



**Annual General Meeting**  
**Roche Holding Ltd**  
**1 March 2016**

**Address by Severin Schwan**  
CEO of the Roche Group

**(Check against delivery.)**

Shareholders, Ladies and Gentlemen

I would also like to welcome you to this year's Annual General Meeting.

2015 was another extremely good year for your company. We again achieved strong financial results whilst – particularly important for the future of Roche – making significant strides in the development of a number of medicines.

Today I'd like to address two topics:

- Firstly: the full-year results for 2015 and the outlook for the current financial year.
- Secondly: our pipeline progress, especially in relation to multiple sclerosis. I want to show you what this condition is all about and what our new medicine ocrelizumab means for patients.

*Now to my first topic.* On 28 January we provided a detailed briefing on our full-year performance at our press conference. Allow me to summarise the key financial results.

## Operating results

In billions of CHF		2015	2014	Growth in %		
				CHF	local <sup>1</sup>	
<b>Sales</b>		<b>48.1</b>	47.5	+ 1	+ 5	
- Pharmaceuticals		37.3	36.7	+ 2	+ 5	
- Diagnostics		10.8	10.8	0	+ 6	
<b>Core operating profit</b>		<b>17.5</b>	17.6	- 1	+5	<b>+ 7*</b>
<b>Core earnings per share (CHF )</b>		<b>13.49</b>	14.29	- 6	+ 4	<b>+ 7*</b>

<sup>1</sup> At constant exchange rates.  
\* Excluding the one-time income from the sale of filgrastim rights in 2014.

We met all the targets we set ourselves at the start of 2015.

Sales in the Pharmaceuticals Division rose 5% at constant exchange rates. Our entire oncology portfolio continues to grow strongly; as does immunology.

The Diagnostics Division increased its sales by 6% at constant exchange rates – again well ahead of the market growth – thanks to consistently high demand in Professional Diagnostics.

Core earnings per share developed well with a rise of 4% at constant exchange rates. Excluding the one-time benefit (of CHF 428 million before taxes) related to the divestment of filgrastim rights in 2014, core earnings per share rose by 7%, significantly outperforming sales. On the same basis, core operating profit was also up 7%.

## Outlook

Outlook for 2016	
<b>Group sales growth<sup>1</sup></b>	Low- to mid-single digit growth
<b>Growth core earnings per share<sup>1</sup></b>	Ahead of sales growth
<b>Dividend</b>	Further dividend increase in Swiss francs

<sup>1</sup> At constant exchange rates.

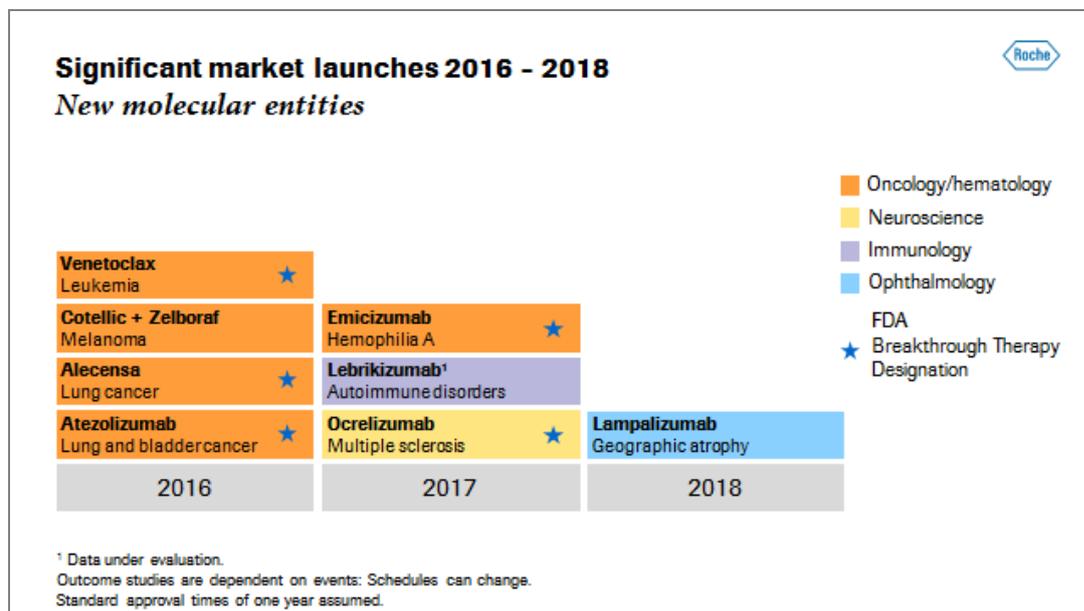
We expect to see further positive growth in 2016: We anticipate low- to mid-single digit sales growth (at constant exchange rates). And we are also aiming once again to grow core earnings per share (at constant exchange rates) faster than sales growth.

