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In 2014, we made significant progress partnering and supporting healthcare patient groups, carers and organisations in the field of mental health. Specifically, we focused very heavily on social inclusion, which is often overlooked in mental healthcare and yet is one of the biggest challenges. One of the concrete results of a subsequent grant award was the publication of the Oxford Health Policy Forum, *Schizophrenia: Time to Commit to Policy Change* report. This document, written by leading international

psychiatrists and advocacy groups, recommends a five-point policy programme to address the problem of social inclusion. We are also actively participating in a number of initiatives created by the G7 World Dementia Council, as well as facilitating the bringing together of patient and caregiver groups in the recently established International Dementia Forum. This forum aims to advance understanding of the impact dementia has on the daily lives of patients and their families, and the role therapeutics can play.

We also brought 137 delegates together from all over the world, between them covering 12 different therapeutic areas, with our International Experience Exchange in Vienna, Austria, to share best practice in bringing about policy change and understanding in care. A similar event was held for 59 delegates representing patient groups from the ASEAN region in Kuala Lumpur, Malaysia. The Chugai Academy for Advanced Oncology, which was founded by Chugai, a member of the Roche Group, has also established a similar event – the Japan Experience Exchange for Patient Organizations, which held two meetings in 2014.

Another initiative during the year was to build on the findings of a Roche-funded, but completely independent report, *The State of Oncology in 2013*. Based on the report findings,

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**35 COUNTRIES REPRESENTED**  
AT THE ROCHE INTERNATIONAL PATIENT GROUP EXCHANGE IN 2014

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Roche Latin America hosted a forum in Guadalajara, Mexico, to discuss how to improve cancer care. Today, the disease is responsible for 20% of all deaths in Mexico. Experts from the region came together, concluding that with the right level of political will, Latin America could provide a global model in cancer control which could be used in other regions.

### Educating healthcare professionals

For healthcare professionals, we conduct training sessions in the proper use of our products, as well as publish and present our research findings to help physicians and others stay abreast of the latest information on diagnostic tests and treatment options. The more understanding medical practitioners have of our drugs and diagnostic products, the better treatment will be for patients. To help achieve this, we publish an extensive range of educational and instructional materials, and host or support medical congresses and events.

One example is our commitment to providing medical education in therapeutic areas where there is significant unmet need. Our ongoing support of the annual European Society for Medical Oncology (ESMO) congress ranges from major financial sponsorship, a science-focused booth and educational symposia, to grants and fellowships for scientists and doctors to participate in and contribute to the success of the congress. In 2014, Roche was honoured by ESMO for ongoing support of Clinical Fellowships and Translational Fellowships. In Japan in 2014, the Chugai Academy for Advanced Oncology held its annual conference

with 200 of Japan's top oncologists hearing from world experts about the latest developments in cancer treatment and research.

### Increasing awareness of disease

Education and understanding of disease and the treatment available is very important in improving access to healthcare. Roche undertakes disease awareness programmes all over the world, to help patients understand a disease, its risks, treatments and avoidance strategies. In the United Arab Emirates (UAE), hepatitis C is a serious problem. This is a disease that often has no symptoms and in the UAE there is urgent need for education about the risk of infection from contaminated instruments and certain traditional habits. To raise awareness of hepatitis C in the UAE, we launched the National Hepatitis C Awareness Campaign in late 2012, together with the Emirates Gastroenterology & Hepatology Society. By 2014, the campaign had reached over 40% of the population – 3.5 million out of 8.5 million people.

In Indonesia, we are working to increase understanding of breast cancer and access to screening. We have an early-detection campaign for oncology doctors, general practitioners, family welfare programme trainers and midwives, to teach healthcare professionals the proper technique for a clinical breast exam. The campaign is conducted in partnership with the Indonesia Cancer Foundation and GE Healthcare Indonesia. In 2014, 1,600 doctors, midwives and family welfare programme trainers were trained.

## A selection of Roche initiatives in 2014 to improve access to healthcare

Initiative	Country (countries)	Description	Impact in 2014
AmpliCare	sub-Saharan Africa, parts of South America and Asia	Multi-faceted programme enabling early diagnosis of infants born to HIV positive mothers	1.3 million infants tested for HIV
Changing Diabetes® in Children*	9 countries in Africa and South-East Asia	Increase access to care for children with type 1 diabetes	13,200 children received free care
Genentech Access to Care Foundation	USA	Help patients who are uninsured or denied coverage to receive Roche/Genentech medicines free of charge	Over 40,000 patients supported
SPHERE training programme	12 markets in Asia	Train surgeons, pathologists and lab technicians to improve breast cancer testing	10,726 healthcare professionals trained
Mobile breast cancer screening buses	North Africa	Provide free mammographies to women in remote desert areas	Over 250,000 women screened
Patient assistance programme	China	Improve awareness, testing and treatment of breast and gastric cancer	11,446 patients treated with Herceptin
Roche Scientific Campus	Africa	Purpose-built training centre to train lab technicians and strengthen diagnostics capabilities	488 lab technicians trained from 25 countries
Second brand programme	Egypt	Increase access to Hepatitis C treatment through differential pricing via a second brand	34,139 patients treated
Transnet-Phelophepa healthcare train	South Africa	Provide general healthcare, disease awareness, health education in rural areas	Over 375,000 people reached

\* Novo Nordisk programme



**“I want people to see Africa as a continent of opportunities.”**

*Charles Fordjour*

*Charles is passionate about increasing patient access to treatment in Africa. He is the project leader of the Roche Africa Strategy, which aims to improve access to innovative medicines in sub-Saharan Africa.*

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# A mission to improve healthcare in Africa

*CHARLES FORDJOUR knows the medical realities of Africa. His story shows how one person's perseverance and ability to motivate others can make a difference.*

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I grew up in a village in the Brong Ahafo region of southern Ghana. My father was a civil servant and my mother was a schoolteacher. Both had modest salaries, and they struggled to support me and my seven brothers and sisters.

While the other boys were out playing soccer, I often had to stay in bed with a high fever, sweating and nausea. Because I was ill so often, the other kids called me 'sickler'.

Many years later, I learned that the cause of my illness was probably malaria. This disease kills more than 5,000 children every week in Africa.

As a consequence of my illness, I had a lot of time to read. I devoured every book I could get my hands on. That helped me in school, and soon I became the best pupil in class.

When I was in secondary school, I went to see a pharmacist and told him about the regular bouts of fever. He prescribed the Roche anti-malarial medicine Fansidar and my symptoms disappeared! That is when I decided to become a pharmacist.

I worked my way through university by transporting raw materials and mixing medicines that lecturers sold in their own pharmacies. After graduating, I joined the Roche affiliate in Ghana in 1998 as a sales representative. The teaching hospitals that I called on were more than eight hours apart by car over dusty, badly maintained roads that turned to mud in the rainy season.

One day, I arrived at a hospital and saw that a young girl was in a coma due to a bacterial infection. The doctor told me that he wanted to treat her with the Roche antibiotic Rocephin, but it was too expensive. I pleaded with him to treat the girl for at least the first 48–72 hours to give her

a fighting chance. When I left, I gave him my remaining free sample vials of the antibiotic.

Three days later, I returned to the hospital. The doctor asked me if I knew the child who was running through the halls, laughing and playing. He explained that it was the same girl who had been in a coma. I almost wept.

That doctor was instrumental in writing a protocol that became institutional policy in that teaching hospital in Ghana for treating severe infections with the Roche antibiotic for the first 48–72 hours. That change in healthcare policy has saved many lives.

I worked my way up to being the Field Force Manager of the Roche affiliate in Ghana, and in 2008 was asked to become Country Manager of Nigeria, Africa's most populous country with over 170 million people.

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**FOUR**  
TIMES MORE PEOPLE HAVE  
**HEPATITIS THAN HIV**  
IN SUB-SAHARAN AFRICA<sup>2</sup>

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# AN ESTIMATED 53,000 WOMEN DIE FROM CERVICAL CANCER IN AFRICA EVERY YEAR<sup>3</sup>

In Nigeria, healthcare authorities were mainly focused on the communicable diseases like malaria, tuberculosis and HIV. These decision-makers were unaware of the real disease burden of hepatitis and women's cancers.

*“Patient access in Nigeria to hepatitis diagnosis and treatment has increased dramatically.”*

We worked with the global organisation of Roche for a grant to obtain reliable epidemiological figures, starting with hepatitis. When the data was analysed, the prevalence of hepatitis in the population was 12%—significantly higher than the 8% estimate provided by the World Health Organization (WHO) at the time and three times higher than the prevalence of HIV.

That shocked healthcare authorities into action. Now there is a national policy in Nigeria to diagnose and treat hepatitis B and C. Roche Diagnostics has leased sophisticated screening tools at a minimal charge. Roche Pharmaceuticals has made a large price reduction for the hepatitis drug Pegasys.

As a result, patient access in Nigeria to hepatitis diagnosis and treatment has increased dramatically. Lives are being saved, but there is still much to be done. We are now working to implement the same approach for breast, ovarian and cervical cancer.

*“I am passionate about creating a healthcare environment in Africa with good diagnostic centres, affordable medicines and broad insurance coverage.”*



**Charles wants to achieve** a breakthrough in patient access to medicines and tests in Africa.

I am convinced that our experience in Nigeria can serve as a blueprint for the rest of sub-Saharan Africa. This is a dynamic, urbanising region that already has 50 cities with a population of more than one million. By 2040, the population is expected to reach two billion.

To achieve a breakthrough in patient access on this continent, we must invest for the long term and work with local authorities to shape healthcare policy. Roche cannot do this alone. We need to partner with international foundations, private companies and non-governmental organisations such as the UN and WHO.

I believe we can eradicate hepatitis and greatly improve cancer treatments. And I want Roche to be known as a leader in finding solutions.

<sup>2</sup> Global statistics AIDS.gov; Pan-African Medical Journal 2015; WHO: Globalcan | <sup>3</sup> WHO. Cervical Cancer.

# Responsible business

# 32 MILLION

Swiss francs to support **patient organisations**

## 101

countries where the  
**Roche Group Speak-Up Line** is in operation

## 5,000

**business partner representatives**  
completed training on the Roche Supplier Code of Conduct



## 166

**supplier sustainability audits**

# Integrity is at the core of everything we do

*WE DEMAND THE HIGHEST STANDARDS of ethics and integrity from all our employees and business partners. Our commitment goes well beyond the legal and regulatory requirements for compliance: it is a fundamental part of how we do business.*

In 2014, we continued to strengthen compliance, both throughout our operations as well as with our external partners. During the year, 98.7% of our employees were trained on a new integrity directive, which was launched at the end of 2013. This directive is designed to further specify and clarify the expectations outlined in the Roche Group Code of Conduct and it focuses on four areas: bribery and granting of advantages; gifts and entertainment; dealing with business partners; and conflict of interest.

*We believe that integrity is key to our long-term success.*

Two additional directives were also formalised during the year; the first on interaction with healthcare professionals and organisations; and the second on grants, sponsorships and donations. Training and education on both directives will begin in 2015.

All employees at Roche are trained on the Code of Conduct, which is supported by a Help & Advice Line for employees to seek guidance on the interpretation of the Code. The aim is to create an open culture to discuss issues and prevent violations, and employees are also able to report non-compliant behaviour. We do not tolerate retaliation against employees raising a compliance concern in good faith. In 2014, 80 employees contacted the Roche Group Speak-Up Line, which is now available in 53 languages in 101 countries. In 2014, we also expanded the scope of our Code of Conduct reporting system to include all allegations of breaches, whether material or not, across all Roche affiliates. This increases transparency and gives us a more comprehensive picture of how non-compliance allegations are handled locally. Overall, with the new reporting system, the Chief Compliance Officer received 512 reports relating to alleged violations of the Code of Conduct. The vast majority of reports related to personal integrity, such as

conflict of interest, abuse of company assets, expense fraud, harassment and discrimination. The remainder related to violations of company integrity, such as good practice in marketing, antitrust and false records. Out of 512 allegations, 104 were unfounded, 164 are still under investigation, and 244 were founded. All allegations are subject to careful investigation and, if allegations are founded, adequate sanctions are taken. 157 employment contracts were terminated on the grounds of unethical behaviour. 13 agreements with business partners were also terminated for the same reason.

We expect the same standards from our business partners, as we do for ourselves. Our Roche Supplier Code of Conduct is included in contracts and we offer training in support. In 2014, we also launched a new internet site to give guidance on compliance-related topics for current and prospective business partners. This guidance includes the Code, as well as an anti-corruption compliance questionnaire. We also conducted 166 supplier sustainability audits worldwide, using a risk-based approach. We had more than 500 findings from these audits and collaborated with the suppliers involved to resolve them quickly. We conducted 44 follow-up audits. For more information please see our Suppliers website ([www.roche.com/sustainability/for\\_partnership/suppliers.htm](http://www.roche.com/sustainability/for_partnership/suppliers.htm)).

**98.7%**  
OF OUR EMPLOYEES  
WERE TRAINED ON A NEW  
INTEGRITY DIRECTIVE



## Increasing transparency

At Roche, we believe transparency is critical to a productive and responsible business environment.

Clinical trial results from Roche-sponsored studies are reported on Roche-trials.com and ClinicalTrials.gov, as well as published in journals and at congresses. The Roche Data Sharing Policy reflects our commitment to increasing transparency and sharing of clinical trial information, whilst safeguarding patient confidentiality and the regulatory process. The policy provides the opportunity to request global clinical study reports and other summary reports. In addition, researchers may obtain access to analysable patient-level data from our clinical trials after their requests have been reviewed and approved by an independent panel of experts. Access is approved on the basis of scientific merit. In both cases, data is anonymised to respect the privacy of patients participating in our trials in accordance with relevant laws and regulations.

We work closely with healthcare institutions and patient organisations in areas where we have particular expertise and can provide support and education. We fund many kinds of activities including seminars for professionals and patient organisations, as well as workshops and training.

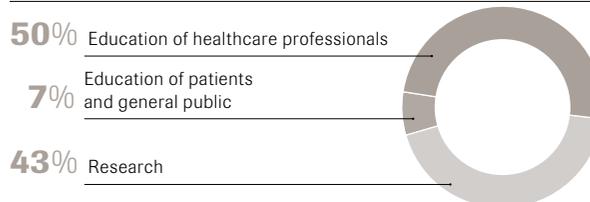
Roche remains independent of any political affiliation; however, we do support a number of associations and political institutions. In Switzerland, we spent around 9.5 million Swiss francs, which includes payments to Interpharma, economiesuisse, scienceindustries, SwissHoldings and various chambers of commerce, financial assistance to trade unions and donations to political parties at the cantonal and federal level. Donations to political parties are each in the low-double-digit thousand Swiss

franc range and overall less than 3% of total contributions and donations.

Our employees in the United States 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 2014, employees donated 328,252 US dollars to political campaigns through these committees.

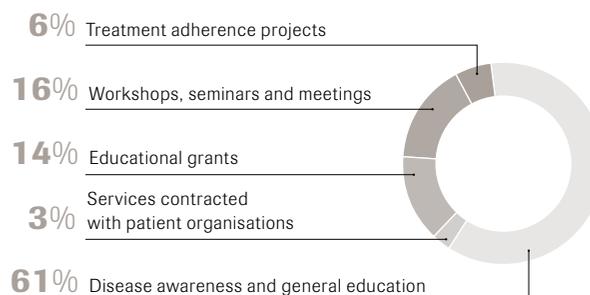
### Contributions to healthcare institutions

Total amount: **136** million Swiss francs



### Contributions to patient organisations

Total amount: **32** million Swiss francs



# Engaging with our stakeholders

Engaging with our stakeholders is essential for understanding their expectations, needs and concerns. By embedding their feedback into our strategy and our daily business, we are able to address our common issues and develop long-term solutions.

We interact with our stakeholders through a variety of communication channels, such as corporate websites and other publications. In addition, we participate in more formal and structured engagement, such as meetings, forums and other events, and carry out consultations and surveys.

We have established Group-wide guidelines and policies to govern our interactions with key stakeholder groups. We capture stakeholder concerns at a local level and re-channel them to the global list of strategic communication priorities. This helps us incorporate stakeholder interests into our strategic plans, as well as focus our communication on topics of most relevance to our stakeholders.

## Political and industry engagement

As well as engaging with healthcare professionals and patient organisations, we are also active in consulting with government officials, industry bodies and other stakeholders such as think tanks and academic institutions to participate in debate and develop effective laws, regulations and policies for public health. Key areas for discussion in the EU in 2014, for example, were regulations on a number of topics, including clinical trials; the Innovative Medicines Initiative (IMI2); data protection; and medical devices and *in vitro* diagnostic tests.

In the US, the landscape remained heavily influenced by the development of healthcare reform and the ensuing debates around it. Genentech worked closely with its

stakeholders in 2014 to contribute our expertise on issues such as insurance coverage expansion, biosimilars, drug safety and security, corporate tax and payment and delivery reform.

All employees working with government officials are expected to follow our good practice guidelines and act in an appropriate ethical and professional manner.

## Non-financial reporting

We have adopted the Global Reporting Initiative (GRI) G4 reporting guidelines, which we disclose at the core application level. We also report a number of additional indicators that are relevant to our business and stakeholders which go beyond the requirements for the core level.

## Materiality

To ensure we have identified the topics that affect our stakeholders and that are relevant for our long-term success, we have conducted a materiality analysis at the corporate level amongst our key stakeholders, in line with our Strategic Framework, and described on the related Roche website (see page 172). In a first step, in 2013 we defined an integrated process, criteria for inclusion and main drivers for the materiality assessment. In a second step, in 2014 we gathered stakeholder feedback through various internal and external sources, conferences as well as regular interviews and one-on-one discussions conducted by Roche experts. This enabled us to include the topics from those stakeholder groups that we consider most important to our business and to the healthcare sector: patient organisations, employees, media, investors, payers, regulators and governments. We also identified key corporate business risks and opportunities through our internal risk framework (see page 100).



In a final step, we combined those various insights and identified 21 material topics that stood out as highly relevant to us and our key stakeholders, and with a significant economic, environmental or social impact. These 21 material topics are reflected in our business priorities. We build concrete actions relating to them in our operational activities, and measure performance through defined indicators as described on the related Roche website (see page 172).

The process and the results of our materiality analysis have been endorsed by the Roche Corporate Sustainability Committee and by our Chief Executive Officer.

Moving forward, we will maintain constant engagement with our key stakeholders at a global and local level and regularly update our materiality analysis.

## Step 1

Defining the materiality process

### Preparing our assessment

- Confirm process, criteria and drivers to assess materiality of key topics
- Determine ability to influence topics and opportunities for differentiation

## Step 2

Collecting stakeholder feedback

### Views from our stakeholders

- Identify key stakeholders
- Collect feedback through surveys and internal experts

### View from Roche

- Identify key corporate business risks and opportunities through our established risk framework

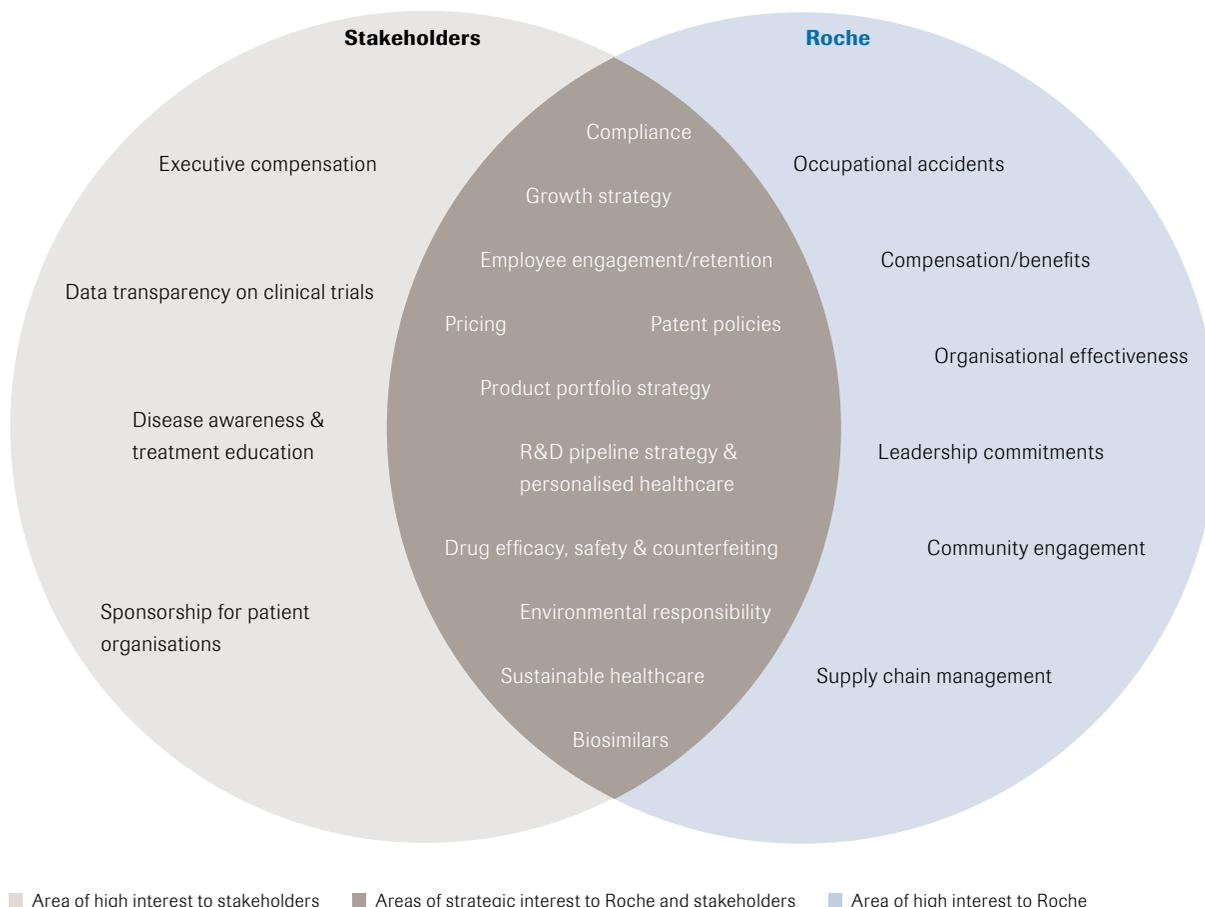
## Step 3

Identifying material topics

### Our 21 material topics

- Map the most significant economic, environmental and social topics for our long-term success
- Address through operational activities and align with our strategic priorities
- Plan ongoing pro-active engagement with key stakeholders

### Material topics actively managed by Roche



# Managing risk and crisis

We have in place a full Risk Management Policy, which sets out our approach for identifying, managing and reporting internal and external risks and opportunities. We also use stakeholder feedback to help manage social, environmental and economic risks and opportunities.