Given these expectations, Roche – as Mr Franz mentioned – also intends to continue its attractive dividend policy this year.

## Pipeline

We seek to develop medicines and diagnostics that mean tangible added value for physicians and patients alike in therapeutic areas with high unmet medical need.

This brings me to the *second topic* of my speech: Our pipeline progress, especially in relation to multiple sclerosis.



We expect to bring up to eight new medicines to market by 2018 – there have never been so many product launches over such a short period in the history of Roche.

This is the gratifying result of the extraordinarily positive clinical trial results we presented over the course of last year for novel compounds in hematology, cancer immunotherapy and multiple sclerosis (MS).

However the results are impressive not only in quantitative, but also in qualitative terms. The US Food and Drug Administration (FDA), for example, granted Breakthrough Therapy Designations to four of our medicines. This enables truly innovative medicines to be approved and made available to patients more quickly.

In the first two months of this year alone, these four medicines were joined by a further three. (As Mr Franz mentioned), a total of twelve of our investigational medicines have been granted this recognition – a record number of which we are proud.

One of these is ocrelizumab, which we expect to bring to market next year. The study results for this medicine were spectacular: Ocrelizumab represents a milestone in the treatment of multiple sclerosis. – Allow me to go into the disease and the success story of our new medicine in a little more detail.

## Ocrelizumab / multiple sclerosis

**Multiple sclerosis (MS)** 

- Chronic inflammatory disease of the brain and spinal cord
- Cannot be cured

**Possible symptoms**

- Vision and balance problems
- Speech difficulties
- Bladder function issues
- Muscle weakness/walking difficulties:

Around half of all MS patients will need a wheelchair at some stage



*Healthy brain*      *Advanced MS*

Multiple sclerosis (MS for short) is an autoimmune disorder, i.e. a disease in which our body's own natural defences – the immune system, which is supposed to protect us against pathogens such as bacteria and viruses – misguidedly attacks our own body.

In the case of MS, it is the central nervous system which is under attack, including the brain, our body's "control centre". MS usually begins in early adulthood (between 20 and 40) .

The symptoms vary from patient to patient – so there is no "typical" MS patient. That's also why MS is called the "disease with 1,000 faces". MS can affect everything connected with our brain and our nerves: How we see, speak, walk, think – in short, how we function.

Symptoms frequently include muscle weakness, muscle stiffness (known as spasticity), but also difficulties concentrating and remembering. Some people lose control over their bladder. Often MS patients ultimately face life in a wheelchair.

Vision problems of different kinds are another symptom. One of our colleagues (Sallie, MS patient) recalls how she woke up blind one day. Her vision returned after four months.

The worst aspect for many patients (and their relatives) is the fact that no one knows how the disease will develop – and that there is still no cure.

## History

**History**  
*Focus on T cells*



> 100 years ago	1950s	1980/90s	2004	2015
<b>Cause of MS</b> Inflammation in the central nervous system	<b>T cells</b> Focus of research	<b>B cells</b> New approach meets with scepticism  <b>T cells</b> First treatments	<b>B cells</b> Roche starts various MS trials  Setback leads to new insights	<b>Ocrelizumab</b> New hope for patients with multiple sclerosis
				

Although scientists have known for over a century that MS involves inflammation in the nervous system, we are only now really beginning to understand what happens here at the biological level.