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 reviewed by 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, classroom training, workshops and risk roundtables are in place to improve the understanding of risk and help employees manage them appropriately. In 2014, a Risk Forum concept involving a group of internal thought leaders was launched in order to raise risk awareness across the organisation.

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 and deliver a minimum, acceptable level of key products and services. A Group BCM policy and guideline is in place, facilitating a consistent and aligned local implementation. We are currently rolling out the new BCM framework across the Group to make sure Roche's operations are resilient and capable of effectively responding to major disruptions.

We have also updated our Group Influenza Pandemic Policy and supporting materials based on the latest World Health Organization Interim Guidance. This guidance, which is risk based, is to be evaluated at a national/local level. The Group Policy reiterates our strategy to promote preventative measures to reduce infection risk, such as social distancing, personal protective equipment, vaccination provision (where possible), and to use antivirals as part of an influenza pandemic management plan.

## Sustainability risks and opportunities

Business sustainability risks include risks affecting multiple parts of the company, as well as risks which may have longer term impact. In 2014, Roche enhanced its Business Sustainability Risk Assessment approach, which allows us to assess emerging risks on an annual basis and to integrate these into our existing Group Risk Management Process. Using this approach, potential business sustainability risks were identified from literature review, risk intelligence sources and workshops with the Corporate Sustainability Committee. Each of these risks was then assessed by an expert cross-functional team resulting in a short list of five business sustainability risks that have now been integrated into our 2014 Group Risk Management Process.

### The five business sustainability risks identified for 2014 are:

- Earthquake (Basel, Tokyo, South San Francisco)
- Inadequate strategies for Cloud, mHealth (use of mobile devices), eHealth (use of electronic devices) and social media
- Cyber attack
- Issue response not yet optimised
- Third-party relationships

# Safeguarding patients

Our priority is to make sure that the therapeutic benefits of a medicine outweigh the risks of side effects. Any medicine can cause side effects and it is important for us to understand and monitor adverse events that patients may have experienced whilst on our medicines. To this end, we regularly audit the quality of our processes and systems internally, in addition to supporting regulatory authority inspections. We also maintain strict product recall procedures to ensure that we can withdraw products rapidly should quality or safety problems arise.

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*We have a systemised process to ensure that every product is safe and effective throughout its lifecycle.*

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All Roche employees are required to complete training on adverse events and immediately report any issue relating to the safety or quality of our medicines. Adverse events are stored in a global database, reviewed by a qualified physician and reported promptly to the appropriate regulatory authorities, as required. Any report to the company of an adverse event experienced by a patient on a Roche drug is included in the company's safety database, which is used to regularly evaluate whether the benefits of a medicine still outweigh the risks.

Following an internal quality review at the end of 2011, Roche identified some unreported missed adverse events from its Patient Assistance Program in the United States. Following discussions with the relevant health authorities, Roche conducted a retrospective global search to identify any

unreported adverse event reports and completed a safety assessment for each impacted product.

In November 2013, the European Medicines Agency (EMA) confirmed the Roche assessment that, based on all available safety information, the benefit-risk balance of the medicines concerned was not impacted. All medicines remain authorised without changes to the treatment advice for patients and healthcare professionals. Corrective and preventative actions resulting from the health authority inspections have been completed or are being completed.

A further re-inspection by authorities in November and December 2013 resulted in additional findings, which are being addressed. In parallel, EMA has initiated a procedure to investigate whether Roche had infringed some legal obligations relating to the reporting of the adverse events. On 14 April 2014, EMA issued its report to the European Commission, which is now deciding how to proceed with this matter.

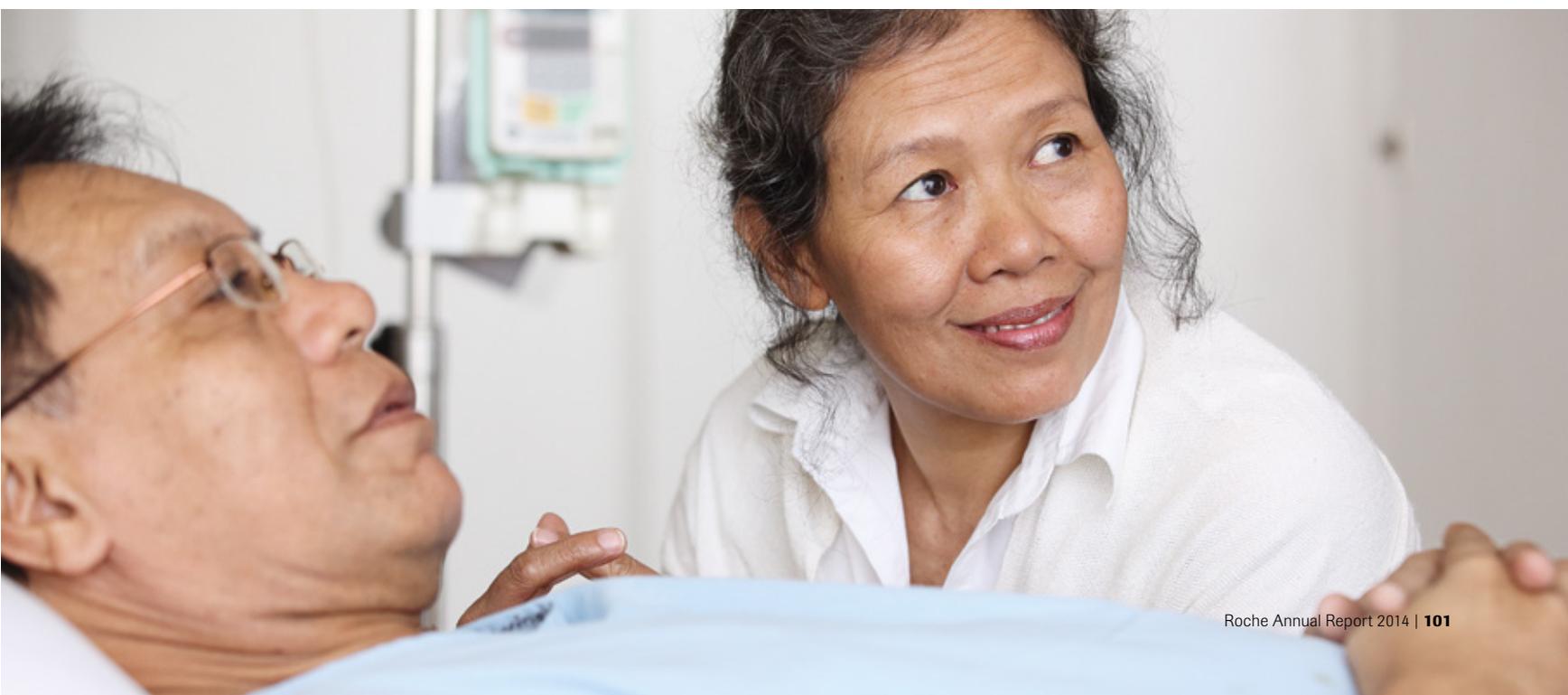
We have reinforced our processes throughout the organisation to optimise our understanding, management and communication of the safety profile of our medicines.

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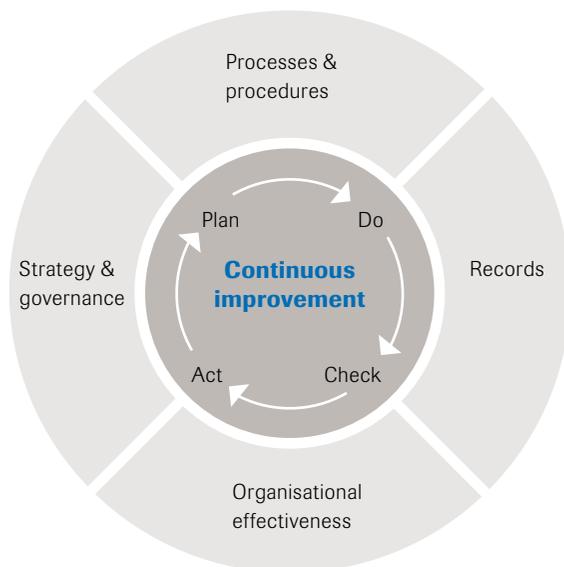
*We strive to go above and beyond what is required to protect the health and safety of the patients who rely on our products.*

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We are fully committed to meeting the highest standards of Good Clinical Practice (GCP) and Good Pharmacovigilance



**Strengthening compliance across the organisation**



Practice (GVP) regulations and to meeting the evolving expectations of health authorities around the world. We have a Medical Compliance organisation that sets strategy and standards, and provides full visibility of all quality and compliance activities.

Our new quality management system sets out the structure, responsibilities and procedures to help us identify, measure, control and enhance core quality and compliance processes. Alongside this, we are simplifying all global processes and procedures, as well as the associated documents and training. To support the implementation of the new quality management system, more than 160,000 training assignments were completed in 2014.

To ensure that any significant compliance issues can be quickly tracked and acted upon, in 2014 we developed new procedures for corrective action. This involved the introduction of tracking and reporting tools, in addition to a comprehensive suite of training materials and guidance on how to conduct a root cause analysis. They will be rolled out in 2015.

**9,000**  
**EMPLOYEES WERE**  
**TRAINED ON NEW QUALITY AND**  
**COMPLIANCE PROCESSES IN 2014**

We have also separated our commercial and medical organisations, differentiating clearly between non-promotional activities of a medical or scientific intent and promotional activities. This separation has also allowed for fully transparent budgeting and costs, as well as new definitions of roles and responsibilities.

In support of this separation, we have established a Pharma Healthcare Compliance Office to ensure clear governance, oversight and decision-making across the organisation.

**Anti-counterfeiting and supply chain control measures**

Counterfeiting of medical products is a serious and growing global problem. The World Health Organization (WHO) defines a counterfeit medicine as 'one which is deliberately and fraudulently mislabelled with respect to identity and/or source.' It estimates that counterfeiting, substandard formulation, contamination, fakery, and active ingredient substitution constitute a 431 billion US dollar market.<sup>1</sup>

Illegally imported medicines may also not have been stored or handled properly and could be contaminated, damaged or degraded. Patients are the ultimate victims of this criminal activity.

In answer to increasing global supply chain challenges and international criminal activities, in 2010, Roche initiated a ten-year programme to increase security in our supply chain. We are implementing a number of new technologies including overt and covert anti-counterfeiting features, 2D barcoding, mass serialisation techniques, tamper-evident packaging as well as tracking and tracing systems. In 2014, we increased supply of serialised products significantly, particularly those for China and the US.

On completion of the programme, which is anticipated by 2018, every Roche product, folding box, case and pallet will have a unique identification. With the cooperation of health authorities and other trading partners, this will ultimately enable tracking and tracing from our manufacturing facilities, through all global distribution channels and, then, to the patient.

We are also working with international trade organisations in support of industry-wide efforts to improve the safety and security of the pharmaceutical supply chain. In addition, we collaborate with health authorities, law enforcement bodies and other government agencies in the countries where our products are sold on traceability guidelines and regulations.

We continue to explore the potential of new technologies to support a worldwide trend towards digitisation of drug supply chains. With ongoing advances in technology, we expect intelligent packaging to allow for more interaction within the healthcare systems, driving innovation and efficiencies in other areas of our operations and in healthcare generally.

*Roche is using new technologies, including 2D barcoding and tamper-evident packaging, to bolster supply chain security.*

### **Biosimilars**

Biologic medicines (manufactured from biological sources) have become an essential part of modern medicine. Demand continues to rise for innovative Roche biologics such as MabThera/Rituxan, Actemra/RoActemra, Kadcyla and Perjeta, as they play an important role in improving the lives of patients.

At the same time, a second group of products has been developed and commercialised, which their manufacturers claim are similar to the original biologic medicine, biosimilars. As the name implies, these products are similar, but not identical, to the original product. To meet the claim of being similar and follow the guidelines set by the WHO, a biosimilar must be 'similar in terms of quality, safety and efficacy to an already licensed reference product'.<sup>2</sup>

Producing biosimilars is, however, far more complicated than producing generic versions of off-patent, chemically synthesised medicines. The complex molecular structure and unique manufacturing process required make these products difficult to reproduce.

The challenges in producing biosimilars have given rise to a third group of products: non-comparable biologics. This new term has been proposed by the International Federation of Pharmaceutical Manufacturers and Associations to describe those medicinal products that are intended to copy the original biologics, but fail to meet science-based standards for direct comparison. They also do not meet WHO guidelines for quality, safety and efficacy.

The clinical profile of non-comparable biotherapeutic products cannot be expected to be the same as the innovator biological medicine, and remains unknown due to lack of quality side-by-side assessment showing similarity and/or lack of comparative clinical data. These potentially significant differences could put patients at risk of poor health outcomes.

### *Non-comparable biologics of unknown quality and clinical profile can pose a significant burden to healthcare systems and society.*

Our view is that the risk of non-comparable biologics to patients and public health must be minimised or eliminated by appropriate comparative evaluations that are consistent with WHO guidelines for biosimilars. The implementation of such oversight, however, is uneven globally. Some national regulatory agencies have appropriate frameworks in place, whilst others are in the process of adapting theirs. We continue, meanwhile, to implement our strategy to innovate, expand and protect our biologic medicines and keep ahead of potential competition. We have amended the Roche position on biosimilars reflecting new developments and it can be found on [roche.com](http://roche.com).

<sup>1</sup> WHO. Essential medicines and health products: General information on counterfeit medicines. | <sup>2</sup> WHO. Guidelines on evaluation of similar biotherapeutic products (SBPs) 2009.



**“Medical treatment  
is just one part of  
the solution.”**

*Lee Dunster*

*Lee has been instrumental in creating an International Working Group with patient groups and policy makers to work towards a more holistic view of treating schizophrenia. He is also helping to build a global network for improving Alzheimer's care.*

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# Understanding the wider implications of mental illness

*LEE DUNSTER believes that social inclusion is an extremely important facet of mental illness treatment. He is working with organisations worldwide to improve support for people in this very challenging area.*

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I have looked at diseases and their impact on people from many different perspectives. I began my career as a research scientist in microbiology and then went on to run a World Health Organization (WHO) collaboration centre in Kenya for viral hemorrhagic fevers like Ebola and Rift Valley fever. My wife and I helped to set up an early response and diagnostic network in East Africa for these diseases, which remains active to this day. Drawing on this experience, I worked as an adviser to the WHO in Egypt, focusing on regional preparedness to support measles eradication. From there, I became the Head of Research and Information for the UK Multiple Sclerosis Society, where I was able to bring about fundamental change to research funding and create a new programme focused on non-medical intervention to improve quality of life for patients.

I joined Roche in 2010 working in Global Public Policy and a year later I found myself in a new role to support our efforts to improve treatment for people living with schizophrenia.

Most of us think of schizophrenia in connection with the 'visible' symptoms: hallucinations, delusions and self-harm. In fact, the 'hidden' symptoms of schizophrenia – a lack of motivation, speech problems, withdrawal from people – can be even more debilitating over the long term, leading to isolation and exclusion from family and society.

Roche was developing a treatment to address these hidden symptoms of schizophrenia. From the outset, however, it was clear that treatment alone would be unlikely to provide meaningful change and improve everyday living for people with schizophrenia. My goal as Senior International Public

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## ONE IN FOUR PEOPLE WORLDWIDE ARE LIVING WITH A MENTAL DISORDER<sup>3</sup>

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Policy Manager was to bring together policy experts and mental health associations from around the world, so we could understand the needs of people affected by schizophrenia. We learned that real benefits would come when society provided the support and opportunities which could only be achieved by many different stakeholders working together.

A milestone in our international collaboration was the critically acclaimed report, made possible by a grant from Roche, 'Schizophrenia: Time to Commit to Policy Change'. This report brought together leading psychiatrists and advocacy groups to provide concrete recommendations for policy change.

Collaborations with patient organisations from Europe, the United States, Canada, Australia, Japan, Hong Kong, South Africa and Brazil, resulted in the formation of the International Working Group (IWG) on Social Inclusion and Schizophrenia. Many of these organisations had little, if any, regular contact with each other, yet all shared a common goal.

# 44

## MILLION PEOPLE WORLDWIDE ARE LIVING WITH DEMENTIA<sup>4</sup>

The aim of working together was to identify how policy changes could respond to the needs of people affected by schizophrenia and introduce new initiatives to improve lives.

We found that the 'hidden' symptoms of schizophrenia could be tackled by increasing social inclusion and challenging stigma. This is also true for managing many other types of mental illness. By sharing experience we can identify opportunities to integrate people with schizophrenia into society. This includes education and jobs that help individuals regain self-esteem, independent living and social interaction.

Personal experience has helped shape my thinking about social inclusion. I have a 12-year-old daughter with autism and it remains a struggle to convince local authorities to provide support to include her in everyday activities like mainstream schooling. My wife and I want her to have the same opportunities as everyone else to develop her talents and lead a full and independent life.

*“By working to overcome the stigma associated with mental illness, we can provide opportunities for inclusion into society.”*

There were high hopes for the Roche therapy, bitopertin, for treating schizophrenia. Unfortunately, in the final stages the trials failed to demonstrate sufficient efficacy and were halted early in 2014. Nevertheless, the studies did generate valuable data that were openly shared with the medical community and provided insights for developing future treatments and the design of clinical trials.



**Lee is developing** a dementia forum with leading patient associations in the field of Alzheimer's disease.

Even though the clinical programme ended, Roche continues to support social inclusion and the efforts of the International Working Group. As the IWG knows, changing policy is a lengthy process and this is just the beginning.

As Roche develops its presence in the field of neuroscience, we are building on the experience gained from the International Working Group. Recently, I have started to develop a dementia forum with leading patient associations in the field of Alzheimer's disease. The insights being gained from this partnership with patient groups are shaping the way we conduct research and development as well as policy objectives across the Roche neuroscience portfolio, which includes multiple sclerosis, Alzheimer's disease, autism and Down's syndrome.

*“Effective treatment requires a vision of the whole person and all the factors influencing an individual's quality of life.”*

In all of these areas, social inclusion plays a crucial role. Effective treatment requires a vision of the whole person and all the factors influencing an individual's quality of life. Whilst medical treatment is important, it is just one part of the solution.

3 WHO. World health report: Mental disorders affect one in four people. | 4 Alzheimer's Association. Alzheimer's & dementia e-news.



# People

**81%** of our employees  
**are proud to work for Roche**

**71%** overall employee  
**engagement**

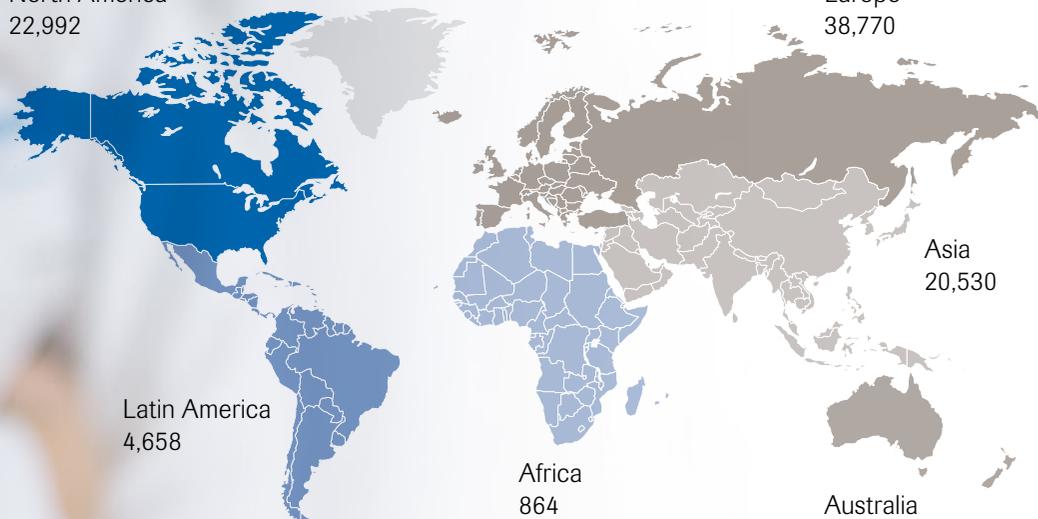
**Average employee profile**

 with Roche for **9 years**  
**3 years** in current role  
**41 years** old

**88,509**   
employees

North America  
22,992

Europe  
38,770



Latin America  
4,658

Africa  
864

Asia  
20,530

Australia  
695

# Engaging and energising our people

***GREAT COMPANIES** are defined by people who embrace a shared sense of purpose, put extra energy and passion into their jobs and identify with common goals. That is the kind of engagement we aim for at Roche.*

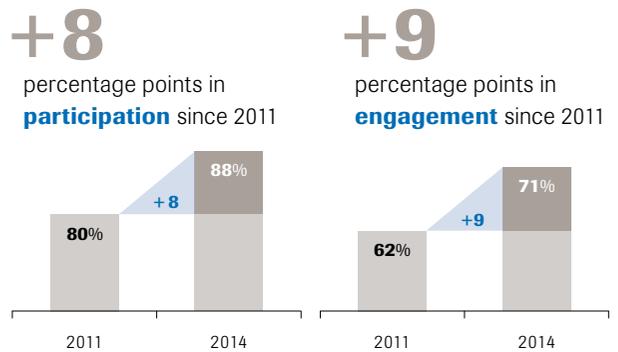
Our concept of engagement reflects the evolving needs of our workforce and the world around us. To stay aligned with what drives our employees, we ask for feedback at regular intervals through our Global Employee Opinion Survey (GEOS). This survey includes questions that measure engagement through drivers and statements about belief, commitment and action.

Employees take GEOS seriously because they know their opinions matter and concrete actions will be taken based on their feedback. The first survey results in 2011 resulted in the development of our Leadership Commitments, which have become the foundation of how we manage and lead people at Roche.

*Engagement is directly linked to our business success.*

Research shows that the level of engagement is a strong long-term predictor for organisational performance.

## Global Employee Opinion Survey results



Our target was to achieve 80% employee engagement by end 2014. We achieved 71%, but this result still puts us among the best in class in our industry.



## Applause from peers across the globe

People at Roche work with colleagues from multiple functions at locations around the world. With the online tool Applause, employees can now recognise each other directly through eCards or reward point nominations. It is simple, fast and widely appreciated. Launched in 2014, Applause is now live in 200 Roche affiliates, 109 countries and ten languages.