Accordingly, for a long time it wasn't clear either how one might intervene therapeutically. In the 1950s, research started to focus on the T cells (known as the immune system's killer cells). It was understood that these good immune cells misguidedly attack the nerve fibres in the brain – and it didn't take long to convince experts that T cells were the beginning and the end for MS.

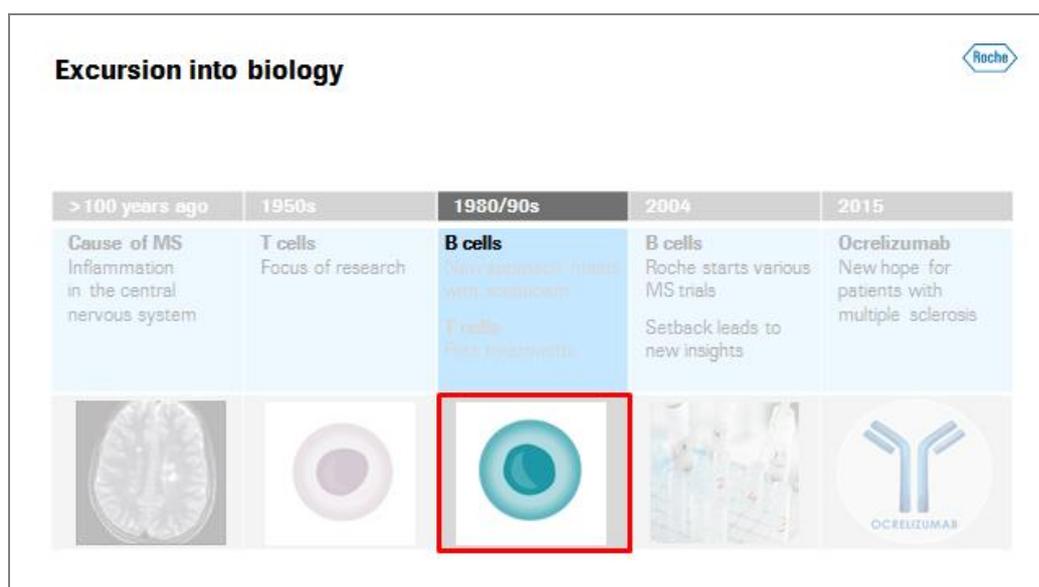
This theory appears to be well-founded, at least in part: Quite a few medicines (influencing the T cell function) have been brought to market over the last 20 years. But there was a problem: The first medicines approved for MS had a relatively benign safety profile, but they were not very efficacious. Newer medicines were more efficacious, but they were associated with potentially serious safety risks. For this reason, even today, many physicians tend to prescribe “weak” medicines at the beginning and only switch to “stronger” medication at a later stage (as the disease progresses) – a solution that doesn’t provide the patient with the most potential benefit. Consequently, there is a real need for new treatment options for MS.

It was not until later, during the 1980s, that a small group of physicians and researchers (one being Dr Hauser, whom you will see shortly in a video) became convinced that although T cells cause significant damage, the *B cells*, likewise a component of our immune system, may play a greater role in MS than had previously been assumed.

The medical community was highly sceptical of this approach. Around this time, our researchers in San Francisco, USA, also suspected B cells of playing a role in MS, and – in the face of much criticism from the scientific community – we (at Roche) were open to this idea and commenced our first proof-of-concept studies.

## B cells

Allow me to delve briefly into biology. Let’s first take a look at the B cell.



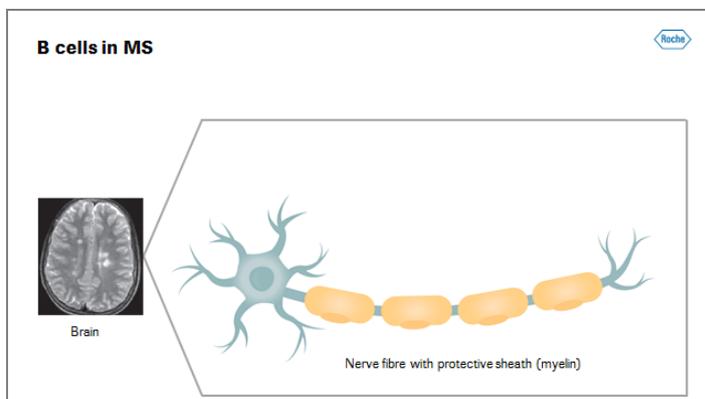
What does a B cell do, and what role does it play in MS? One could spend hours answering this question – I propose to give a much-simplified account of their function and focus on the most important aspects (for this story).