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**198,367**  
**PEER-TO-PEER RECOGNITIONS**  
 AMONGST OUR EMPLOYEES IN 2014

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## Recognising and rewarding employees

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*Recognition is a key driver of employee engagement. People want to be acknowledged and appreciated by others.*

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The results of the Global Employee Opinion Survey have triggered a paradigm shift in the culture of Roche. Recognition is now firmly embedded in our Leadership Commitments. In 2014, we launched an innovative programme of peer-to-peer recognition: Applause. And whilst the emphasis is on recognising colleagues, managers are notified each time an employee receives an Applause award.

We strive for a performance-driven culture. This is based on continuous dialogue and feedback between managers and employees. In 2014, 89% of employees surveyed in an internal 'pulse check' agreed that 'feedback discussions with my manager support both my day-to-day tasks and my development at Roche.'

In terms of compensation, we try to strike a balance between a highly competitive base salary and performance-linked rewards. In addition to bonuses linked to individual achievements, Roche offers rewards linked to the overall success of the company.

There are also numerous benefits for employees that vary from site to site. These may include discounts on buying Roche stocks, pension schemes, health insurance, childcare, on-site fitness, medical facilities, flu vaccinations, preventative health screenings, discounts with local retailers and transportation to the workplace. We also offer an International SOS service to all employees and their dependents if an emergency situation arises when travelling or living abroad.

In 2014, a Wellbeing Week was held for the second consecutive year at 110 Roche sites around the world. A wide range of activities were organised around four main themes: healthy lifestyle, emotional wellbeing, prevention practices and wellbeing resources.

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**71%**  
**OF EMPLOYEES ARE**  
**SATISFIED WITH THEIR**  
**BENEFITS AT ROCHE<sup>1</sup>**

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<sup>1</sup> Results Global Employee Opinion Survey 2014.

# Appreciating everyone's contribution

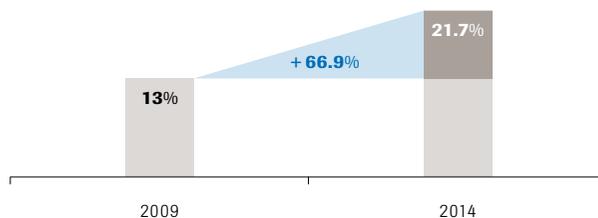
At Roche, we strive to create an environment where everyone regardless of gender, race, ethnicity, sexual preference or religious background can contribute to our mission of delivering innovative diagnostics solutions and developing life-saving drugs.

*Diversity and inclusion is a high priority.*

For us, diversity and inclusion is a high priority. We want diversity to go beyond the visible differences to include different educational backgrounds, professional knowledge, personality types, thinking styles and life experiences. We actively support and encourage an environment where everyone feels free to speak his or her mind. Only in that way can we discover the best ideas and develop truly innovative solutions.

In 2014, senior leaders and some members of the Corporate Executive Committee participated in various diversity and

## Female representation among key leadership positions



Our goal was to achieve 20% of women representation in key leadership positions by the end of 2014. With an achievement of 21.7%, we exceeded this target.

**48% WOMEN**  
IN TOTAL WORKFORCE

**40% WOMEN**  
IN MANAGEMENT LEVEL

inclusion events in many Roche sites across the world. These events demonstrate our commitment and enthusiasm to become a more diverse and inclusive organisation. These activities marked a fundamental shift toward viewing diversity and inclusion as a critical success factor for our business and an element of successful leadership at all levels of the company. To maintain this momentum, we have diversity champions leading these efforts at our largest sites.

Various parts of our worldwide organisation are at different points on the diversity and inclusion journey. While certain corporate goals apply worldwide, there is freedom for affiliates to adapt to local culture and priorities.

## Common understanding of diversity and inclusion

In 2014, the Roche Corporate Executive Committee discussed and agreed on what diversity and inclusion means at our company. These definitions help to ensure that all employees across the globe share a common understanding.

Diversity refers to 'the mix': a wide range of visible and invisible differences that exist among people. These include, but are not limited to, values, beliefs, physical differences,

## How diversity and inclusion is linked to future growth

Emerging markets will be the most important growth driver for Roche over the next five to ten years. To succeed in these markets, we must reflect their diversity in our decision-making. This means ensuring that more global leaders are recruited from countries such as China, Brazil, Turkey or Russia. And vice-versa, we encourage Roche leaders from developed countries to share best practices and gain hands-on experience in emerging markets.

Creating a diverse group of decision-makers is only half the story. Practicing inclusion is equally important. At Roche, our leaders need to draw out expertise and knowledge from different cultural norms. Integrating a wide range of perspectives is crucial to developing new medicines or

access programmes that address the local needs of customers and patients.



Daniel O'Day, Chief Operating Officer, Roche Pharmaceuticals

ethnicity, age, gender, experiences, thinking styles, backgrounds, preferences and behaviours.

Inclusion refers to 'making the mix work': proactive behaviours that create an environment in which all people

are actively included, treated fairly and respectfully, have equal access to opportunities and resources, and can be themselves while contributing fully to the organisation's success.

## Preparing the workplace of the future

Our world is changing rapidly, particularly in terms of demographics, employee expectations and technology. In industrialised countries in Western Europe and Japan, for example, the median age of the population is steadily increasing while birth rates are decreasing, which means shortages of skilled labour in the years ahead.<sup>2</sup>

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*As a global company, Roche is thinking ahead about what these trends mean for the future workplace.*

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As more experienced employees postpone their retirement in many developed countries and early-in-career people begin employment, five generations will be working together, from traditionalists and baby boomers to generations X, Y and Z.

These different generations have common requirements as well as different values and priorities. Keeping these diverse

groups of people engaged and productive requires leadership competence that is sensitive towards individual needs, as well as flexible solutions in terms of compensation, work arrangements, technology, professional development and social responsibility.

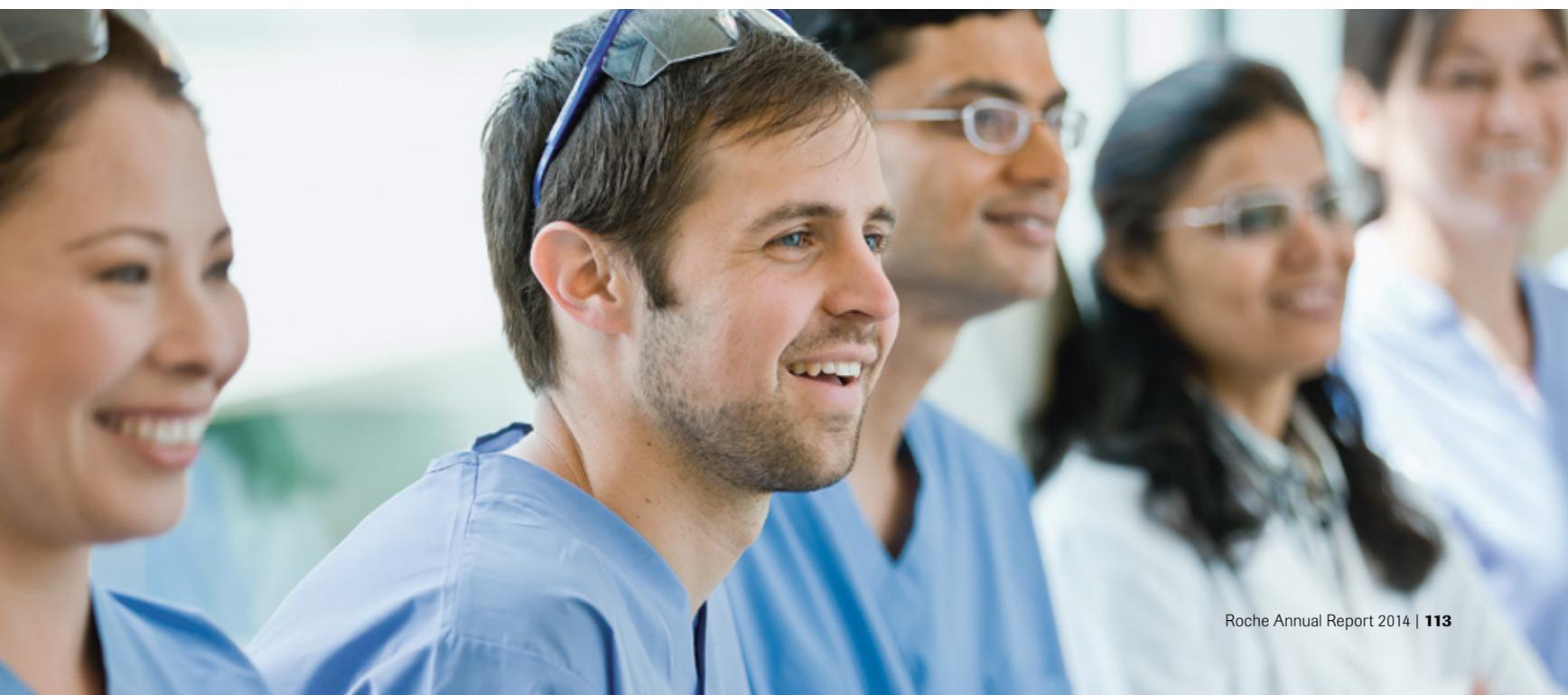
To attract and retain the best talent, Roche has a broad outreach programme that includes a strong presence on social media platforms such as Facebook and LinkedIn.

Beyond traditional recruiting at universities and business schools, we collaborate actively with academic institutions through webinars and by sharing business cases. Roche also offers a number of internships and post-doctoral research positions.

Roche has taken an innovative approach to seeking out the most capable people by positioning globally aligned 'talent scouts' in priority areas of our business. These specialists proactively search for qualified candidates and build diverse talent pipelines for positions that are difficult to fill and critical for our business. Talent scouts also help to cover any prioritised gaps in our internal succession planning.

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<sup>2</sup> World population ageing 2013, Department of Economic and Social Affairs, United Nations.



### Building for the future

Roche is investing over three billion Swiss francs in new research infrastructure and attractive workspaces at Basel headquarters over the next ten years. The first part of the construction project, Building 1, is slated for completion in 2015. It will feature open communication zones to enhance collaboration among employees and modular office spaces that can be adapted for the required mix of single offices,

open plan offices and meeting rooms. Building 1 will not only be the tallest building in Switzerland, but also one of the most energy efficient, using waste heat generated from production processes for warmth and ground water for cooling. State-of-the-art video conferencing and telepresence technology will limit the need for travel, further helping us to keep our environmental footprint under control.

## Developing the full potential of our leaders

The results of GEOS in 2011 were a catalyst in clarifying the expectations we have for managing and leading people at Roche. Intensive workshops, involving many managers at different levels, produced succinct, clearly worded leadership commitments that have been embraced by managers at all levels of our company. These commitments were cascaded through our global organisation, with our leaders giving personal examples of what they mean in daily practice. Developed by Roche for Roche, these commitments are our basis for good leadership.

In 2014, these commitments continued to be translated into tangible processes that define the way we manage and lead people. The leadership commitments are now embedded in our performance management tool, 360-degree appraisals of managers, employee recognition and the interview guide for hiring new leaders.

Our leadership commitments are also a touchstone for every development programme we design around leadership. In 2014, over 1,500 managers went through the Leading@Roche suite of programmes. Catalyst addresses personal leadership strengths and challenges with regard to leading through change. Leading Leaders@Roche is about increased self-awareness and the ability to build trust, commitment and engagement with people in complex environments. Leading People@Roche focuses on bringing our Leadership Commitments to life through role modelling.

The results of GEOS in 2014 show that employees appreciate the approach we are taking. Since 2011, the scores for Senior Leadership have risen 9 percentage points, 11 percentage points for People Focus, and 23 percentage points for Keeping Promises.

In addition to developing our current leaders, we also have a well-defined succession and talent management process to ensure that Roche has a robust and diverse pool of qualified candidates for critical positions. We identify leadership 'high potentials' early in their career and provide them with targeted development.

### Leadership experience in emerging markets

Roche is adapting its leadership programmes to reflect global megatrends. As most of the world's future economic growth will come from emerging markets, Roche is investing heavily in these countries. This includes our Leadership Acceleration Programme in Pharmaceuticals, which encourages leaders from developed countries to do job rotations in emerging markets and vice-versa. The goal is to achieve a critical mass of diverse experience in our decision-making to reflect the special needs of patients, physicians, healthcare providers and other stakeholders in these areas of the world.

**80%**  
OF KEY POSITIONS  
FILLED WITH **INTERNAL**  
**CANDIDATES** IN 2014

**4.4** MILLION  
VISITS ON OUR CAREER  
WEBSITE IN 2014

## Our Leadership Commitments

"I firmly believe that each person at Roche deserves a great leader. Every day I strive to lead by example, consistently demonstrating our values of Integrity, Courage and Passion."

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

## Making the most of employee careers

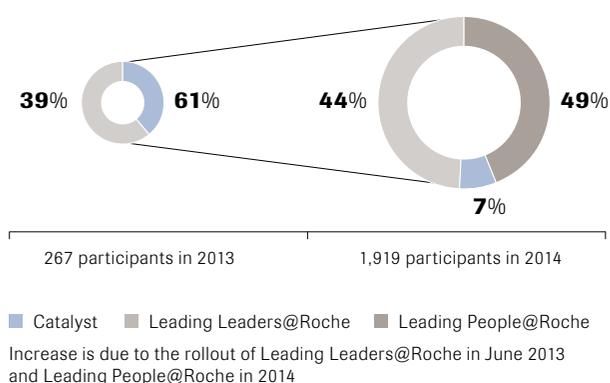
Personal initiative and self-awareness are the starting points for employee development at Roche. We offer a number of online tools to help individuals identify strengths as well as skill gaps and then plan the training or job experience that is needed to achieve their career goals.

Our leaders are focused on people, not just business results. An important part of their job is to help employees with self-assessment and career planning through structured conversations, supported by practical guidelines.

Roche has a well-developed online jobs marketplace that offers opportunities around the world, including personalised alerts when desired job profiles are posted. Employees who want the experience of working in another function or country can pursue shorter-term secondments or job rotations and then return to their previous jobs. We recognise that time to learn and develop outside of Roche is also important. Once certain criteria have been met, employees may also take time off from their work through sabbatical programmes.

Roche is a learning organisation that invests heavily in training courses to improve the skill base of our people. This includes a huge online offering that employees can access from any location and complete at their own pace.

### Global Leadership Development





“A unique chance  
to share my skills  
and a life-changing  
experience.”

*Katrin Kühhirt*

*During a Roche secondment year in Uganda, Katrin touched the lives of many children at an orphanage. She adapted to the realities of local healthcare needs, made lasting contributions and gained new insights about herself.*

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# Learning to overcome personal barriers

*KATRIN KÜHHIRT demonstrated the leadership skills and courage it takes to leave her normal life behind and work for an entire year in Africa.*

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I have always felt a deep sense of satisfaction in helping others. Perhaps it goes back to my childhood in East Germany before the Berlin Wall fell. I remember vividly the thrill of receiving packages of food and clothing from relatives in West Germany.

Thanks to the hard work of my parents, I was able to finance my education as a pharmacist. I had intended to do volunteer work after graduation, but instead took a position in 2003 at Roche in Basel, Switzerland.

My current job is Quality Site Manager for Solid Dosage Forms. That means I inspect third-party manufacturers to ensure the quality of the drug-making process. Whenever I walk into a pharmacy, I can see Roche medicines that have been a part of my work.

I never forgot my desire to do humanitarian work. In 2013, I got my chance with the Roche secondment programme. This programme allows employees who meet certain criteria to spend up to one year on a hands-on project in some of

the world's poorest countries. By sharing their skills and knowledge, employees have a human impact that goes beyond conventional financial aid. They return to their jobs with invaluable insights into healthcare needs in other parts of the world.

I chose to work with the Kids of Africa programme in Uganda. This Swiss-based charity has created a school, a farm, a healthcare clinic and ten individual homes run by local foster mothers for orphaned and abandoned children. Their motto is 'We are family.' The children are not put up for adoption but grow up together in a healthy environment and receive an education so they can contribute to society. I liked this combination of self-help and sustainability.

My first months in Uganda were not easy. I was not used to the tropical heat and humidity, and food that mostly consisted of rice, beans and a corn-flour mash known as posho. The projects that I had planned didn't materialise immediately. Accustomed to work at a rapid pace in Switzerland, I had to learn to slow down.

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OVER  
**28%**  
OF THE LOCAL POPULATION LIVES  
MORE THAN 5 KILOMETRES AWAY  
FROM A HEALTH FACILITY<sup>3</sup>

ABOUT  
**20%**  
OF UGANDANS LIVE ON  
**LESS THAN**  
A DOLLAR A DAY<sup>4</sup>

---

*“The projects that I had planned didn’t materialise immediately. Accustomed to work at a rapid pace in Switzerland, I had to learn to slow down.”*

I had not been particularly good with kids before, so it was a steep learning curve. After settling in, I helped some of the older children prepare for school exams and taught courses on hygiene, diseases, sexual education and first aid.

I soon realised that many children could not see properly. I organised eye examinations and raised money through my network of family and friends in Europe to purchase eyeglasses. It is amazing what a difference a simple pair of glasses can make in the life of a child.

Other initiatives had a connection to my professional training. I improved the process for purchasing and storing medicines. I filled out medical records on simple notecards for each child, set up a sick bay and put together first-aid kits.

When the day nurse left, the children often came to me when they were hurt. I learned to overcome my fear of blood and helped them bandage their wounds. I also accompanied kids on visits to doctors and hospitals.

One day, I made a trip to a local hospital with one of our boys to have a cyst on his throat removed. In the waiting room, a young girl approached me with a warm smile. Her right arm had been amputated above the elbow and her face was severely scarred by burns. My first reaction was to turn away, but she would not let me. Still smiling, she looked into my eyes and led my hand to the stump of her arm. Then she traced the burn marks on her face with my fingers. It was an intense moment of acceptance and love. That little girl taught me something profound about my humanity, about overcoming my own barriers to reach out to others.

*“It is remarkable that a company sends an employee abroad for a full year of personal development...”*

One of the biggest challenges during my year with Kids of Africa was taking charge of all ten children in our house while the regular ‘mummy’ was away. For four weeks, I got the kids ready for school, cleaned, washed clothes and cooked, as well as entertained and counselled them.

I also mentored several children, including Kevin. He was a stubborn boy who barely spoke and avoided eye contact. Gradually, I gained his trust and we grew very close. Kevin is like a son to me now, and we talk on the phone regularly.

Helping those children in Uganda has transformed me. I am now more open to people and freer with my emotions. At work, I am more focused on what is really important.

The experience has also strengthened my connection to Roche. It is remarkable that a company sends employees abroad for a full year of personal development while continuing to pay their salaries and guaranteeing their jobs when they return.

The mission of our company is help people with innovative medicines. In some small way, my year in Uganda was an extension of that philosophy. By caring for those children, I may have changed some lives. The experience has certainly changed mine.



**Katrin mentored Kevin** during her year in Uganda and still has a close bond with him. Besides that she is financing high school studies for other kids outside of the Kids of Africa community. To help more of these children she founded her own association and sells jewellery and sandals made by a local artist ([www.mukisa.ch](http://www.mukisa.ch)).

3 Ministry of health. Uganda’s health sector strategic and investment plan: Promoting people’s health to enhance socio-economic development 2010/11–14/15. | 4 The Republic of Uganda. Poverty status report 2014: Structural change and poverty reduction in Uganda.

# Environment and Community



**12.9%**  share in **sustainable energy**

**11.5%** improvement in **eco-balance**

**23.6%** reduction of **Roche accident rate**

**20 YEARS**  
supporting **mobile healthcare clinic** in South Africa

# Reducing our environmental footprint whilst production and sales grow strongly

*AT ROCHE, Safety, Security, Health and Environmental Protection (SHE) forms an integral part of our operations. We approach it with the same level of commitment as we do with any business-related activity, striving for continuous improvement wherever possible and economically viable.*

We monitor our performance regularly to ensure compliance with our high standards and objectives, as well as ensuring that our processes and equipment are state of the art. Prevention, however, is the key to effective SHE management to which we devote special attention. Our main tool is a professional risk management.

In addition to spending 221.2 million Swiss francs for environmental purposes, our investments and operating cost for safety and security amounted to 391.2 million Swiss francs. Hence, the total spending for SHE measures in 2014 was 612.4 million Swiss francs, compared with 637.8 million Swiss francs in 2013, a decrease of approximately 4%.

## Mid-term SHE goals\*

**20%** share of **sustainable energy**

**20%** improvement in **CO<sub>2</sub> emissions** per employee

**20%** improvement of **energy consumption** per employee

**< 0.06** **Roche accident rate**

**15%** improvement of **eco-balance** per employee

**< 0.01** **Roche illness rate**

\*Goals for 2020 based on 2010 figures.

Our total investments for SHE projects amounted to 309.7 million Swiss francs, an increase of 38% compared with 2013.

### Improving and monitoring performance

As a company with global production operations, Roche is exposed to risks that could possibly damage people, goods, the environment and our reputation. Audits, consulting and training on environmental protection and occupational health and safety minimise these risks. In Safety, Health and Environmental Protection, we employ 662 people worldwide and additionally 520 people in Security. Expert teams at each Roche site identify risks and develop mitigation plans. They communicate policy and guidelines to employees and other stakeholders and motivate them to implement the necessary measures.

The effectiveness of our SHE management system is reviewed frequently, with employees encouraged to identify areas for improvement and recommend changes as required. Using a database of SHE best practices, our employees frequently share knowledge and exchange new ideas on SHE topics. In 2014, 32 proposals from this database were adopted by other areas within our organisation.

*Education, awareness and training are the best ways to foster employee engagement and responsibility in SHE.*

With this in mind, we conduct regular training sessions, regional conferences and workshops and provide online tools in local languages to employees. In 2014, our employees participated in approximately 245,444 hours of SHE training.

### Audits and assessments

Our policy is to audit critical sites, such as chemical, pharmaceutical and diagnostic manufacturing facilities, every three years and other relevant sites periodically according to risk. These audits assess SHE performance against internal standards and stipulate future improvements. Plant management and local SHE officers conduct more frequent 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, we or third-party auditors retained by us periodically inspect the operations of our suppliers and issue recommendations for improvement. In the event of non-compliance, we may either terminate a contract or refuse to renew it.

### Group SHE audits

	2014	2013	2012	2011
<b>Internal audits</b>				
Follow-up	24	20	17	10
First time	4	10	9	3
<b>External audits</b>				
Follow-up	3	9	10	5
First time	8	21	48	42

In 2014, we followed up on 24 earlier audits and confirmed that improvements had been made in the interim period. Recommended SHE improvements following these audits included increasing the involvement of line management and improving risk analysis.

### SHE materiality

In Group SHE, we are constantly aware of SHE material issues. We regularly gather information concerning SHE-related risks and opportunities from Roche affiliates as well as consult with and listen to our stakeholder groups. In a further step, we match the stakeholder issues with our internal strategic priorities and risks framework to produce our materiality matrix.