B cells (like T cells) are – as mentioned – part of our immune system. They perform different tasks – depending on their stage of development.

One “sort” of B cells is able to recognise specific “foreign invaders” (e.g. the measles virus) – it knows that this is something bad (and identifies it as an “enemy”). Now, to trigger an immune response, it “recruits” fragments of the invader and shows them (a bit like in a “wanted” poster) to the T cells. The T cells now know what they need to look for, and head off to fight the (wanted) invader.

## B cells in MS

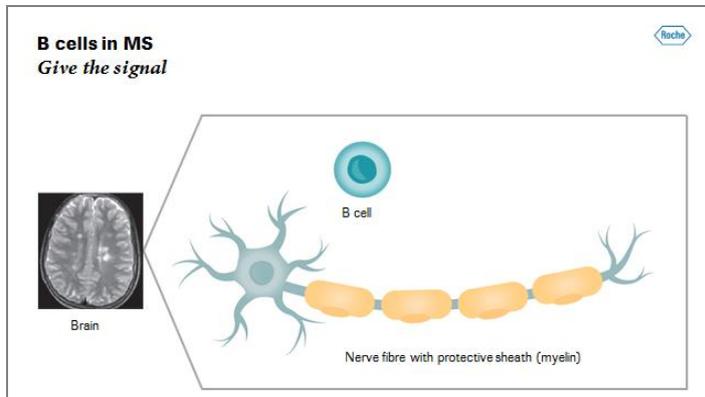
So what do these B cells do in MS? As I mentioned earlier, with MS, part of our immune system is misprogrammed, which means our immune system – the B cells and T cells – attack our own, healthy body. The awful thing is, this takes place in the brain.



Signals are sent from the brain (our “control centre”) via the spinal cord to the rest of our body (or are received from there); these are transmitted by different nerve fibres, which are encased in a protective, insulating sheath (*coloured orange in the picture*), much like the coating around electrical wires.

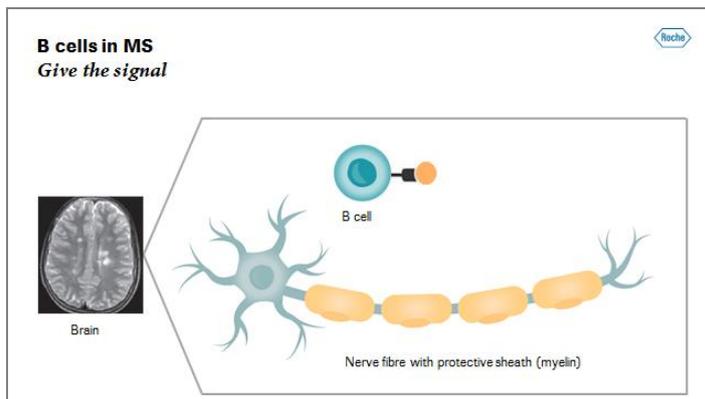
This protective sheath consists of a substance called myelin. It plays an important role in enabling the signals to pass rapidly (along the nerve fibres). If this protective sheath gets

damaged, the signal is transmitted slowly, or not at all (which can lead to the aforementioned symptoms). The B cells now come into play:

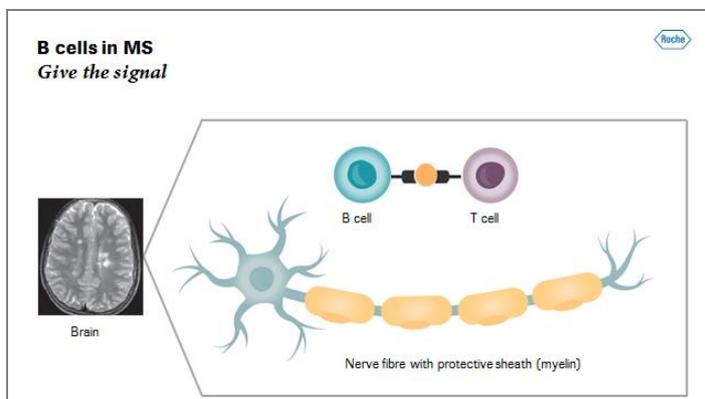


In MS, the B cells erroneously think that the protective sheath encasing the nerves in the brain is an invader.