Using this method we have been able to identify the material topics which stand out as areas of interest to Group SHE and its stakeholders. Such topics are actively managed by Group SHE:

- Climate change
- Compliance
- Diseases of civilisation (see page 27)
- Energy and resources
- Extremism and organised crimes (see page 102)
- IT-systems
- Natural disasters
- Occupational and mental health
- Pharmaceuticals in the environment
- Politics and legislation
- Water

With a clear and defined process, Roche creates progress through target setting. In a series of workshops, aimed at the Roche Group, as well as discussions with internal and external experts, mid-term targets have been set for the period 2015–2020. By knowing our material issues and what we want to achieve we are able to set targets and initiate action plans. The new goals are feasible but challenging and are in the areas of people, environment and business. For more information, see related Roche websites on page 172.

# Occupational and mental health

Absences from work due to occupational accidents and occupational diseases (including unhealthy stress) have a negative impact on the company. Providing a safe and healthy workplace for our employees is therefore a priority. Our primary objectives are to keep the Roche accident rate (RAR) below 0.07 by 2015, 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 per year. RIR corresponds to the number of working days lost due to occupational illness per employee per year.)

## Our approach

As a responsible employer, it is important to us to do everything possible to prevent work-related accidents and illnesses. We therefore continuously improve our occupational health and safety measures. We set realistic goals and run projects aimed at keeping accidents to a minimum. We have established health and safety committees at virtually all Roche sites engaged in technical activities, such as production, laboratories, workshops and warehouses, and at many other sites according to risk levels.

In 2014, we updated one of our Group directives to include mental health protection. As an integral part of any work-place risk assessment, all of our sites will perform an evaluation of risks to mental health. Furthermore, 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 allows all our employees to report and address safety issues. We expect similarly rigorous policies from our contractors.

## Our performance

In 2014, we recorded 373 injuries resulting in a Roche accident rate of 0.052. The number of days lost due to injuries decreased by 21% from 6,324 in 2013. As the number of employees increased the worked hours went up 3% and the RAR went down by 23.6%.

*Accident rates at Roche are very low, but we are working towards further reductions.*

As RAR is at a very low level, single accidents resulting in longer absences can result in sharp fluctuations.

The incidence of reported cases of occupational illnesses increased to 142 in 2014. Furthermore, the related working days lost also increased to 1,547 from 1,268 in the previous year which increased the overall Roche illness rate to 0.016 or 14% higher.

## Employee safety and health

	2014	2013	2012	2011
Roche accident rate	0.052	0.068	0.072	0.067
Roche illness rate	0.016	0.014	0.018	0.025
Number of work-related accidents	373	352	440	390
Work-related fatalities	1	1	1	0
Working days lost per year due to accidents	4,976	6,324	6,036	5,471
Work-related accidents per million working hours	2.18	2.11	2.92	2.67

Our occupational accident and illness profile remains consistent with slips, trips, falls and repetitive strains representing the majority of work-related incidents in 2014. We sincerely regret that a third-party passenger died in a road traffic accident in Indianapolis, Indiana, while carrying out his duties.

SHE INVESTMENTS UP  
**38%**

**85%**  
OF EMPLOYEES CONSIDER HEALTH AND SAFETY TO BE IMPORTANT



# Environmental sustainability

Research, pharmaceutical and diagnostic manufacturing are dependent on natural resources which are becoming increasingly threatened. Roche's environmental strategy aims at using natural resources such as raw materials, fuel and water in a sustainable manner. In doing so, the company decreases its environmental footprint, which, in turn, benefits its stakeholders and society by reducing greenhouse gas (GHG) emissions, preventing water scarcity as well as other environmental and health problems. The less Roche depends on non-renewable resources, the less vulnerable it is to supply constraints and volatile market prices.

At Roche, we generate high-value products with relatively low levels of energy used for our operations. In 2014, the total energy use per million Swiss francs of products sold was 0.273 terajoules, which compares well with other pharmaceutical companies and chemical industries. By setting goals, we are able to expand our business while utilising less energy and hence reduce emissions. As part of our commitment to sustainable development, we proactively seek to employ new and more sustainable technologies and processes which minimise our environmental footprint.

*By 2020, we will achieve a 15% improvement of our eco-balance.*

## Eco-balance

Eco-balance refers to the consumption of energy and resources and the emission of by-products and waste from our business activities. It describes the total environmental impact of our operations. By allocating environmental impact points to ecologically relevant parameters, such as the consumption of natural resources and emissions to air and

water, we obtain a view of the demand we place on the Earth's eco-systems. These points are added up and then related to the total number of employees, which enables us to monitor our environmental impact per employee.

## Eco-balance

	2014	2013	2012	2011
Primary energy	39,101	41,542	41,201	41,374
Raw material	74,932	73,380	67,342	67,042
Water	1,786	1,908	1,919	1,981
Emissions to the air	332,272	370,792	355,015	375,390
Emissions to water	66,657	86,994	53,059	54,988
Landfilled waste	30,508	21,066	26,487	22,967
Eco-balance	545,256	595,683	545,022	563,742
Environmental impact*	5.70	6.44	6.45	6.88
Eco-balance per million CHF of sales	11.49	12.73	11.98	13.25

\* Environmental impact per employee in million impact points.

We have established a Group-wide goal for eco-balance, which allows local site management the freedom to develop locally appropriate strategies and objectives for reducing environmental impact. In 2014, our total environmental impact per employee decreased from 6.44 to 5.70. Approximately 61% comprised emissions to the air, of which approximately 86% was CO<sub>2</sub> from energy use.

Our improvements in decreasing energy consumption, the volume of withdrawn water, emissions to air and water and an increase in headcount had a positive effect on our environmental impact. While the total use of raw material increased, the raw material efficiency (kg of raw materials used per kg of products produced) improved by 8%.

**Natural capital**

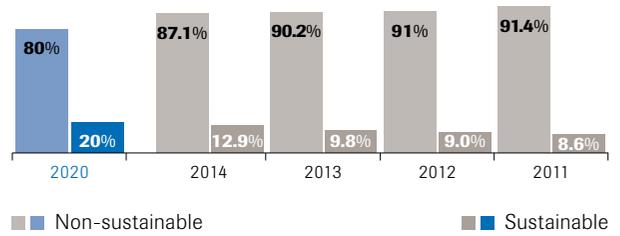
Roche is committed to conserving eco-system services and biodiversity. In order to provide us with an overarching metric which assesses and compares our risks and opportunities across operations, products and supply chains we are exploring the idea of natural capital evaluation. This is a means of placing a monetary value on environmental impacts along the entire supply chain of our business.

Roche is, however, faced with a number of challenges associated with natural capital evaluation such as the lack of a harmonised framework and difficulties to gain access to data if the impact analysed lies beyond the company premises. In general, putting the impacts into a regional context and to find data with adequate quality are also great challenges. We are now investigating the best way forward.

**Energy management**

Roche is committed to minimising its environmental footprint in meaningful ways and contributing to a sustainable energy future. To transform this vision into reality, we have set up energy-saving action plans across our sites. They include the implementation of innovative technologies and continuous upgrading of infrastructure to improve energy efficiency. We purchase energy-efficient equipment, including hybrid and diesel-efficient cars, and we review employees' travel needs. We also change work processes which is a complex task in highly regulated and approved facilities and we are focusing our effects on a steady transition to the use of sustainable energy.

**Share of sustainable energy actual data and goal for 2020**



Today, approximately 87% of the energy used by Roche comes from fossil fuels: non-renewable and depleting sources such as coal, oil and natural gas. As a result, we produce GHG, mainly CO<sub>2</sub>, and other waste products that contribute to climate change and air pollution.

*Our aim is to maximise efficient energy usage and to increase the use of sustainable energy, while continuing to expand our global business.*

**Cutting-edge technology for optimised constructions**

We partnered with the Department of Energy's FLEXLAB at Lawrence Berkeley National Laboratory, California, (picture below) to use state-of-the-art technology to optimise energy efficiency of new buildings. Mounted on a rotating platform, it provides a realistic model of the new building to test the effects of sunlight on building temperature, measure the thermal properties of walls and windows, and get a precise idea about the comfort of the internal environment for employees. This data was incorporated into the design of

The FLEXLAB provides state-of-the-art technology to optimise energy efficiency of new buildings, helping to save energy and water.



new buildings, which will significantly reduce heating and cooling demand for energy and water.

### Energy intensity and consumption

Roche is actively reducing energy intensity (measured at Roche by energy used per employee), as well as increasing its use of energy from sustainable sources. Energy conservation benefits the environment by avoiding air pollution and reducing GHG emissions, and benefits Roche by lowering costs and increasing reputational value. The efficient use of energy also ensures business continuity and a sustainable future for generations to come.

Our goal is twofold. First, we aim to reduce energy intensity in gigajoules (GJ) per employee by 20% by 2020, from 2010 levels. By about 2050, we expect to reduce energy consumption per employee by approximately 50% from 2005 baseline levels. Second, we plan to increase the proportion of sustainable energy used to 20% of total energy consumed by 2020.

In 2014, our energy consumption decreased by 3.7% while sales grew 5%, thus decoupling energy consumption from the growth of business. Our energy-saving activities resulted in a:

- 4.7% decrease in energy used in buildings and stationary equipment (gas, fuel oil, waste, electricity, district heating)
- 5.5% decrease in car fuel consumption
- 27.0% increase in sustainable energy use, bringing the total share of sustainable energy to 12.9% of consumption

Our reduction efforts around business travel started to show effect in 2014. Although the energy consumption from air travel increased, it only did so by 0.4% compared to 2013, now comprising 20.6% of the total energy consumption.

In 2014, our energy intensity improved by 7.5% reaching 136 GJ/employee by the end of the year. We have, therefore, successfully reached and surpassed the Roche Group mid-term energy goal of 158.4 GJ/employee as well as taking one more step towards reaching our 2020 goal of 140.8 GJ/employee.

In absolute terms, we have decreased our overall energy consumption by 10.5% over the last five years. Our energy intensity has behaved similarly decreasing from 176 GJ/employee in 2010 to 136 GJ/employee in 2014.

### Solar power

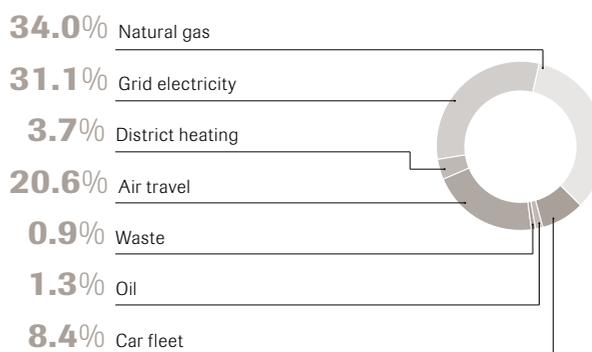
Genentech's newest tool for minimising its impact on the environment is the sun. A new 490 kilowatt photovoltaic system represents its first foray into the world of solar energy and is a step forward in Roche's global efforts to use 20% of its energy needs from sustainable sources by 2020. The power generated provides electricity for the Dixon, California, US, site. Power can be generated pretty much all year round as there is adequate sunshine, even in winter. The solar arrays, which are installed on new parking lot canopies as well as the building's roof, also offer shade from

the Californian sun for approximately 50 vehicles. Furthermore, four electric vehicle chargers were added, allowing employees to plug in their electric cars and purchase electricity needed for the commute home.

### Energy Consumption terajoules

	2014	2013	2012	2011	2010
Total energy	12,968	13,470	13,279	13,371	14,486
Energy from sustainable sources	1,679	1,322	1,192	1,147	817
Energy consumption per employee (GJ/employee)	136	147	158	164	176

### Energy use by type



### Air emissions

Our aim is to avoid, reduce, and control air pollutants in line with our eco-balance goals. Despite the increased production resulting from our continued strong growth, it is our overall objective to keep emissions to the air at the low levels we have achieved in the past few years.

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

**Emissions to air tonnes**

	2014	2013	2012	2011
VOCs	120	114	122	124
Particulates	26	31	20	20
Nitrogen oxides	254	227	254	222
Sulphur dioxide	5	7	5	8

Emissions to air from Roche sites are at a very low level, which means that new processes or activities, as well as the timing of sampling, can result in fluctuations as seen in the past few years.

**Greenhouse gas emissions and climate change**

In 2014, 39.1% of our GHG emissions originated from within our own facilities (scope 1) and amounted to 362,582 tonnes. GHG emissions originating from the transformation of purchased energy consumed by us (scope 2) made up 40.5% of the total and amounted to 376,159 tonnes.

Roche's responsibility to the environment means we actively drive programmes which reduce GHG emissions. As the majority of our GHG emissions originate from the transformation and use of energy, our goal for improving energy efficiency also applies to GHG emissions, i.e. a 20% reduction, measured in tonnes per employee by 2020 from 2010 levels. We do not favour the use of carbon offset as an alternative to driving our own efforts to reduce emissions. We expect to achieve further reductions by substituting fossil fuels with energy from sustainable sources.

*Our combined scope 1 and 2 GHG emissions were cut by 10%.*

This reduction was achieved by implementing energy-saving measures, reducing the amount of fuel we use to heat, cool and operate our sites.

Transportation via our logistics service providers also contributes to GHG emissions. To reduce our CO<sub>2</sub> footprint in transportation we need to monitor our overall emissions in terms of our carbon accounting system. In 2013, we

developed a software-based IT tool to calculate our intercompany and direct delivery shipments that uses one standard for all of our logistics service providers. This will provide the data basis required to manage these scope 3 emissions in the coming years. It is certified as being compliant with EU (ISO Standard 16258) requirements. Shipments for all modes of transportation are assessed on a single shipment basis, which allows us to identify emissions drivers and focus on methods for emission reduction.

Another initiative to reduce GHG emissions at Roche is to reduce our use of halogenated refrigerants, which are used in cooling equipment and can remain in the atmosphere for a long period of time. Since 2004, we have made significant progress reducing emissions of halogenated hydrocarbons, eliminating all halons and reducing fully halogenated compounds by 90%, except at the US Genentech and Ventana sites, which came later into the reduction programmes and have later target dates. Our plan was to reduce halogenated refrigerants by 90% at all Roche sites by 2015. However, recent acquisitions and the lack of alternatives in some countries means that fulfilling this goal by 2015 is unrealistic. We nevertheless continue to examine alternatives and work with refrigeration suppliers to make further reductions. For companies integrated into the Roche Group more recently, separate timelines are being set.

**Halogenated hydrocarbons tonnes**

	2014**	2013	2012	2011
Inventory	167.3	176.4	172.1	181.9
Emissions	2.6	3.7	2.6	3.8

\*\* Change in scope relating to ownership and percent occupancy of a building.

**Carbon Disclosure Project**

In 2014, the Carbon Disclosure Project (CDP) ranked Roche second in the healthcare, pharmaceuticals and biotech sector of the DACH region (Austria, Germany, Switzerland). Roche scored 99% in the Carbon Disclosure Index and achieved a Carbon Performance Rating of A-. This score qualified us for the Climate Disclosure Leadership Index for the second successive year. The disclosure score confirms that we understand the business issues related to climate

**CO<sub>2</sub> equivalent emissions metric tonnes**

	2014	2013	2012	2011	2010 (base year)
Scope 1	356,348	396,588	388,061	419,306	451,073
Halogenated hydrocarbons	6,234	6,548	6,014	7,092	6,507
Scope 2	376,159	418,214	432,103	443,583	448,460
Scope 3*	189,714	188,924	177,678	160,632	171,261
Total	928,455	1,010,274	1,003,586	1,030,613	1,077,301
Total emissions per million CHF of sales (tonnes)	19.56	21.60	22.06	24.23	22.69

\* Includes CO<sub>2</sub> from business flights.

change and are building climate-related risks and opportunities into core business. Roche's performance score signals that we are measuring, verifying and managing our carbon footprint. The CDP publishes these two indices in order to increase transparency of GHG emissions reporting.



### Water management

Our business is dependent on reliable supplies of high-quality water. Almost all chemical, biotech, pharmaceutical and diagnostics manufacturing processes involve water as a reagent, solvent, cleaning and cooling agent. For the pharmaceutical industry globally, poor quality water is resulting in higher costs for purification and greater risk of product contamination. We also use water as an energy carrier in refrigeration and heating installations.

### Our approach

Roche is aware that the demand for fresh water is increasing and an effective water management is crucial to avoiding water scarcity. Therefore, Roche sites are either working on or implementing programmes to reduce water consumption and recycle or reuse water. In our view, water supply and use is best managed and monitored locally. For that reason, our 2015–2020 SHE-Goal is to reduce water consumption per employee by 10%, weighted according to the water stress for that region.

We also support global efforts to promote water protection and conservation and to improve access to clean drinking water. Furthermore, we aim to reduce total waste water toxicity by 10% by 2020 from a 2015 baseline. In the meantime, we continue to investigate reliable performance indicators and measurement methods for establishing a waste water toxicity baseline.

More than half of the water we draw is used in cooling circuits. Even though this water is not chemically contaminated, we analyse it before it is directly discharged. The rest is purified in treatment plants before it is released to waterways.

### Our performance

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

- Reducing discharges of toxic and poorly biodegradable substances and heavy metals
- Reducing the generation of waste water
- Treating or pre-treating waste water, with ozone in some cases, for non- or poorly-degradable contaminants.

Our use of water has remained relatively unchanged over the past years. In 2014, we withdrew 18.4 million m<sup>3</sup> of water from different sources. Of this, approximately 16% was consumed, becoming a constituent part of a product, being vaporised in refrigeration or air conditioning plants or used for irrigation. 53% of the water was not chemically contaminated and could therefore be directly discharged. 31% was sent to treatment plants as chemically contaminated waste water, resulting in the discharge of 141 tonnes of organic matter and 236 kilogrammes of heavy metals.

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*A small increase in discharges compares favourably with our 5% sales growth seen in 2014.*

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Roche is aware which of its sites are located in regions where water is scarce and thus a valued commodity. These sites monitor the water situation locally and have procedures in place which ensure efficient water usage and business continuity. Water-related issues can affect our reputation and investors are increasingly showing interest in our water policy and performance. Therefore, Roche participated in the CDP's water programme in 2014.

### **Waste management**

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.

### **Our performance**

Waste is a parameter of our eco-balance and, as such, our waste reduction targets are reflected in our goal to improve the Group's eco-balance by 15% by 2020 compared to 2010. Waste reduction goals are set at the local level primarily because of large year-to-year fluctuations in waste from construction and demolition activities. In 2014, for example,

Roche produced 27,142 tonnes of chemical waste and 31,794 tonnes of general waste which comprised 15,064 tonnes of construction and demolition waste. Activities at our sites in Clarecastle, Ireland; Indianapolis, Indiana; and Nutley, New Jersey contributed to the increase seen in 2014.

### **Natural disasters**

Roche has operations in regions of the world which are susceptible to natural disasters such as earthquake, tornados, flooding. The financial risk of such an event is, however, minimal. In the necessity of having to suspend procedures due to a natural disaster, Roche has the possibility to transfer operations to another site thereby ensuring a continual supply and access to our products. To minimise the damage to our operations we have managed this issue by, for example, ensuring that threatened sites are earthquake-proof or built to withstand tornados.

## Security

Protecting our employees, physical assets, critical information and the integrity of our brands and products are principal concerns to Roche.

One focus in 2014 was the launch of the Global Logistics Security Programme in the Pharmaceuticals Division. The goal is to improve, systematically, the protection of our products from theft or manipulation during transportation or storage in own or third-party warehouses. A small team led by Global Pharma Supply Chain and comprising security and logistics experts from different regions, performed training sessions and delivered guidance on risk assessment and auditing for the local logistics security officers.

A second security focus in 2014 was set by the Latin American Security Workshop held in Rio de Janeiro, Brasil. Site security officers from all sites in Latin America discussed challenges and good practices on three key topics for the region: personnel security, logistics security and product counterfeiting.

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*Preventative measures are a priority in all aspects of security.*

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Furthermore, a new Group Directive was issued in the reporting year to give guidance on adequate security measures for exposed Roche personnel and their families working in high-risk countries.

### **IT system security**

Roche is continually aware of the issues surrounding the security and vulnerability of its IT systems and the ever growing necessity to protect its intellectual property. The implications of digital fraud go far beyond the financial risks. Despite the protective measures already being taken by Roche, the occurrence of cyber-attack is considered possible. In an effort towards minimising such events, we identify attackers and threats, assess the likely target, assess the impact of an attack on the organisation and finally, identify which assets are of high impact and require prioritising in terms of protection.



## Pharmaceuticals in the environment

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 metabolic processes following normal patient use. By far, patient use is generally recognised as the primary contributor.

Evidence suggests that the exposure to the resulting 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.

Roche is acting on concerns about the impact of pharmaceuticals on the environment by considering the entire lifecycle of its products, of which many are crucial diagnostic tests or life-saving medicines. We have two goals: first to safeguard the eco-system; and secondly, to protect our business against potential long-term financial and reputational risks.

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*Some of Roche's best-selling antibodies are judged to represent no significant risk to the environment.*

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Rituxan, Avastin, Herceptin and Lucentis are monoclonal antibodies which generated a large proportion of Roche's Group sales in 2014. They belong to a defined class of active pharmaceutical ingredients (APIs) exempt from the European Medicines Evaluation Agency (EMA) guideline on environmental risk assessment. They have a low excretion rate and are judged to present no significant risk to sewage works and surface waters. They are therefore termed 'benign in nature' and constitute environmentally sustainable compounds. All of our chemical products are, however, subjected to a rigorous environmental risk assessment.

## Legislation and compliance

We meet all local laws or regulations. However, our Group 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 eleven consecutive years prior to 2014, we incurred no significant fines for SHE-related violations. In 2014, we incurred no fines.

# Focusing on remediation management

Waste is an inevitable by-product of any industrial operation – the pharmaceutical sector is no exception. Since 1896, Roche has been researching, developing, manufacturing and marketing high-quality innovative solutions for unmet medical needs. By its very nature, the synthesis of chemical and pharmaceutical substances results not only in the desired compound, but also in by-products which ultimately have to be disposed of as chemical waste. Historically, insufficient know-how along with a lack of appropriate technical resources resulted in landfilling as the common disposal method. However, with improved knowledge of geological characteristics and adverse impacts associated with chemical contamination of soil and groundwater, we are faced with a potential long-term risk for people and the environment.

*Roche accepts full responsibility for all waste generated from our operations, including that previously deposited in landfills.*

Roche believes that existing landfills which contain hazardous wastes thereby threatening the environment should be addressed proactively, even if this means applying solutions exceeding the country's legal framework.

Roche deposited waste material in the Kesslergrube landfill in Grenzach, Germany between the mid-1950s and 1961. A former gravel pit, the now turned landfill received wastes for 15 years thereafter. In 2005, the evolving legislation on contaminated site management triggered a historical, multi-

phase technical investigation. Based on the findings, in 2013 the competent authorities decided that the landfill required remediation. After two years of refined planning, a complex remediation project was permitted. Before the excavation work commences the required infrastructure will be finalised, comprising a bypass road, a new temporary ship landing dock and a 20 metre deep pile wall surrounding the excavation pit.

The project is on track to be completed by 2021. The area to be remediated will be enclosed and all waste material, including contaminated soil down to the groundwater, will be removed. This waste will be packed and stored in special transport containers which will then be transported, by rail, to disposal facilities in Europe for thermal treatment. With careful planning and a step-by-step procedure Roche can ensure a safe and efficient execution of a complex remediation programme. The remediation will take place as quickly as possible, however, delivering a flawless execution has utmost priority. After completion of the remediation the area will be available for industrial re-development. Further information available at [www.kesslergrube.com](http://www.kesslergrube.com)

In 2013, Roche ceased business operations at its site in Nutley, New Jersey, after 84 years. To facilitate the sale and repurposing of the property, Roche accelerated its remediation efforts, which are under the oversight of the New Jersey Department of Environmental Protection (NJDEP) and the US Environmental Protection Agency.

Roche has already taken initial cleanup action to address soil and groundwater contamination while it prepares and submits final remediation plans to NJDEP for approval.

*At the site in Nutley, New Jersey, soil samples were collected and evaluated as part of extensive remediation efforts.*



Remediation is a complex process and a wide range of technologies are being explored to determine the best remedies to clean up the site safely and quickly. As part of the Nutley site environmental investigation, over 7,000 soil samples were collected and evaluated.

The cleanup of soil is expected to be completed by the end of 2015. Groundwater cleanup will take longer and Roche is conducting quarterly monitoring, which will continue for several years to ensure that the remedies are having a positive impact on contamination. After divesting the site which is anticipated by the end of 2015, Roche will retain responsibility for the environmental cleanup, monitoring and remedial activities on the Nutley site.

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*Not only does Roche actively manage its historical contaminated site issues, we also strive to avoid future liabilities.*

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The remediation process also involves being transparent with local officials and residents in the communities surrounding the Nutley site regarding the extent of the contamination, its impact and how Roche plans to address it. As such, Roche hosted two public meetings in May and October 2014, and will host additional meetings in the future. Further information available at [www.rocheusa.com](http://www.rocheusa.com).



“Sustainability  
is part of everything  
we do.”

*Katie Excoffier*

*Katie switched careers to become Sustainability Manager at Genentech. Her enthusiasm and ability to connect people have moved the needle in engaging employees and reducing the company’s environmental footprint.*

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# Employees drive sustainability

*BROAD EMPLOYEE PARTICIPATION has helped Genentech reduce energy and water usage by 33% and waste by 47% in five major buildings in only two years.*

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In 2005, after 20 years of working in R&D and management for a leading laboratory equipment manufacturer in California, US, I decided to take some time off. During that break, I saw a compelling documentary about the urgency to act on climate change. It inspired me to re-evaluate my career goals and reflect on how I could contribute to positive change.

I decided to pursue an MBA in Sustainable Management, which led to a job as a sustainability intern at Genentech in 2007. I knew the reputation of the company from my scientific background in genetics and from living in the San Francisco Bay Area. So, I was thrilled to be hired full-time as Sustainability Manager in 2009.

Sustainability is a cross-functional issue that often requires expertise and input from a range of different people. An important part of my job is to connect the right people and resources from across Genentech to make things happen. I have assembled a Sustainability Council to develop our sustainability strategy and goals and to encourage cross-functional collaboration. I also liaise with other companies to share best practices in sustainability and to leverage our collective influence to realise sustainability benefits.

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*“One of my tasks is to connect the right people and resources to make things happen.”*

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When I started my position as Sustainability Manager, there was already a successful programme called ‘Green Genes’ that engaged employees in environmental sustainability, and part of my role was to provide deeper opportunities for employees to live out their commitment to sustainability in

**COSTS SAVED:**

**> 1.5  
MILLION USD**

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a meaningful way at work. Many employees are environmentalists at home, but were not sure how to bring that lifestyle into the workplace. By enlisting employees as sustainability ambassadors and through educational outreach, we were able to overcome that challenge.

During my tenure, Green Genes has grown to 2,800 of the total of 12,000 Genentech employees – a leading benchmark in terms of employee engagement in sustainability. In addition, we have about 300 Green Guides with a deeper level of training and environmental expertise. These Guides lead teams on Energy, Water, Recycling, Transportation, Wellbeing and Green BioPharma. I work with each team to set up activities such as recycling month, Earth Week, beach cleanups, Lunch & Learns and other awareness events.

That high level of engagement and evolved organisational structure gave us a solid foundation for a new initiative in 2012. Alongside other leading companies, we participated in the US Green Building Council’s Best Buildings Challenge and committed to reducing energy, waste and water usage by 20% within just two years. Our aim was to achieve these

reductions on a per-employee basis in five of our high-occupancy buildings, which included energy- and water-intensive lab buildings.

One of the challenges we faced as we launched the initiative, known internally as Dash to 20, was a lack of detailed data. So, we installed new water meters, smart lighting sensors and Wi-Fi-enabled energy-use strips in office cubicles. With more specific information, we were able to prioritise our efforts and share progress with employees through touch screen dashboards in the Dash buildings.

In June 2014, we concluded Dash to 20 with results that exceeded our expectations, reducing energy and water usage by 33% and waste by 47% per employee. The financial returns on our investments showed that sustainability also makes good business sense.

*“We saved 12.5 million gallons of water over two years, helping to conserve during a historic drought in California.”*

The water savings were particularly important for our community, given that we are based in California, which is experiencing one of the worst droughts in its history. In some areas, farmers are struggling to irrigate their crops, and wells for drinking water are drying up. By fine-tuning our airconditioning systems, replacing water-thirsty lawns with drought-resistant landscaping and other initiatives, we saved 12.5 million gallons (47,312,000 litres or 47.312 m<sup>3</sup>) of water over two years. Our efforts helped to prevent mandatory water restrictions that might jeopardise our production of life-saving medicines.

The energy-efficient new building currently under construction will contribute to these efforts by significantly reducing heating and cooling demand for energy and water. The construction was optimised by using the innovative FLEXLAB technology (see page 126).



**Green Genes** – Engagement for environmental sustainability exists at high levels, employees welcome suggestions to implement it at their workplace.

In partnership with the USGBC Building Health Initiative, we are joining with other companies to make buildings as healthy as they can be for occupants. The first important step is to require increased transparency from suppliers about the content of building materials and office furniture, so that we can make more informed decisions about what to purchase.

I see an increasing number of employees who want to do something for the environment. If we build on that momentum and mobilise our colleagues, families and friends, we can make a meaningful difference in our impact on the world around us.

ENERGY AND WATER  
CONSUMPTION  
**DOWN BY**  
**33%**

**47%**  
**DECREASE**  
**IN WASTE**

# Making a difference with philanthropy

*SINCE ITS FOUNDATION almost 120 years ago, Roche has been committed to supporting people in need through innovative and sustainable partnerships. We carefully choose our projects based on criteria such as commitment, collaboration, and continuity to ensure the engagement and impact will be long-lasting.*

## *Pillars of our philanthropic engagement*

*Community and environment involvement*

*Humanitarian and social projects*

*Science and education*

*Art and culture*

*Our focus: ongoing initiatives, sustainable projects and sponsorship.*

### **Sustainable health partnerships**

The Transnet-Phelophepa Healthcare Train, a mobile clinic bringing medical care and medicines to remote communities in South Africa, celebrated its 20<sup>th</sup> anniversary in 2014. As the main external sponsor, Roche is proud of the initiative's success and significant impact. Since its start, Phelophepa\* has provided primary care, dental and eye checks, treatments for diagnosed conditions, health education and counselling to about 5.8 million people.

*Counselling on hygiene and prevention could improve the health of many people in villages visited by the trains.*

It is a service that many people in the region have come to rely on. Every year, Phelophepa's two medicalised trains visit a combined total of about 70 communities, many of which have only one doctor for as many as 5,000 patients. The trains are operated by resident staff and a team of volunteer student doctors and nurses. Since the first journey in 1994, Phelophepa counts over 20,000 volunteers whose

contribution is an essential component of the programme's sustainability.

Recognised around the world for its innovation and immense service to its people, Phelophepa has twice won the Sigma Theta Tau Award, a prestigious nursing award, and the United Nations Public Services Award.

In Japan, Chugai Pharmaceutical Co., Ltd., a member of the Roche Group, also had a milestone anniversary of one of their hallmark philanthropic projects in 2014. For 30 years running, Chugai has donated specially equipped para-transit vehicles to five organisations providing welfare services to senior citizens and disabled people throughout Japan. Since the programme began, Chugai has donated over 200 of these vehicles to support people receiving long-term nursing care at home.

Meanwhile, the Roche Children's Walk gives every employee the chance to raise funds for children in need. Half of the donations are given to local projects and the rest goes to support schools and orphan day care centres in Malawi. In 2014, 128 Roche sites participated in the Children's Walk, which is the largest number of participating sites since the first walk in 2003. So far, donations have helped to support



over 17,000 orphan children with school uniforms and over 5.6 million meals.

#### **Innovative disaster response**

Roche also provides support and donations following natural disasters. In order to ensure a sustainable response, we collaborate from an early stage with local Roche affiliates and on-site implementation partners. Our contributions range from material goods and logistic support to transfer of knowledge and experience.

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*When a natural disaster occurs, Roche listens to the needs on the ground and works with local partners to provide sustainable support.*

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Typhoon Yolanda, one of the strongest tropical storms ever recorded, devastated several parts of the Philippines in November 2013. Many small, poverty-stricken coastal communities, such as Naborot Island in the province of Iloilo, were among the worst hit. In 2014, to help with restoration efforts, Roche Philippines committed to support 5,000 families and collaborated with MyShelter Foundation to install solar bottle lights in homes on Naborot. The innovative technology uses a recycled one-litre plastic bottle, small solar panel, battery and LED light to provide a free source of eco-friendly light. Installed through MyShelter Foundation's Liter of Light project, an initiative supported by Roche Philippines, the bottle lights now brighten over 28,000 homes.

\* 'Phelophepa' in Tswana and Sotho dialects means good, clean health.

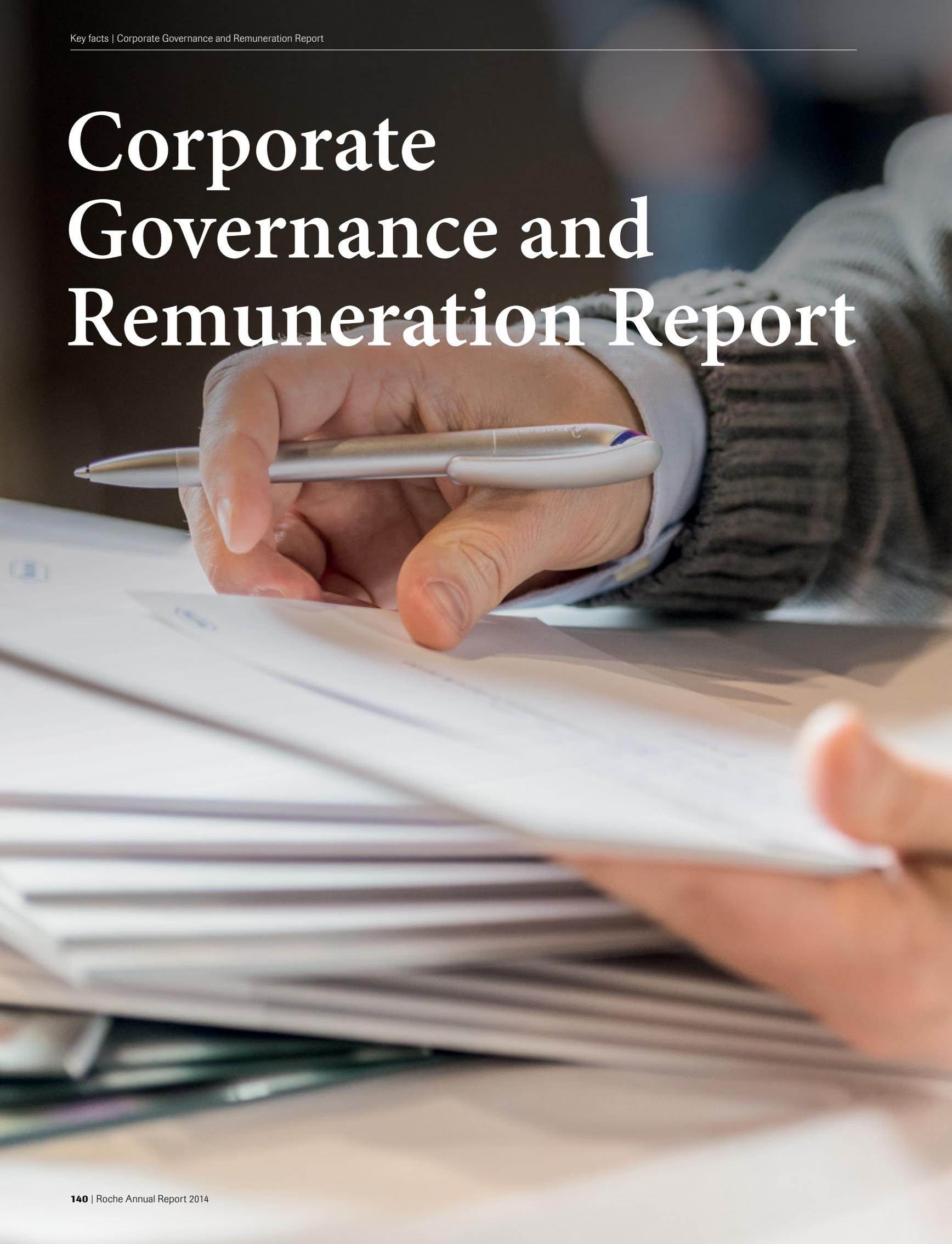
Another important initiative in the reporting year was a disaster relief for earthquake victims in China. After a severe earthquake killed more than 600 and injured 3,000 people in Ludian County in Yunnan Province in August 2014, Roche China immediately activated a disaster response plan, reaching out to the local Red Cross and donating the value of about 145,000 Swiss francs and 15,000 doses of Rocephin. In addition, Roche China employees organised fundraising activities to support ongoing disaster response efforts in the region.

#### **Supporting innovation in arts and science**

Roche also supports groundbreaking contemporary art, cultural projects and activities that explore the parallels between innovation in art and in science. This forms the basis for the unique collaboration between Roche, the Lucerne Festival and the Lucerne Festival Academy. With *Roche Commissions* and *Roche Young Commissions*, we again funded two philanthropic activities that promote non-mainstream classical contemporary music composers.

In 2014, Olga Neuwirth was named the winner of *Roche Commissions* series. The Austrian composer ranks among the most important figures in contemporary classical music today. Her compositions will be premiered in 2016 and performed by the Lucerne Festival Academy Orchestra.

# Corporate Governance and Remuneration Report

A close-up photograph of a person's hand holding a silver pen over a stack of papers. The hand is wearing a dark, textured sweater. Another hand is visible at the bottom right corner, holding the edge of the papers. The background is blurred, showing more papers and a desk.

After its **foundation in 1896**, Roche over the years specialised as a leader in research-focused healthcare with combined strengths in pharmaceuticals and diagnostics.

**In 2014, for the 6<sup>th</sup> consecutive** year, Roche has been recognised by the Dow Jones Sustainability Indexes (DJSI) **as the Group Leader in sustainability** within the pharmaceuticals, biotechnology and life sciences industry.

# 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 2014, for the 6<sup>th</sup> consecutive year, Roche has been recognised by the Dow Jones Sustainability Indexes (DJSI) as the Group Leader in sustainability within the pharmaceuticals, biotechnology and life sciences industry. 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.<sup>1</sup>

The printed Annual Report contains selected links to the Roche website ([www.roche.com](http://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.

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<sup>1</sup> [http://www.roche.com/about\\_roche/corporate\\_governance.htm](http://www.roche.com/about_roche/corporate_governance.htm)

# Board of Directors

In implementing the 'Ordinance against excessive compensation in listed corporations' (Verordnung gegen übermäßige Vergütungen bei börsenkotierten Aktiengesellschaften [VegüV]), at the 96<sup>th</sup> Annual General Meeting (AGM) of Roche Holding Ltd, on 4 March 2014, shareholders approved corresponding required amendments of the Articles of Incorporation and elected all members of the Board of Directors standing for election, the Chairman of the Board of Directors, the members of the Remuneration Committee and the independent proxy for a one-year term.

Shareholders elected Christoph Franz as new Chairman of the Board of Directors succeeding Franz B. Humer. Franz B. Humer and William M. Burns decided not to stand for re-election and retired from the Board. Furthermore, the AGM elected André Hoffmann, Pius Baschera, John I. Bell, Paul Bulcke, DeAnne Julius, Arthur D. Levinson, Andreas Oeri, Severin Schwan, Peter R. Voser and Beatrice Weder di Mauro as members of the Board of Directors for a new term of one year as provided by the Articles of Incorporation. For the first time the AGM elected Christoph Franz, André Hoffmann, Arthur D. Levinson and Peter R. Voser as members of the Remuneration Committee.

At its organising meeting immediately following the AGM, the Board of Directors has determined the structure and composition of its remaining committees as shown below (composition as at 31 December 2014, see also pages 12

to 13 and page 146 'Board of Directors and Corporate Executive Committee').

The Board of Directors also already introduced and executed on the occasion of the AGM on 4 March 2014, the mandatory votes on remuneration, as well as the remote electronic ballot by means of authorisations and instructions to the independent proxy.

On 4 September 2014, Arthur D. Levinson has resigned from the Board of Directors and the Remuneration Committee with immediate effect.

At the forthcoming AGM on 3 March 2015, the Board of Directors nominates the Chairman, all remaining Members of the Board of Directors for re-election and the following members of the Board of Directors as members of the Remuneration Committee: Christoph Franz, André Hoffmann, Peter R. Voser. Additionally, the Board of Directors nominates Bernard Poussot and Richard P. Lifton for election to the Board of Directors. Moreover, Bernard Poussot is nominated by the Board of Directors for election as a new member to the Remuneration Committee.

As in 2014, the Board of Directors nominates BDO AG as the independent proxy for the period from 2015 until the conclusion of the 2016 ordinary Annual General Meeting of Shareholders for election by the AGM.

	Name (year of birth)			First elected
<b>Board of Directors</b>	Dr Christoph Franz (1960)	C, D*, E	Chairman	2011
	André Hoffmann (1958) (representative of the shareholder group with pooled voting rights)	A, C*, D, E	Vice-Chairman	1996
	Dr Andreas Oeri (1949) (representative of the shareholder group with pooled voting rights)	A*, E		1996
	Prof. Pius Baschera (1950)	A, E		2007
	Prof. Sir John Irving Bell (1952)	B, E		2001
	Paul Bulcke (1954)	B, E		2011
	Dame DeAnne Julius (1949)	B*, E		2002
	Dr Severin Schwan (1967)	F		2013
	Peter R. Voser (1958)	C, E		2011
	Prof. Beatrice Weder di Mauro (1965)	B, E		2006
<b>Secretary to the Board of Directors</b>	Dr Gottlieb A. Keller (1954)			
<b>Honorary Chairman of the Board of Directors</b>	Dr Fritz Gerber (1929)			

A Corporate Governance and Sustainability Committee.

C Remuneration Committee.

E Non-executive director.

\* Committee chairperson.

B Audit Committee.

D Presidium/Nomination Committee.

F Executive director.

# Corporate Executive Committee

In 2014, memberships of the Corporate Executive Committee remained unchanged.

Richard Scheller, Head of Genentech Research and Early Development (gRED) and member of the Enlarged Corporate Executive Committee retired on 31 December 2014. As of 1 January 2015, Michael D. Varney, former Head of Small Molecule Drug Discovery, became Head of gRED and member of the Enlarged Corporate Executive Committee of Roche.

Information on each member of the Corporate Executive Committee and of the Enlarged Corporate Executive Committee is listed below (composition as at 31 December 2014, see also pages 18 to 19 and page 146 'Board of Directors and Corporate Executive Committee').

	Name (year of birth)	Position
<b>Corporate Executive Committee</b>	Dr Severin Schwan (1967)	CEO of the Roche Group
	Daniel O'Day (1964)	COO Division Roche Pharmaceuticals
	Roland Diggelmann (1967)	COO Division Roche Diagnostics
	Dr Alan Hippe (1967)	Chief Financial and IT Officer
	Silvia Ayyoubi (1953)	Head Group Human Resources
	Dr Gottlieb A. Keller (1954)	General Counsel
	Osamu Nagayama (1947)	Chairman and CEO Chugai
<b>Enlarged Corporate Executive Committee</b> Until 31 December 2014 As of 1 January 2015	Dr Richard Scheller (1953) Dr Michael D. Varney (1958)	Head Genentech Research and Early Development (gRED)
	Prof. John C. Reed (1958)	Head Roche Pharma Research and Early Development (pRED)
	Dr Stephan Feldhaus (1962)	Head Group Communications
	Dr Sophie Kornowski-Bonnet (1963)	Head Roche Partnering
	Per-Olof Attinger (1960)	
<b>Secretary to the Corporate Executive Committee</b>		
<b>Statutory Auditors of Roche Holding Ltd</b>	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)	
<b>Chief Compliance Officer</b>	Dr Urs Jaisli (1956)	

# 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 four business areas: 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 31 to the Roche Group Consolidated Financial Statements ('Subsidiaries and associates', page 113).
- Major shareholders are listed in the Finance Report, Notes 21 and 30 to the Roche Group Consolidated Financial Statements ('Equity attributable to Roche shareholders' and 'Related parties', pages 84 and 111) and in Note 4 to the Financial Statements of Roche Holding Ltd ('Significant shareholders', page 144). In addition, significant shareholders are published on the relevant webpage of the disclosure office of SIX Exchange Regulation [http://www.six-exchange-regulation.com/obligations/disclosure/major\\_shareholders\\_en.html](http://www.six-exchange-regulation.com/obligations/disclosure/major_shareholders_en.html).
- André Hoffmann, Vice-Chairman of the Board of Directors and Chairman of the Remuneration Committee, 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 shareholder group with pooled voting rights and receive the remuneration set forth in the Remuneration Report on page 157 and in the Finance Report, Note 30 to the Roche Group Consolidated Financial Statements ('Related parties', page 111). 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 143). Additional details are contained in the Articles of Incorporation of Roche Holding Ltd.<sup>2</sup>
- Movement in recognised amounts during the last three financial years are detailed in the Finance Report, Notes to the Financial Statements of Roche Holding Ltd (page 144).
- 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 20 to the Roche Group Consolidated Financial Statements ('Debt', page 79).
- Information on employee stock options is provided in the Finance Report, Note 26 to the Roche Group Consolidated Financial Statements ('Equity compensation plans', page 96), including detailed information on the 'Stock-settled Stock Appreciation Rights (S-SARs) Plan', the 'Roche Restricted Stock Unit Plan', the 'Roche Performance Share Plan', 'Roche Connect' and the 'Roche Option Plan'.
- Roche has issued no options apart from employee stock options as provided in the Finance Report, Note 26 to the Roche Group Consolidated Financial Statements ('Equity compensation plans', page 96) 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.

<sup>2</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

### 3 Board of Directors and Corporate Executive Committee

- Information on each member of the Board of Directors (including the years of their first election) and on each member of the Corporate Executive Committee is listed on pages 143 to 144. Members of the Board of Directors have no age limit or restriction on their term of office. Curricula vitae of all current and of former members (of the last five years) of both bodies and other information (including information on board memberships, additional positions, memberships and activities) are available and continuously updated on the Internet.<sup>3</sup>
- Rules pursuant to article 12 para. 1 point 1 VegüV on the number of permitted activities of the Board of Directors and the Corporate Executive Committee members are outlined in §22.4 of the Articles of Incorporation of Roche Holding Ltd.<sup>4</sup>
- Since 2014 the Annual General Meeting elects all members of the Board of Directors, the Chairman of the Board of Directors and the members of the Remuneration Committee on an annual basis in elections in which each nominee is voted on separately (see §18 of the Articles of Incorporation of Roche Holding Ltd<sup>4</sup> and the Minutes of the 96<sup>th</sup> Annual General Meeting of Roche Holding Ltd, held on 4 March 2014<sup>5</sup>).
- With the exception of Severin Schwan none of the members of the Board of Directors in office at the end of 2014 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 proceeding the current reporting period and they are for lack of existing business connections with any Group subsidiary independent.
- The Principles of Governance (principles of delegation and competence, reservation of powers and management of a group of companies) of the executive bodies of the company include economic, environmental and social topics. The principles together with the internal organisation of the Board of Directors, 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.<sup>6</sup>
- 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.<sup>7</sup> Their composition and chairpersons as at 31 December 2014 are described on page 143. Each committee's authorities and responsibilities are defined in detail in the Bylaws of the Board of Directors.<sup>8</sup>
- All the committees 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 (MIS), 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.
- The Board of Directors has established a system of controls which is continuously monitored by the Audit Committee, by the Corporate Governance and Sustainability Committee and by the Board of Directors and consists of the following elements:
  - Report on operating and financial risks (risk management system)

The Roche Group has established a risk management process covering the entire company with a system in place to identify and manage all type of risks potentially affecting its business (including economic, environmental, and social impacts, risks and opportunities and containing stakeholder input). The Board of Directors is the highest governance body involved. Roche's Risk Management Policy 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. All material risks are reviewed by the Board on a yearly basis. The process is subject to regular reviews, with findings presented to the Audit Committee or the full Board. The effectiveness of the risk management process is monitored by the Group Risk Advisory team and the overall process is regularly reviewed by external auditors (last external review in 2013 with findings presented to the Corporate Executive Committee and to the Audit Committee of the Board).

<sup>3</sup> [http://www.roche.com/about\\_roche/management/board\\_of\\_directors.htm](http://www.roche.com/about_roche/management/board_of_directors.htm) and [http://www.roche.com/about\\_roche/management/executive\\_committee.htm](http://www.roche.com/about_roche/management/executive_committee.htm)

<sup>4</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

<sup>5</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/annual\\_general\\_meetings.htm](http://www.roche.com/about_roche/corporate_governance/annual_general_meetings.htm)

<sup>6</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

<sup>7</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/committees.htm](http://www.roche.com/about_roche/corporate_governance/committees.htm)

<sup>8</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

For details on risk management, including risk factors and the Risk Management Policy see 'Risk Management & Compliance' on our website.<sup>9</sup> Financial risk management is specifically described in the Finance Report.<sup>10</sup>

- System of internal controls over financial reporting (see pages 125 and 127 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 149
- Chief Compliance Officer and Compliance Officers in subsidiaries, see page 150
- Safety, Health and Environmental Protection Department<sup>11</sup>
- Corporate Sustainability Committee<sup>12</sup>
- Science and Ethics Advisory Group (SEAG), for issues relating to genetics and genetic engineering (established in 1999)<sup>13</sup>
- 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.

## Board and Board committees attendance 2014

	Board	Presidium/ Nomination Committee	Remuneration Committee	Audit Committee	Corporate Governance and Sustainability Committee
<b>Number of meetings</b>	<b>9</b>	<b>5</b>	<b>3</b>	<b>5</b>	<b>3</b>
Ch. Franz	8	4	3	4*	2*
A. Hoffmann	9	5	3	–	3
P. Baschera	9	–	–	–	3
J.I. Bell	9	–	–	5	–
P. Bulcke	8	–	–	5	–
D. Julius	8	–	–	5	–
S. Schwan	9	–	–	5*	–
A. Oeri	8	–	–	–	3
P.R. Voser	9	–	3	–	–
B. Weder di Mauro	8	–	–	5	–
Franz B. Humer (until 4.3.2014)	1	1	–	1*	–
William M. Burns (until 4.3.2014)	1	–	–	–	1
A.D. Levinson (until 4.9.2014)	3	–	1	–	–

– Not a member of that committee.

\* Invited as a guest to these Board committee meetings.

<sup>9</sup> [http://www.roche.com/corporate\\_responsibility/business\\_ethics/risk\\_management\\_and\\_compliance.htm](http://www.roche.com/corporate_responsibility/business_ethics/risk_management_and_compliance.htm)

<sup>10</sup> Additional information is provided in the Finance Report, Note 29 to the Roche Group Consolidated Financial Statements, 'Risk management', page 102.

<sup>11</sup> [http://www.roche.com/corporate\\_responsibility/environment.htm](http://www.roche.com/corporate_responsibility/environment.htm)

<sup>12</sup> [http://www.roche.com/corporate\\_responsibility.htm](http://www.roche.com/corporate_responsibility.htm)

<sup>13</sup> [http://www.roche.com/research\\_and\\_development/who\\_we\\_are/how\\_we\\_work/ethics\\_in\\_rd/ethical\\_conflicts.htm](http://www.roche.com/research_and_development/who_we_are/how_we_work/ethics_in_rd/ethical_conflicts.htm)

- 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 2015:

26 December 2014 to 28 January 2015

1 April to 22 April 2015

26 June to 23 July 2015

1 October to 22 October 2015

Black-out periods can be changed by the Chairman of the Board of Directors if circumstances warrant.

- In 2014, the Board of Directors met for 9 meetings, generally each from 3 to 6 hours in length\*\*; in addition once for a full-day meeting\*\* and once for a 3-day visit to a major subsidiary\*\*. The Board committees met as follows in 2014:
  - Presidium of the Board of Directors/Nomination Committee: 5 meetings (approx. 2 hours each\*\*)
  - Remuneration Committee: 3 meetings<sup>14</sup> (approx. 2 to 3 hours each\*\*)
  - Audit Committee: 5 meetings (approx. 3 to 4 hours each\*\*)
  - Corporate Governance and Sustainability Committee: 3 meetings (approx. 3 hours each\*\*).
- The composition of the Board’s committees has remained unchanged since 4 March 2014 (with the exception of members of the Board of Directors who retired).
- The Board of Directors regularly conducts an assessment (self-assessment/assessment by third parties via electronical survey) 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 4.4 (annex) of the SIX Directive on Information relating to Corporate Governance.

#### 4 Remuneration, shareholdings and loans

- All details regarding remuneration, shareholdings and loans (content and method of determining the compensation and the shareholding programmes, basic principles and elements of compensation and shareholding programmes for serving and former members of the Board of Directors and Corporate Executive Committee, together with a description of the authorities and procedure for determining such) are set forth in the separate Remuneration Report on pages 152 to 167 and in the Finance Report, Notes 21 and 30 to the Roche Group Consolidated Financial Statements (‘Equity attributable to Roche shareholders’ and ‘Related parties’, pages 84 and 111), and are listed in Note 6 to the Financial Statements of Roche Holding Ltd (‘Board and Executive shareholdings’, page 145).

- Following rules on Remuneration, shareholdings and loans for the Board of Directors (Board) and the Corporate Executive Committee (CEC) are set forth in the Articles of Incorporation (AoI)<sup>15</sup>:

Content	Rules in AoI <sup>15</sup> for	
	Board	CEC
Rules on the principles applicable to performance-related pay	\$25.1–6	\$25.1–6
Rules on the principles to the allocation of equity securities, convertible rights and options	\$25.7	\$25.7
Additional amount for payments to members of the Executive Committee appointed after the vote on pay at the General Meeting of Shareholders		\$24.5
Rules on loans, credit facilities and post-employment benefits	\$25.1 and 3	\$25.2 and 3
Rules on the vote on pay at the AGM	\$24	\$24

#### 5 Participatory rights of shareholders

- The participatory rights of shareholders are defined in Roche’s Articles of Incorporation<sup>15</sup>. 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 28 days before the date of the meeting.
- The rules on the issue of instructions to the independent proxy and rules on the electronic participation in the AGM are laid down in the corresponding invitation to the AGM and are not regulated in the Articles of Incorporation.

\*\* These figures indicate the actual length of meetings and do not include the directors’ extensive pre-meeting preparations and post-meeting follow-up activities.

<sup>14</sup> Remuneration Committee members recuse themselves from deliberations and decisions on matters that affect their interests.

<sup>15</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

## 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 4 March 2014, 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 144). 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<sup>16</sup>). The statutory auditors participated in 5 meetings of the Audit Committee in 2014.

The reports of statutory auditor on the Consolidated Financial Statements and on the Financial Statements can be found on pages 126 and 149, 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):

	2014	2013
	(millions of CHF)	
Auditing services	20.5	19.5
Audit-related services		
– Accounting	-	0.4
– Assurance	1.3	1.0
Tax services	1.2	1.3
Other services	0.7	0.5
<b>Total</b>	<b>23.7</b>	<b>22.7</b>

The statutory auditors are elected each year by the Annual General Meeting.

Auditing services are provided as legally required.

Audit-related services include assurance and accounting services provided by auditors but which are not necessarily provided by the statutory auditor. These services include audits of pension funds and employee benefit plans, internal control reviews which go beyond the legal requirements, and other attestation services, comfort letters, consents and consultation.

Tax services include services with respect to compliance, tax returns and tax advice except those services related to the audit of tax.

Other services include advice relating to process improvements, regulations and trainings.

The company has a formal policy governing the engagement of the statutory auditor for non-audit services. The policy prohibits certain services from being provided but permits certain other services up to limits agreed by the Audit Committee. Each potential non-audit service engagement is reviewed against this policy before any authority to proceed is given.

## 8 Relationship to the independent proxy

In recent years, BDO AG served as the independent proxy and for the first time at the Annual General Meeting on 4 March 2014, shareholders elected BDO AG as the independent proxy for the period from 2014 until the conclusion of the 2015 ordinary Annual General Meeting of Shareholders. BDO AG was paid in 2014 for its services according to expenditure totalling 22,421 Swiss francs (2013: 12,506 Swiss francs).

The rules on the issue of instructions to the independent proxy and rules on the electronic participation in the AGM are laid down in the corresponding invitation to the AGM and are not regulated in the articles of incorporation.

<sup>16</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

## 9 Information policy

- As provided by §34 of the Articles of Incorporation<sup>17</sup>, 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.<sup>18</sup>
- All relevant information and documents, including all media releases, investor updates<sup>19</sup> 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 30 61,  
fax +41 (0)61 688 41 96.
- 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.

Additional information, including details on specific contact persons, is available on the Internet.<sup>20</sup>

## 10 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<sup>21</sup> 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'. Starting in December 2013 a new compliance tool on Group level, the so-called Roche Group Code of Conduct Help & Advice Line, was introduced which strives to provide guidance in case of questions or

uncertainties about the interpretation of the Roche Group Code of Conduct and its reference documents. It furthermore will serve as a platform for ideas and suggestions concerning those documents.

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 management receives specific and concrete information about an alleged violation of the Roche Group Code of Conduct in one of certain pre-defined categories.<sup>22</sup> 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.

## 11 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).

<sup>17</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

<sup>18</sup> <http://www.roche.com/media.htm>

<sup>19</sup> <http://www.roche.com/investors.htm>

<sup>20</sup> <http://www.roche.com/investors/contacts.htm>

<sup>21</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/code\\_of\\_conduct.htm](http://www.roche.com/about_roche/corporate_governance/code_of_conduct.htm)

<sup>22</sup> [http://www.roche.com/corporate\\_responsibility/business\\_ethics/risk\\_management\\_and\\_compliance.htm](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 its entire people. Recognition of this forms the basis of our remuneration policy and system.

At Roche we strive to create new innovative 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 shareholders (until 2014: dividend increase for the 27<sup>th</sup> year in a row).

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 Stock-settled Stock Appreciation Rights (S-SARs) Restricted Stock Units (RSUs) and Performance Share Plan (PSP) 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
- A balanced mix of long- and short-term remuneration components
- Market competitiveness
- Fairness and transparency in remuneration decisions

## 2. Remuneration decision process

Each year the Remuneration Committee of Roche's Board of Directors meets at least twice and decides 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] Restricted Stock Units [RSUs] and policy decisions on pension benefits). The terms of Performance Share Plan (PSP) awards are decided annually by the Board of Directors, acting upon recommendations from the Remuneration Committee. In 2014 for the first time, total aggregate amounts which are based on these decisions were submitted to the General Meeting for approval implementing the 'Ordinance against excessive compensation in listed corporations' (Verordnung gegen übermäßige Vergütungen bei börsenkotierten Aktiengesellschaften [VegüV]). The General Meeting shall vote annually and with binding effect on the approval of the remuneration (that the Board of Directors has resolved) of the Board of Directors and the Corporate Executive Committee (for details see 4. and 5.).

The Remuneration Committee tracks market data on salaries at other leading global pharmaceuticals companies<sup>1</sup> and reports its findings to the full Board. The external consulting firm PricewaterhouseCoopers (PwC) assists Roche in performing market comparisons and in advising the Remuneration Committee. 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<sup>2</sup> and are also outlined in the sections below on the principles governing specific remuneration components.

<sup>1</sup> Peer set for 2014: Abbott Laboratories, AbbVie, Amgen, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck & Co., Novartis, Pfizer, Sanofi, Takeda (compared to 2013: without Becton Dickinson).

<sup>2</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

### 3. Summary of main activities in 2014

The following were the key developments and decisions in 2014:

- Over the past three years – which have proven decisive for the Performance Share Plan – the year end prices of non-voting equity securities (NES) increased by 70% and the value of shares by 61%. This has led to a 94.0 billion Swiss francs rise in the value of our company, from 138.5 billion Swiss francs to 232.5 billion Swiss francs, which represents an 68% increase.\*
- Roche shares rose from 247.40 Swiss francs to 267.75 Swiss francs over the past year and its non-voting equity securities from 249.20 Swiss francs to 269.90 Swiss francs. Roche's value rose in line by 17.8 billion Swiss francs, from 214.7 billion Swiss francs to 232.5 billion Swiss francs, over 2014.\*
- Dividends have risen every year steadily over the past 27 years, and a dividend of 6.728 billion Swiss francs was distributed in 2014.
- The Remuneration Committee (assisted by the consultancy of PwC) regularly tracked the base pay of Roche directors and members of the Corporate Executive Committee against market data on payments at other leading global pharmaceuticals companies (see footnote 1) and at other major Swiss companies<sup>3</sup>.
- The base salaries (fixed) paid to Corporate Executive Committee (CEC) members, except for Roland Diggelmann, remained unchanged in 2014.
- The bonus (variable) paid to CEC members for the 2014 financial year will consist entirely of cash payments (except in the case of CEO Severin Schwan) and reflects the sales growth and the increase of core earnings per share at Constant Exchange Rates (CER), and the progress of the product development 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 160).
- 2013, Restricted Stock Units (RSUs) – rights to receive non-voting equity securities after a three-year vesting period plus a value adjustment (being the amount equivalent to the sum of the dividend paid during the vesting period attributable to the number of non-voting equity securities for which an individual award has been granted) – were introduced as a new remuneration component partially replacing S-SARs and options. The value of S-SAR awards is reduced to 65% and the 35% balance will be awarded in the form of RSUs. 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.

- Performance Share Plan (PSP) awards (variable): For the PSP cycle 2012–2014 175% of the targeted NES will be awarded (2013: PSP 2011–2013: 175% of the targeted NES awarded). In the case of the PSP 2007–2009, PSP 2008–2010, PSP 2009–2011 and PSP 2010–2012 cycles, there were no pay-outs or awards of targeted NES. The plan's key performance metric for an award, the Total Shareholder Return (TSR), is calculated as a three-month moving average at constant CHF exchange rates (see 'E. Performance Share Plan [PSP]', page 161).
- In 2012 the Remuneration Committee decided that the Chief Executive Officer (CEO) and other CEC members must acquire Roche shares and/or non-voting equity securities (NES) equivalent to two annual base salaries (CEO) and one annual base salary (other CEC 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 164).

For all further details please refer to the following sections of this Remuneration Report<sup>4</sup>.

<sup>3</sup> ABB, Credit Suisse, Holcim, Nestlé, Swiss Re, UBS, Zurich Insurance Group, Actelion, Nobel Biocare, Sonova, Straumann, Synthes.

<sup>4</sup> See also in the Finance Report, Note 30 to the Roche Group Consolidated Financial Statements ('Related parties', page 111) and Note 6 to the Financial Statements of Roche Holding Ltd ('Board and Executive shareholdings', page 145).

\* Calculations on the basis of total number of shares and NES.

#### 4. Remuneration components

Base pay, bonuses, blocked non-voting equity securities (NES), awards of Stock-settled Stock Appreciation Rights (S-SARs), Restricted Stock Units (RSUs) and a Performance Share Plan (PSP) support the fundamental aims of Roche's remuneration policy. These remuneration components are linked to the employees' performance, 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 Chairmen of the Board's remuneration and the amount of each remuneration component paid to each member of the Corporate Executive Committee for the 2014 financial year.

As in the previous year, in 2015, the Board of Directors will separately submit the total aggregate bonuses of the Chairmen of the Board of Directors and of the Corporate Executive Committee to the General Meeting for the 2014 financial year for retrospectively binding approval.

The maximum amounts of the total aggregate remuneration (excluding bonuses) of the Board of Directors and of the Corporate Executive Committee for the period between the ordinary General Meeting 2015 and the ordinary General Meeting 2016 will be tabled in 2015 as in the previous year for the General Meeting's prospectively binding approval (see 5 B.).

##### A. Base pay

Base pay (cash payment) is determined for each position based on salary market data of other leading global pharmaceuticals companies (see footnote 1) and of other major Swiss companies (see footnote 3) and reflects individuals' abilities, experience and performance over time. Pay adjustments are likewise linked to individual performance and take into account prevailing market conditions and the company's overall financial situation.

The Remuneration Committee makes and reviews the final decision on the individual base pay 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 of value creation in a business year 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, product development 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.

In December at the end of a reporting year or in January following a reporting year the Remuneration Committee decides 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 and/or blocked shares).

##### 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)

In 2013 Restricted Stock Units (RSUs) – rights to receive non-voting equity securities and/or shares after a three year vesting period plus a value adjustment (being the amount equivalent to the sum of the dividend paid during the vesting period attributable to the number of non-voting equity securities for which an individual award has been granted) – were introduced as a new remuneration component partially replacing S-SARs. The value of S-SAR awards was reduced to 65% and the 35% balance is awarded in form of RSUs.

RSU awards are allocated individually at the Remuneration Committee's discretion and will be vested to the recipient after three years only. Thereafter, resulting non-voting equity securities may remain blocked for up to 10 years.

##### E. Performance Share Plan

The members of the Corporate Executive Committee and other members of senior management (currently some 150 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 (see footnote 1).

In 2014 there were three overlapping performance cycles (PSP 2012–2014, PSP 2013–2015 and PSP 2014–2016), of which PSP 2012–2014 closed on 31 December 2014.

The payment of the Performance Share Plan is 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/RSUs and PSP) relative to fixed base pay**

Criteria	Bonus	S-SARs/RSUs	PSP
Individual <b>target value</b> , assessed in consideration of the performance of competitors (see footnote 1) and the macro-economic development (in % relation to value of base pay)	Max. 100%	65% S-SARs 35% RSUs	33.33% (Based on annual base pay measured at 1 January of first year of cycle)
<b>Minimum</b> <b>Maximum</b> (in % relation to value of base pay)	0% 200% (Cash payment/ blocked NES/shares)	0% 150% (Value development determined by performance [plus a value adjustment for dividends] of NES after grant)	0% 66.66% (Value development determined by performance [starting with PSP 2013–2015 cycle plus a value adjustment for dividends] of NES after grant)
<b>Performance criteria</b>	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, product development 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
<b>Split in %</b>			
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

### A. Resolution

Each year the Remuneration Committee of Roche's Board of Directors decides the remuneration of Board members and members of Roche's Corporate Executive Committee (base pay, bonuses, S-SARs, RSUs and policy decisions on pension benefits). The terms of the Performance Share Plan are decided 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 (see footnote 1) and at major Swiss companies (see footnote 3) 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 and in the Articles of Incorporation after the approval of changes by the General Meeting on 4 March 2014<sup>5</sup> and are also outlined in the preceding sections of this report on the principles governing specific remuneration components.

The salaries and bonuses of the Chairman of the Board of Directors and members of the Corporate Executive Committee were decided by the Remuneration Committee, taking into account revisions to Roche's remuneration policy, market comparisons and management changes.

The remuneration of the Vice-Chairman 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 of PwC) tracked these cash payments of Roche directors against market data on directors' pay at other leading global pharmaceuticals companies (see footnote 1) and other major Swiss companies (see footnote 3).

### B. Policy on and procedure for submitting total Board and Executive remuneration for shareholder approval at the Annual General Meeting

Each year at the Annual General Meeting (AGM) shareholders approve the total remuneration decided by the Board of Directors' Remuneration Committee for the Board of Directors and the Corporate Executive Committee.

According to the approval at the AGM 2014, Roche has committed itself to obtaining separate and binding shareholder approvals of the total remuneration paid to the Board of Directors and to the Corporate Executive Committee as follows.

#### a) Retrospective approval

Total aggregate bonus amounts for the Corporate Executive Committee and the Chairman of the Board of Directors for the financial year just ended will be submitted *retrospectively* at each ordinary AGM for separate and binding approval.

#### b) Prospective approval

All other Board and Executive aggregate remuneration will be submitted *prospectively* by the Board of Directors for separate and binding approval for the period between two ordinary AGMs.

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 the 2014 financial year and include comparisons with the remuneration paid in the previous years.

#### 5.1 Remuneration of members of the Board of Directors.

In 2014 the members of the Board of Directors<sup>6</sup> received the fixed remuneration in cash payments shown in the 'A. Remuneration of members of the Board of Directors' table on page 157 for their Board activities. Roche paid legally required employer's contributions of total 155,431 Swiss francs to Swiss social security programmes providing retirement, disability and unemployment benefits (AHV/IV/ALV) for the members of the Board of Directors beside the legally required contributions separately stated for Christoph Franz and Franz B. Humer.

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 2015.

With the exception of Christoph Franz, Franz B. Humer (bonus in form of blocked shares) and Severin Schwan members of the Board of Directors were not awarded any shares, non-voting equity securities, S-SARs or RSUs for 2014.

In his capacity as a member of the International Advisory Council (IAC) of Chugai Pharmaceutical Co., Ltd. André Hoffmann received honoraria amounting to a total of 20,000 US dollars (18,298 Swiss francs). Arthur D. Levinson received payments for his consulting work and for serving on the Board at Genentech amounting to 124,862 US dollars (114,236 Swiss francs) until his resignation from the Board of Directors on 4 September 2014. William M. Burns received honoraria amounting to a total of 15,000 US dollars (13,724 Swiss francs) for serving as a member of the Board of directors of Chugai Pharmaceutical Co., Ltd. of which he retired in March 2014. Since October 2014, William M. Burns as a new member of the International Advisory Council (IAC) of Chugai Pharmaceutical Co., Ltd. received honoraria amounting to a total of 5,000 US dollars (4,574 Swiss francs).

<sup>5</sup> [http://www.roche.com/about\\_roche/corporate\\_governance/article\\_of\\_incorporation.htm](http://www.roche.com/about_roche/corporate_governance/article_of_incorporation.htm)

<sup>6</sup> For a list of members, their positions and their committee memberships and chairmanships see page 143.

## A. Remuneration of members of the Board of Directors

	2014			2013		
	Remuneration 2014 (in CHF)	Additional compensation 2014 for committee members/chairs <sup>7</sup> (in CHF)	Additional special compensation 2014 (in CHF)	Remuneration 2013 (in CHF)	Additional compensation 2013 for committee members/chairs <sup>7</sup> (in CHF)	Additional special compensation 2013 (in CHF)
Ch. Franz	(see 'B. Total remuneration paid to the Chairman of the Board of Directors')			300,000	30,000	
A. Hoffmann	400,000 <sup>8</sup>	–	18,298 (see page 156)	400,000 <sup>8</sup>	–	
P. Baschera	300,000	30,000		300,000	30,000	
J.I. Bell	300,000	30,000		300,000	30,000	
P. Bulcke	300,000	30,000		300,000	30,000	
D. Julius	300,000	60,000		300,000	60,000	
A. Oeri	300,000	60,000		300,000	60,000	
S. Schwan	(See '5.2 Highest total remuneration paid to Severin Schwan as a member of the Corporate Executive Committee', remuneration received in his primary function as CEO and reflected in total remuneration for the Corporate Executive Committee)			(See '5.2 Highest total remuneration paid to Severin Schwan as a member of the Corporate Executive Committee', remuneration received in his primary function as CEO and reflected in total remuneration for the Corporate Executive Committee)		
P.R. Voser	300,000	30,000		300,000	30,000	
B. Weder di Mauro	300,000	30,000		300,000	30,000	

## Remuneration of members of the Board of Directors retired in 2014

Franz B. Humer	3,853,045 <sup>9</sup>	–	3,137,418 <sup>10</sup>	8,728,814	50,000	–
W.M. Burns	75,000 <sup>11</sup>	–	18,298 (see page 156)	300,000	30,000	23,171
A.D. Levinson	225,000 <sup>12</sup>	22,500 <sup>12</sup>	114,236 (see page 156)	300,000	30,000	276,656
B. Gehrig	n.a.	n.a.	n.a.	72,220	–	–
L.J.R. de Vink	n.a.	n.a.	n.a.	54,200	–	–
<b>Total</b>	<b>6,653,045</b>	<b>292,500</b>	<b>3,288,250</b>	<b>12,255,234</b>	<b>410,000</b>	<b>299,827</b>

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.

9 Prorated remuneration for serving as Chairman of the Board for the period January to March 2014 amounting to CHF 1,000,000, bonus award of CHF 2,791,950 (in form of shares blocked for 10 years [calculation of number of shares based on the share price at the date of transfer in April 2015 after approval at the AGM 2015], calculation of value in consideration of reduction of value due to blocking period of 10 years [reduced market value: 55.839%] to be submitted for shareholder approval at the AGM 2015), employer contributions to employee stock purchase plan Roche Connect (prorated for the period January to March 2014) amounting to CHF 18,750, payments for tax consulting services (CHF 34,214) plus prorated remuneration Pension funds/MGB (Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung [employee profit-sharing foundation supplementing occupational pension benefits]) of CHF 939. Additionally, employer contribution to AHV/IV/ALV of CHF 1,152,438 (2013: CHF 379,434) was paid that does not form part of compensation.

10 Franz B. Humer received in his advisory capacity to the Presidium 3,000,000 Swiss francs. Said remuneration was included in the amount of total remuneration of the Board of Directors (ordinary General Meeting 2014 to ordinary General Meeting 2015) which shareholders approved at the AGM 2014. The total amount was paid in 2014. In 2014, Franz B. Humer received honoraria amounting to a total of USD 150,200 (CHF 137,418) for serving as a member of the International Advisory Council (IAC) and as a new member of the Board of Directors of Chugai Pharmaceutical Co., Ltd. starting 1 April 2014.

11 Prorated remuneration for the period January to March 2014.

12 Prorated remuneration for the period January to September 2014.

AUDITED

**B. Total remuneration paid to the Chairman of the Board of Directors**

As Chairman, Christoph Franz received total remuneration for 2014 as shown below. The Remuneration Committee's bonus proposal (adopted in late 2014) in respect of the 2014 financial year (payable in April 2015) will be put for shareholder binding vote at the 2015 ordinary Annual General Meeting (AGM).

Severin Schwan, executive member of the Board of Directors, received his remuneration in his primary function as CEO. It is reflected as the highest total remuneration paid to a member of the Corporate Executive Committee and included in the total amount paid to the Corporate Executive Committee.

**Total remuneration paid to the Chairman of the Board of Directors**

AUDITED	Ch. Franz as Chairman of the Board of Directors		Ch. Franz as Member of the Board of Directors
	2014 (in CHF)		2013 (in CHF) <sup>13</sup>
	Salary (in cash)	3,408,340*	See 'A. Remuneration of members of the Board of Directors', page 157
Bonus	558,390**		
Pension funds/MGB <sup>14</sup> /insurances	68,047		
<b>Total (value)</b>	<b>4,034,777<sup>15</sup></b>		

\* Prorated remuneration as member of the Board of Directors for the period March to December 2014 and as Chairman of the Board of Directors for the period March to December 2014.

\*\* Bonus award (in form of shares blocked for 10 years [calculation of number of shares based on the share price at the date of transfer in April 2015 after approval at the AGM 2015], calculation of value in consideration of reduction of value due to blocking period of 10 years [reduced market value: 55.839%] to be submitted for shareholder approval at the 2015 AGM).

**C. Stock-settled Stock Appreciation Rights (S-SARs)**

On 31 December 2014 Severin Schwan (being the only member of the Board of Directors holding S-SARs due to his position as CEO) and the members of the Corporate Executive Committee held Stock-settled Stock Appreciation Rights (S-SARs) as shown in the '10. S-SARs' table on page 167.

**E. Board remuneration subject to approval at the Annual General Meeting**

**a. Submission of the Chairmen's total aggregate bonuses for a binding vote at the Annual General Meeting**

Remuneration to the Chairman of the Board of Directors includes a bonus award of 558,390 Swiss francs in form of shares blocked for 10 years as shown above 'B. Total remuneration paid to the Chairman of the Board of Directors'. The Board of Directors will submit the Remuneration Committee's bonus proposal (adopted in late 2014) for the Chairman of the Board, Christoph Franz, in respect of the 2014 financial year (payable in April 2015) together with the bonus proposal adopted at the same time for the former Chairman of the Board, Franz B. Humer, in respect of the 2014 financial year (payable in April 2015) of 2,791,950 Swiss francs in form of shares blocked for 10 years, see 'A. Remuneration of members of the Board of Directors', page 157, footnote 9 as a total amount of 3,350,340 Swiss francs (in form of shares blocked for 10 years, excluding legally required employer's contributions to AHV/IV/ALV) for

**D. Total remuneration paid to the Board of Directors**

For the 2014 calendar year the members of the Board of Directors received remuneration including bonuses totalling 11,131,154 Swiss francs (2013: 12,965,060 Swiss francs), excluding additional employer's contribution paid to AHV/IV/ALV totalling 1,495,453 Swiss francs (2013: 579,927 Swiss francs) that does not form part of compensation. Aggregate: 12,626,607 Swiss francs (2013: 13,544,987 Swiss francs).

There are no loans or credits granted to the members of the Board of Directors.

No additional remuneration was paid.

<sup>13</sup> For detailed calculation of the remuneration for 2013 and 2012 see Annual Report 2013, pages 135–136.

<sup>14</sup> MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).

<sup>15</sup> Additionally, employer contribution to AHV/IV/ALV of CHF 187,584 (2013: CHF 19,326) was paid that does not form part of compensation.

the shareholder binding vote to the 2015 ordinary Annual General Meeting (AGM).

### b. Submission of the Board's total aggregate future remuneration for a binding shareholder vote

The Board of Directors proposes that the 2015 ordinary AGM approve Board remuneration totalling not more than 10,000,000 Swiss francs (excluding legally required employer's contributions to AHV/IV/ALV and excluding bonuses) for the period ending at the 2016 ordinary AGM (at the ordinary AGM 2014 approved remuneration for the period ordinary AGM 2014 to ordinary AGM 2015 totalling not more than 11,000,000 Swiss francs [excluding bonuses]). For comparison from 2013 ordinary AGM to ordinary 2014 AGM actual remuneration amounted to 10,046,691 Swiss francs, [excluding legally required employer's contributions to AHV/IV/ALV and excluding bonuses].

### 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 152 to 156 of this Remuneration Report.

Severin Schwan, executive member of the Board of Directors, received his remuneration in his primary function as CEO. It is reflected as the highest total remuneration paid to a member of the Corporate Executive Committee (see below) and included in the total amount paid to the Corporate Executive Committee (see 'H. Total remuneration paid to the members of the Corporate Executive Committee', page 163).

### Highest total remuneration paid to Severin Schwan as a member of the Corporate Executive Committee

	2014 (in CHF)	2013 <sup>16</sup> (in CHF)	2012 (in CHF)
Salary	4,000,000	4,000,000	4,000,000
S-SARs (Grant value according to trinomial model for American call options <sup>17</sup> )	2,600,131	2,600,151	4,000,000
RSUs (Restricted Stock Units)	781,694 <sup>18*</sup>	781,687*	
Pension funds/MGB <sup>19</sup> /insurances	553,246	545,416	747,229
Roche Connect	100,008	100,008	100,008
Subtotal	8,035,079	8,027,262	8,847,237
Bonus			
– Blocked non-voting equity securities/shares	1,340,136 <sup>20*</sup>	1,116,780*	2,512,755*
PSP	2,574,419 <sup>21</sup>	2,736,881	1,137,058
<b>Total (value)</b>	<b>11,985,408<sup>22</sup></b>	<b>11,916,938</b>	<b>12,537,385</b>

\* Calculation of value of non-voting equity securities/shares in consideration of reduction of value due to blocking period of 10 years (reduced market value: 55.839%).

16 For detailed calculation of the remuneration for 2013 and 2012 see Annual Report 2013, page 137.

17 Number of S-SARs 2014: 54,453, grant value according to the trinomial model for American call options: CHF 47.75. 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 160.

18 Number of RSUs 2014: 5,551, grant value CHF 252.19 (NES average market price over a 90 days period prior to the grant date on 6 March 2014) per RSU, calculation of value in consideration of reduction of value due to an additional blocking period of 10 years (reduced market value: 55.839%).

19 MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).

20 Shares blocked for 10 years (calculation of number of shares based on the share price at the date of transfer in April 2015 after approval at the AGM 2015), calculation of value in consideration of reduction of value due to blocking period of 10 years (reduced market value: 55.839%).

21 Total estimated value for 2014: PSP 2012–2014: Award of 175% of the originally targeted NES awarded for 2012–2014 (15,888 NES in total), spread over the relevant period of time i.e. 1/3 for the year 2014, value calculated using the year-end price as at 31 December 2014, CHF 269.90 per non-voting equity security (NES). PSP 2013–2015 and 2014–2016: Estimated value calculated using the year-end price as at 31 December 2014, CHF 269.90 per non-voting equity security (NES), based on the number of NES originally targeted (7,314 NES and 5,413 NES, respectively) subject to changes in the number and value of NES awardable under the plan on 31 December 2015 and 31 December 2016, respectively, and spread over the relevant period of time, i.e. 1/3 for the year 2014. The Board of Directors will vote on the actual allocation of originally targeted NES on 31 December 2015 and 31 December 2016, respectively, according to the TSR achieved.

22 Includes an annual expense allowance (CHF 30,000) and payments for tax consulting services (CHF 5,774). Additionally, employer contribution to AHV/IV/ALV of CHF 1,261,596 (2013: CHF 1,284,456) was paid that does not form part of compensation.

AUDITED

## Remuneration of the remaining members of the Corporate Executive Committee

### A. Base pay (in CHF)

AUDITED	Annual salary	Annual salary	Annual salary
	2014	2013	2012
S. Ayyoubi	1,200,000	1,200,000	1,200,000
R. Diggelmann	1,150,000	1,000,000	647,750
A. Hippe	2,100,000*	2,100,000*	2,100,000*
G.A. Keller	1,500,000	1,500,000	1,500,000
D. O'Day	2,000,000	2,000,000	1,575,000
<b>Total</b>	<b>7,950,000</b>	<b>7,800,000</b>	<b>7,022,750</b>

\* 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 2014 based on the performance 2014 against the agreed objectives. The total aggregate amount of bonuses will be brought forward for a binding vote by the Annual General Meeting 2015.

Except for Severin Schwan, all members of the Corporate Executive Committee will receive the bonus 2014 as a 100% cash payment which is due in April 2015. Severin Schwan will receive the bonus 2014 in form of Roche shares which are blocked for 10 years. Bonus payment is due in April 2015 (see page 159).

### Bonus

AUDITED	Bonus	Bonus	Bonus
	for 2014	for 2013	for 2012
	Total	Total	Total
	(in CHF)	(in CHF)	(in CHF)
S. Ayyoubi	1,500,000	1,400,000	1,700,000
R. Diggelmann	1,300,000	1,200,000	600,000
A. Hippe	2,000,000	1,900,000	2,200,000
G.A. Keller	1,300,000	1,200,000	1,500,000
D. O'Day	3,000,000	2,500,000	2,300,000
<b>Total</b>	<b>9,100,000</b>	<b>8,200,000</b>	<b>8,300,000</b>

### C. Stock-settled Stock Appreciation Rights (S-SARs)

The S-SARs shown in the '10. S-SARs' table on page 167 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).<sup>23</sup>

The numbers of S-SARs, the strike prices, expiry dates and grant values for S-SARs are shown in the '10. S-SARs' table on page 167. The numbers of S-SARs as calculated at the time of issue have been entered as values in the table on page 161 and on page 159.<sup>24</sup>

<sup>23</sup> 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](http://www.roche.com/trinomial_model.pdf)

<sup>24</sup> See strike prices in table '10. S-SARs', page 167.

**Stock-settled Stock Appreciation Rights (S-SARs)**

	S-SARs 2014 (value in CHF)	S-SARs 2013 (value in CHF)	S-SARs 2012 (value in CHF)	AUDITED
S. Ayyoubi	780,140	780,024	1,200,000	
R. Diggelmann	780,140	650,256	366,150	
A. Hippe	1,040,138	1,040,104	1,600,000	
G.A. Keller	975,246	975,166	1,500,000	
D. O'Day	1,300,280	1,300,185	1,300,000	
<b>Total</b>	<b>4,875,944</b>	<b>4,745,735</b>	<b>5,966,150</b>	

**D. Restricted Stock Units (RSUs)**

2013, Restricted Stock Units (RSUs) – rights to receive non-voting equity securities after a three year vesting period plus a value adjustment (being the amount equivalent to the sum of the dividend paid during the vesting period attributable to the number of non-voting equity securities for which an individual award has been granted) – were introduced as a new remuneration

component partially replacing S-SARs. The value of S-SAR awards was reduced to 65% and the 35% balance is awarded in the form of RSUs.

RSU awards are allocated individually at the Remuneration Committee's discretion and will be vested to the recipient after three years only. Thereafter, resulting non-voting equity securities may remain blocked for up to 10 years.

**Restricted Stock Units (RSUs)**

	RSUs 2014 (number)	RSUs 2014 (value in CHF)	RSUs 2013 (number)	RSUs 2013 (value in CHF)	AUDITED
S. Ayyoubi	1,665	419,896	2,107	332,668*	
R. Diggelmann	1,665	419,896	1,755	349,824	
A. Hippe	2,220	312,621**	2,809	559,918	
G.A. Keller	2,081	524,807	2,633	524,836	
D. O'Day	2,775	699,827	3,511	699,848	
<b>Total</b>	<b>10,406</b>	<b>2,377,047</b>	<b>12,815</b>	<b>2,467,094</b>	

Calculation of value 2013: Number of RSUs 2013 multiplied by grant value of CHF 199.33 (NES average market price over a 90 days period prior grant date on 7 March 2013) per RSU (\* calculation of value in consideration of reduction of value due to an additional blocking period of 4 years, reduced market value: 79.209%).

Calculation of value 2014: Number of RSUs 2014 multiplied by grant value of CHF 252.19 (NES average market price over a 90 days period prior grant date on 6 March 2014) per RSU (\*\* calculation of value in consideration of reduction of value due to an additional blocking period of 10 years, reduced market value: 55.839%).

**E. Performance Share Plan (PSP)**

The members of the Corporate Executive Committee and other members of senior management (currently some 150 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 2014 there were thus three cycles in progress (PSP 2012–2014, PSP 2013–2015 and PSP 2014–2016.), whereas PSP 2012–2014 closed on 31 December 2014 with 175% of the targeted NES awarded (2013: PSP 2011–2013: 175% of the targeted NES awarded). In the previous years PSP

2007–2009, PSP 2008–2010, PSP 2009–2011 and PSP 2010–2012 closed 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 peer companies<sup>25</sup>. 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

<sup>25</sup> See footnote 1, page 152.

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 (starting with PSP 2013–2015 cycle plus a value adjustment being the amount equivalent to the sum of the dividend paid during the vesting period attributable to the number of non-voting equity securities for which an individual award has been granted) 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.

In 2014 NES were reserved under the plan for members of the Corporate Executive Committee as shown in the table below and on page 159. The Board of Directors will decide on the actual level of NES or cash equivalent awards for the cycles 2013–2015 and 2014–2016 after the close of the 2015 and 2016 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 2012–2014 cycle (based on a three-month average) with distributed dividends totalling 18.933 billion Swiss francs (2014: 6.728 billion Swiss francs; 2013: 6.340 billion Swiss francs; 2012: 5.865 billion Swiss francs), the TSR of the Roche securities (NES and shares) ranked 5<sup>th</sup>, compared with its peer set of companies operating in the same industry. Therefore, according to the terms of the plan, the participants received 175% of the originally targeted NES (see table below and on page 159 for details).

### Performance Share Plan (PSP)

AUDITED	2014 <sup>26</sup>		2014	2013	2012		
	Target number of NES for PSP 2014–2016	Target number of NES for PSP 2013–2015	Awards of 175% of targeted number of NES for PSP 2012–2014	Total estimated value of PSP awards (2012–2014, 2013–2015 and 2014–2016) (value in CHF)	NES awarded in 2014 for PSP 2012–2014 (value in CHF)	NES awarded in 2013 for PSP 2011–2013 (value in CHF)	No NES awarded in 2012 for PSP 2010–2012 (value in CHF)
S. Ayyoubi	1,624	2,194	4,765	772,206	428,714	412,592	–
R. Diggelmann	1,353	1,828	1,817	449,608	163,424	151,181	–
A. Hippe	2,165	2,925	6,354	1,029,601	571,671	412,592	–
G.A. Keller	2,030	2,742	5,957	965,252	535,931	515,595	–
D. O'Day	2,706	3,657	5,163	1,036,911	464,453	343,813	–
<b>Total</b>	<b>9,878</b>	<b>13,346</b>	<b>24,056</b>	<b>4,253,579</b>	<b>2,164,193</b>	<b>1,835,773</b>	–

### F. Indirect benefits

Employer contributions made in 2014 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 (employer contributions)' table on page 163 and employer contributions as shown on page 159.

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.

<sup>26</sup> Total estimated value for 2014: PSP 2012–2014: Award of 175% of the originally targeted NES awarded for 2012–2014, spread over the relevant period of time i.e. 1/3 for the year 2014, value calculated using the year-end price as at 31 December 2014, CHF 269.90 per non-voting equity security (NES). PSP 2013–2015 and 2014–2016: Estimated value calculated using the year-end price as at 31 December 2014, CHF 269.90 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 2015 and 31 December 2016, respectively, and spread over the relevant period of time, i.e. 1/3 for the year 2014. The Board of Directors will vote on the actual allocation of originally targeted NES on 31 December 2015 and 31 December 2016, respectively, according to the TSR achieved.

**Indirect benefits (employer contributions)**

	2014				2013			
	Pension funds/ MGB <sup>27</sup> / insurances (in CHF)	AHV/IV/ ALV <sup>28</sup> (in CHF)	Roche Connect (in CHF)	Payments for tax consulting services (in CHF)	Pension funds/ MGB <sup>27</sup> / insurances (in CHF)	AHV/IV/ ALV <sup>28</sup> (in CHF)	Roche Connect (in CHF)	Payments for tax consulting services (in CHF)
S. Ayyoubi	90,567	561,427	15,000	2,908	433,257	524,925	10,000	1,620
R. Diggelmann	303,828	160,112	-	-	303,256	84,764	-	1,538
A. Hippe	297,829	326,154	39,996	19,488	298,471	255,820	39,996	23,607
G.A. Keller	439,540	468,787	37,500	-	585,795	437,362	37,500	-
D. O'Day	297,351	619,852	49,992	101,534	297,320	405,781	34,372	21,800
<b>Total</b>	<b>1,429,115</b>	<b>2,136,332</b>	<b>142,488</b>	<b>123,930</b>	<b>1,918,099</b>	<b>1,708,652</b>	<b>121,868</b>	<b>48,565</b>

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**G. Other remuneration, emoluments and loans**

Members of the Corporate Executive Committee additionally receive annual expense allowances of 30,000 Swiss francs, totalling 180,000 Swiss francs. Based on contractual obligations, in 2014, Roche paid to individual members of the Corporate Executive Committee for their children's schooling costs and foreign tax obligation totalling 516,817 Swiss francs. Expense allowances and aforementioned additional payments are included in the total remuneration to members of the Corporate Executive Committee.

In 2014, there are no loans or credits granted to the members of the Corporate Executive Committee.

In 2014 pensions totalling 2,049,180 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. There are no change-of-control clauses in the employment contracts.

**H. Total remuneration paid to the members of the Corporate Executive Committee**

For the 2014 calendar year, the members of the Corporate Executive Committee received remuneration including bonuses totalling 42,904,327 Swiss francs (2013: 41,799,001 Swiss francs) excluding additional employer's contribution paid to AHV/IV/ALV totalling 3,397,928 Swiss francs (2013: 2,993,108 Swiss francs) that does not form part of compensation. Aggregate: 46,302,255 Swiss francs (2013: 44,792,108 Swiss francs).

No additional remuneration other than the above mentioned payments was paid to current or former members of the Corporate Executive Committee.

**I. Executive remuneration subject to approval at the Annual General Meeting****a. Submission of Executive total aggregate bonuses for a binding vote at the Annual General Meeting**

The Board of Directors proposes awarding the members of the Corporate Executive Committee bonuses totalling 10,440,136 Swiss francs in respect of the 2014 financial year (2013: 9,316,780 Swiss francs) excluding legally required employer's contributions to AHV/IV/ALV and will submit this proposed total amount to the ordinary Annual General Meeting (AGM) 2014 for a binding vote.

**b. Submission of Executive total future aggregate remuneration for a binding shareholder vote**

The Board of Directors proposes that the 2015 ordinary AGM approve remuneration for the Corporate Executive Committee totalling not more than 37,000,000 Swiss francs (excluding legally required employer's contributions to AHV/IV/ALV and excluding bonuses) for the period ending at the 2016 ordinary AGM (at the ordinary AGM 2014 approved remuneration for the period ordinary AGM 2014 to ordinary AGM 2015 totalling not more than 36,000,000 Swiss francs [excluding bonuses]; for comparison, from 2013 ordinary AGM to ordinary 2014 AGM remuneration amounted to 32,094,464 Swiss francs, [excluding legally required employer's contributions to AHV/IV/ALV and excluding bonuses]).

The amount of Executive total future aggregate remuneration is composed of base pay, long-term incentives (S-SARs and RSUs, calculated at grant value without considering reductions of value due to blocking periods if applicable) and PSP (calculated at the time of reservation of non-voting equity securities and taking into

<sup>27</sup> MGB: Stiftung der F. Hoffmann-La Roche AG für Mitarbeiter-Gewinnbeteiligung (employee profit-sharing foundation supplementing occupational pension benefits).

<sup>28</sup> AHV/IV/ALV: Swiss social security programmes providing retirement, disability and unemployment benefits.

account their potential to double), contributions to pension benefits (excluding legally required employer’s contributions to AHV/IV/ALV) as well as contributions for expenses, payments for tax consulting services and Roche Connect.

**6. Alignment of interests between managers and shareholders/holders of non-voting equity securities**

The S-SARs, RSUs 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.

**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 and RSUs 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 and RSUs 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	Value
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 2014 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 30 to the Roche Group Consolidated Financial Statements ('Related

parties', page 111) and in Note 4 to the Financial Statements of Roche Holding Ltd ('Significant shareholders', page 144). In addition, as at 31 December 2014 (as at 31 December 2013, respectively) 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 'Security holdings' below and on page 166.

### Security holdings

	(as at 31 December 2014)				(as at 31 December 2013)			
	Shares (number)	NES (number)	Close relatives' security holdings (number/ type)	Others (number)	Shares (number)	NES (number)	Close relatives' security holdings (number/ type)	Others (number)
<b>Board of Directors</b>								
Ch. Franz	–	350	–	–	–	350	–	–
A. Hoffmann	–*	200	–	–	–*	200	–	–
P. Baschera	1	4,600	–	–	1	4,600	–	–
J.I. Bell	300	1,647	–	–	300	1,647	–	–
P. Bulcke	–	1,350	–	–	–	1,350	–	–
D. Julius	350	2,050	–	–	350	2,050	–	–
A. Oeri	–*	187,793	–	–	–*	187,793	–	–
S. Schwan	See 'Security holdings' Corporate Executive Committee on page 166				See 'Security holdings' Corporate Executive Committee on page 166			
P.R. Voser	–	3,600	–	–	–	3,600	–	–
B. Weder di Mauro	200	800	–	–	200	800	–	–
<b>In 2014 retired Directors of the Board</b>								
F.B. Humer	n.a.	n.a.	n.a.	n.a.	7,492	67,725	–	–
W.M. Burns	n.a.	n.a.	n.a.	n.a.	3	84,735	–	S-SARs see Annual Report 2013, page 144
A.D. Levinson	n.a.	n.a.	n.a.	n.a.	–	–	–	–
<b>Total</b>	<b>851</b>	<b>202,390</b>	<b>–</b>	<b>–</b>	<b>8,346</b>	<b>354,850</b>	<b>–</b>	<b>–</b>

\* Shares held by the shareholder group with pooled voting rights not listed.

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**Security holdings**

		(as at 31 December 2014)				(as at 31 December 2013)			
AUDITED	Corporate Executive Committee	Shares	NES	Close relatives' security holdings	Others	Shares	NES	Close relatives' security holdings	Others
		(number)	(number)	(number/type)	(number)	(number)	(number)	(number/type)	(number)
	S. Schwan	91,279	14,065	-	S-SARs/RSUs see 10/11	10,000	68,518	-	S-SARs/RSUs see 10/11
	S. Ayyoubi	8,104	12,923	-	S-SARs/RSUs see 10/11	3	16,032	-	S-SARs/RSUs see 10/11
	R. Diggelmann	-	853	-	S-SARs/RSUs see 10/11	-	836	-	S-SARs/RSUs see 10/11
	A. Hippe	6,970	8,184	-	S-SARs/RSUs see 10/11	2,885	6,851	-	S-SARs/RSUs see 10/11
	G.A. Keller	19,192	7,638	1,100 shares	S-SARs/RSUs see 10/11	2,153	21,413	1,100 shares	S-SARs/RSUs see 10/11
	D. O'Day	3	7,149	-	S-SARs/RSUs see 10/11	3	6,177	-	S-SARs/RSUs see 10/11
	<b>Total</b>	<b>125,548</b>	<b>50,812</b>	<b>1,100 shares</b>		<b>15,044</b>	<b>119,827</b>	<b>1,100 shares</b>	

## 10. S-SARs

	Number of S-SARs held by current and former members of the Corporate Executive Committee on 31 December 2013							
	2014	2013	2012	2011	2010	2009	2008	Total
<b>Corporate Executive Committee</b>								
S. Schwan	54,453	71,472	163,869	-	-	-	-	289,794
S. Ayyoubi	16,338	21,441	49,161	-	-	-	-	86,940
R. Diggelmann	16,338	17,874	15,000	12,732	6,489 <sup>29</sup>	4,263 <sup>29</sup>	5,295 <sup>29</sup>	77,991
A. Hippe	21,783	28,590	65,547	-	-	-	-	115,920
G.A. Keller	20,424	26,805	61,452	-	-	-	-	108,681
D. O'Day	27,231	35,739	53,259	-	-	-	-	116,229
<b>Total</b>	<b>156,567</b>	<b>201,921</b>	<b>408,288</b>	<b>12,732</b>	<b>6,489</b>	<b>4,263</b>	<b>5,295</b>	<b>795,555</b>
Strike price (CHF)	263.20	214.00	157.50	140.10	175.50	145.40	188.90	
Market price per NES on 31 December 2014 (CHF)	269.90							
Expiry date	6.3.2021	7.3.2020	8.3.2019	28.2.2018	4.2.2017	5.2.2016	25.7.2015	
Grant value per S-SAR (CHF)	47.75	36.38*	24.41*	15.38*	23.05*	20.30*	23.61*	
Since 1.1.2012: – Trinomial model for American call options								
* Values according to corresponding annual reports								

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29 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.

## 11. Restricted Stock Units (RSUs)

Number of RSUs held by members of the Corporate Executive Committee on 31 December 2014	RSUs 2014 (number)	RSUs 2013 (number)
S. Schwan	5,551	7,023
S. Ayyoubi	1,665	2,107
R. Diggelmann	1,665	1,755
A. Hippe	2,220	2,809
G.A. Keller	2,081	2,633
D. O'Day	2,775	3,511
<b>Total</b>	<b>15,957</b>	<b>19,838</b>
<b>Grant value</b>	CHF 252.19 (NES average market price over a 90 days period prior grant date on 6 March 2014) per RSU	CHF 199.33 (NES average market price over a 90 days period prior grant date on 7 March 2013) per RSU

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# Report of the Statutory Auditor to the General Meeting of Roche Holding Ltd, Basel

We have audited the accompanying remuneration report dated 26 January 2015 of Roche Holding Ltd for the year ended 31 December 2014. The audit was limited to the information according to articles 14–16 of the Ordinance against Excessive compensation in Stock Exchange Listed Companies (Ordinance) contained in the sections marked with a blue line, including the respective footnotes, on pages 152 to 167 of the remuneration report.

## Responsibility of the Board of Directors

The Board of Directors is responsible for the preparation and overall fair presentation of the remuneration report in accordance with Swiss law and the Ordinance against Excessive compensation in Stock Exchange Listed Companies. The Board of Directors is also responsible for designing the remuneration system and defining individual remuneration packages.

## Auditor's Responsibility

Our responsibility is to express an opinion on the accompanying remuneration report. We conducted our audit in accordance with Swiss Auditing Standards. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the remuneration report complies with Swiss law and articles 14–16 of the Ordinance.

An audit involves performing procedures to obtain audit evidence on the disclosures made in the remuneration report with regard to compensation, loans and credits in accordance with articles 14–16 of the Ordinance. The procedures selected depend on the auditor's judgement, including the assessment of the risks of material misstatements in the remuneration report, whether due to fraud or error. This audit also includes evaluating the reasonableness of the methods applied to value components of remuneration, as well as assessing the overall presentation of the remuneration report.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our opinion.

## Opinion

In our opinion, the remuneration report for the year ended 31 December 2014 of Roche Holding Ltd complies with Swiss law and articles 14–16 of the Ordinance.



KPMG AG

Ian Starkey  
Licensed Audit Expert  
Auditor in Charge

François Rouiller  
Licensed Audit Expert

Basel, 26 January 2015





# Independent Assurance Report on the Roche Corporate Responsibility Reporting

To the Corporate Governance and Sustainability Committee of Roche Holding AG, Basel ('Roche').

We have been engaged to perform assurance procedures to provide limited assurance on the aspects of the 2014 corporate responsibility ('CR') reporting of Roche included in the Annual Report 2014 ('Report').

## Scope and subject matter

Our limited assurance engagement focused on the following data and information disclosed in the CR reporting of Roche and its consolidated subsidiaries for the year ended on December 31, 2014:

- the management of reporting processes with respect to the CR reporting in all material aspects and the preparation of Safety, Security, Health and Environmental protection ('SHE'), contributions and people key figures as well as the related control environment in relation to the data aggregation of these key figures;
- the materiality determination process of Roche at Group level according to the requirements of the GRI G4 guidelines and disclosed on pages 98 to 99 of the Report;
- the SHE key figures (including greenhouse gas emissions for scope 1 & 2 and scope 3 resulting from business travel) in the tables and graphs on pages 120 to 133 and people key figures disclosed on pages 108 to 115 of the Report;
- the consolidated data and information on the Roche Group level in relation to the contributions breakdown, disclosed on page 97 of the Report; and
- the people key figures disclosed on Roche's website within the section 'Non-Financial Reporting' under sub-section 'Performance'.

## Criteria

The management reporting processes with respect to the CR reporting and key figures were assessed against the internal policies and procedures as set forth in the following:

- the Roche Group internal CR 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 G4' published in 2013 by the Global Reporting Initiative (GRI);

- the Roche Group internal Corporate Reporting Manual, Version 2014.2 'Group Reporting Manual-Sustainability Reporting'; and
- the defined guidelines, by which SHE, people and contributions key figures are internally gathered, collated and aggregated;

The accuracy and completeness of CR 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 CR performance.

## Responsibility and methodology

The Roche Corporate Governance and Sustainability Committee is responsible for both the subject matter and the criteria as well as for selection, preparation and presentation of the selected information in accordance with the criteria. Our responsibility is to form an independent opinion, based on our limited assurance procedures, on whether anything has come to our attention to indicate that the identified CR information selected and contained in this report is not stated, in all material respects, in accordance with the reporting criteria.

We planned and performed our procedures in accordance with the International Standard on Assurance Engagements (ISAE 3000) 'Assurance engagements other than audits or reviews of historical financial information'. This standard requires that we comply with ethical requirements, plan and perform the assurance engagement to obtain limited assurance on the identified CR information.

For the subject matter for which we provide limited assurance, the nature, timing and extent of procedures for gathering sufficient appropriate evidence are deliberately limited relative to a reasonable assurance engagement. We have complied with the independence and other ethical requirements of the Code of Ethics for Professional Accountants issued by the International Ethics Standards Board for Accountants, which is founded on fundamental principles of integrity, objectivity, professional competence and due care, confidentiality and professional behaviour.

During 2014 we have not performed any tasks or services to Roche that would conflict with our independence, nor have we been responsible for the preparation of any part of the report; and therefore qualify as independent as defined by the Code of Ethics and applicable legal and regulatory requirements.

### Summary of work performed

Our assurance procedures included, amongst others, the following work:

- **Evaluation of the application of Roche Group guidelines**

Reviewing the application of the Roche Group internal corporate CR and contributions guidelines;

- **Site visits and management inquiry**

Visiting selected sites of Roche's Pharmaceuticals and Diagnostics divisions in the US, India, and Brazil. The selection was based on quantitative and qualitative criteria; Interviewing personnel responsible for internal CR reporting and data collection at the sites we visited and at the Roche Group level to determine the understanding and application of Roche's internal CR guidelines;

- **Assessment of the key figures**

Performing tests on a sample basis of evidence supporting selected SHE, contributions and people key figures (Roche accident rate, energy consumption, greenhouse gas emissions related to energy consumption, halogenated hydrocarbons, water, waste, contributions to healthcare institutions, patient organisations, public policy bodies, and philanthropic organisations, headcount/FTE data, labour practice information, training and hiring costs) concerning completeness, accuracy, adequacy and consistency;

- **Inspection of documentation and analysis of relevant policies and principles**

Inspecting relevant documentation on a sample basis, including Roche Group CR policies, management of reporting structures and documentation; Inspecting the principles of the Roche Materiality Process providing the definition for the development of its adherence to GRI's environmental, social and economic reporting requirements addressing the soundness of the identification process, determination of impacted stakeholders, peer and competition review, integration of relevant regulatory requirements, integration of key organisational values and objectives and report prioritisation of material aspects;

- **Assessment of the processes and data consolidation**

Reviewing the management of/and CR reporting processes for SHE, contributions and people key figures; and Assessing the consolidation process of data at Roche Group level.

We have not carried out any work on data reported for prior reporting periods, nor have we performed work in respect of projections and targets. We have not conducted any work on data other than outlined in the subject matter as defined above.

We believe that the evidence we have obtained is sufficient and appropriate to provide a basis for our assurance conclusions.

### Conclusion

Based on our work performed and described in this report on the identified CR Reporting 2014 nothing has come to our attention causing us to believe that in all material respects:

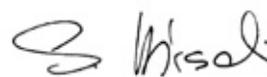
- the Roche Group internal CR reporting guidelines based on the GRI G4 Sustainability Reporting Guidelines as well as the CEFIC Guidelines are not applied;
- the Roche materiality determination process as disclosed does not adhere to the principles and guiding factors (e.g. soundness, stakeholder determination, peer review, relevance of regulatory environment, integration of key organisational values and objectives) defined with GRI G4;
- the internal reporting processes to collect and aggregate SHE, contributions and people data are not functioning as designed and provide an appropriate basis for its disclosure; and
- the CR information mentioned in the subject matter and disclosed within the CR reporting in the Roche Annual Report 2014 and on the referenced webpages is not stated, in accordance with the reporting criteria.

Zurich, 23 January 2015

PricewaterhouseCoopers AG



Christophe Bourgoïn



Stephan Hirschi

# More on the web

## 1 *Business Review*

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About Roche: [www.roche.com/about](http://www.roche.com/about)  
Our Business Priorities: [www.roche.com/priorities](http://www.roche.com/priorities)  
Investors: [www.roche.com/investors](http://www.roche.com/investors)  
Personalised Healthcare (PHC): [www.roche.com/personalised\\_healthcare](http://www.roche.com/personalised_healthcare)  
Sustainability: [www.roche.com/sustainability](http://www.roche.com/sustainability)

## 2 *Pharmaceuticals*

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Pharmaceuticals: [www.roche.com/products](http://www.roche.com/products)  
Pharmaceutical Supply Chain Initiative: [www.pharmaceuticalsupplychain.org](http://www.pharmaceuticalsupplychain.org)

## 3 *Diagnostics*

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Solutions for Diagnostics: [www.roche.com/products](http://www.roche.com/products)

## 4 *Innovation*

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Product Development Portfolio: [www.roche.com/pipeline](http://www.roche.com/pipeline)  
Clinical Trials: [www.roche.com/clinical\\_trials](http://www.roche.com/clinical_trials)  
Patient Safety: [www.roche.com/managing\\_medication\\_safety](http://www.roche.com/managing_medication_safety)  
Research & Development Locations: [www.roche.com/rnd\\_locations](http://www.roche.com/rnd_locations)  
Research Technologies: [www.roche.com/research\\_technologies](http://www.roche.com/research_technologies)  
Patents and Intellectual Property: [www.roche.com/patents](http://www.roche.com/patents)  
Global Standards: [www.roche.com/global\\_standards](http://www.roche.com/global_standards)  
Animal Welfare: [www.roche.com/animal\\_welfare](http://www.roche.com/animal_welfare)

## 5 *Access to Healthcare*

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Access to Healthcare: [www.roche.com/access\\_to\\_healthcare](http://www.roche.com/access_to_healthcare)  
Making Innovation Accessible: [www.roche.com/making\\_innovation\\_accessible](http://www.roche.com/making_innovation_accessible)  
Genentech Access Solutions: [www.GenentechAccessSolutions.com](http://www.GenentechAccessSolutions.com)  
Patient Organisations: [www.roche.com/patient-groups](http://www.roche.com/patient-groups)

## 6 *Responsible Business*

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Non-Financial Reporting: [www.roche.com/investors/reporting/non-financial-reporting](http://www.roche.com/investors/reporting/non-financial-reporting)  
 Materiality: [www.roche.com/materiality](http://www.roche.com/materiality)  
 Key Performance Indicators 2014: [www.roche.com/performance](http://www.roche.com/performance)  
 GRI G4 2014 Index: [www.roche.com/gri-index2014](http://www.roche.com/gri-index2014)  
 Reporting Centre: [www.roche.com/reporting](http://www.roche.com/reporting)  
 Stakeholder Engagement: [www.roche.com/stakeholder\\_engagement](http://www.roche.com/stakeholder_engagement)  
 Code of Conduct: [www.roche.com/code\\_of\\_conduct](http://www.roche.com/code_of_conduct)  
 Roche Supplier Code of Conduct: [www.roche.com/roche\\_supplier\\_code\\_of\\_conduct.pdf](http://www.roche.com/roche_supplier_code_of_conduct.pdf)  
 Business Partner Information: [www.roche.com/businesspartners](http://www.roche.com/businesspartners)  
 Suppliers and Service Providers: [www.roche.com/for\\_partnership/suppliers](http://www.roche.com/for_partnership/suppliers)  
 Responsibility Download Centre: [www.roche.com/positions\\_policies\\_downloads](http://www.roche.com/positions_policies_downloads)  
 Human Rights: [www.roche.com/human\\_rights](http://www.roche.com/human_rights)  
 Risk Management and Compliance: [www.roche.com/risk\\_management\\_and\\_compliance](http://www.roche.com/risk_management_and_compliance)  
 Business Integrity and Responsible Marketing: [www.roche.com/business\\_integrity\\_and\\_responsible\\_marketing](http://www.roche.com/business_integrity_and_responsible_marketing)  
 Anti-Counterfeiting: [www.roche.com/counterfeiting](http://www.roche.com/counterfeiting)

## 7 *People*

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Employees: [www.roche.com/about/people/employees.htm](http://www.roche.com/about/people/employees.htm)  
 Our People: [www.roche.com/people](http://www.roche.com/people)  
 Sustainability for Employees: [www.roche.com/for\\_employees](http://www.roche.com/for_employees)  
 Careers: <http://careers.roche.com>  
 Roche Group Employment Policy: [www.roche.com/employment\\_policy.pdf](http://www.roche.com/employment_policy.pdf)

## 8 *Environment and Community*

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 Our SHE Goals and Performance: [www.roche.com/our\\_she\\_goals\\_and\\_performance](http://www.roche.com/our_she_goals_and_performance)  
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## 9 *Corporate Governance and Remuneration Report*

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F. Hoffmann-La Roche Ltd  
4070 Basel, Switzerland  
Tel. +41 (0)61 688 11 11  
Fax +41 (0)61 691 93 91

**Media Office**

Group Communications  
4070 Basel, Switzerland  
Tel. +41 (0)61 688 88 88  
Fax +41 (0)61 688 27 75

**Investor Relations**

4070 Basel, Switzerland  
Tel. +41 (0)61 688 88 80  
Fax +41 (0)61 691 00 14

**Website**

[www.roche.com](http://www.roche.com)

**Corporate Sustainability Committee**

Tel. +41 (0)61 688 40 18  
E-mail: [corporate.sustainability@roche.com](mailto:corporate.sustainability@roche.com)

**To order publications**

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**Next Annual General Meeting:  
3 March 2015**

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