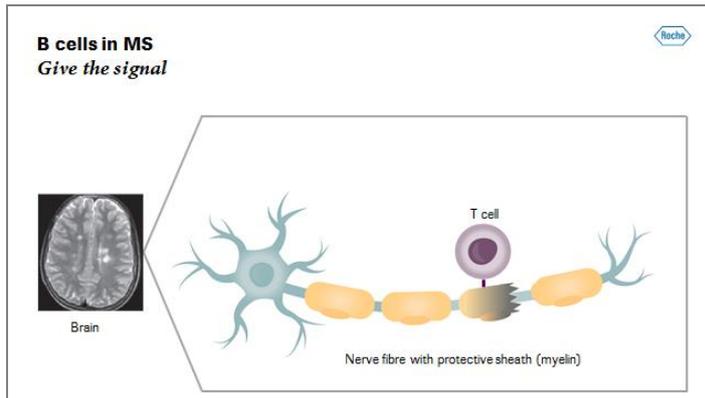
That's why they take (as described previously) a fragment of the protective sheath, using it like a "wanted" poster...



...and summon the T cells...



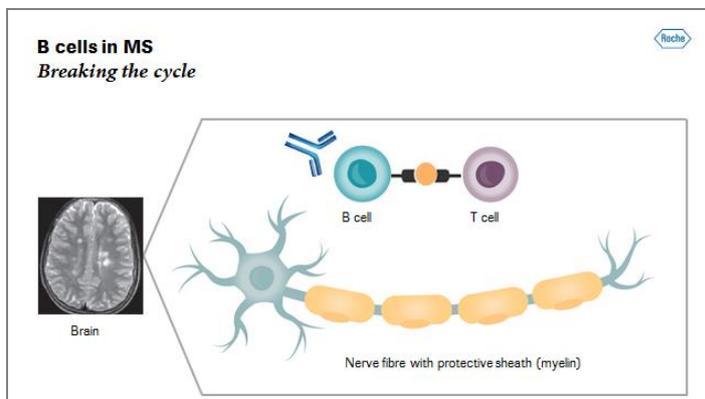
...giving the T cells the order to launch an attack...



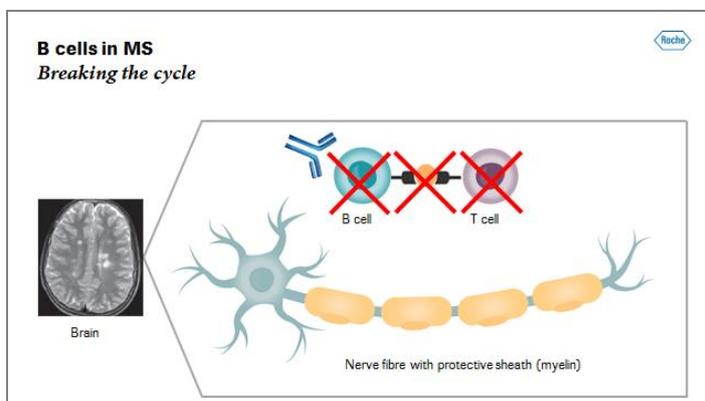
... the T cells then launch an attack on the protective sheath, which leads to inflammation.

With each MS attack, the same thing happens repeatedly: The misguided B cell encounters the protective sheath, thinks it's dealing with an invader, and summons the T cells. The whole process starts again.

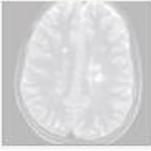
So one of the scientific hypotheses was: If we could only (with the aid of an antibody) decimate these misprogrammed B cells, ...



...we could break the vicious cycle.



## Following the science

Following the science 				
> 100 years ago	1950s	1980/90s	2004	2015
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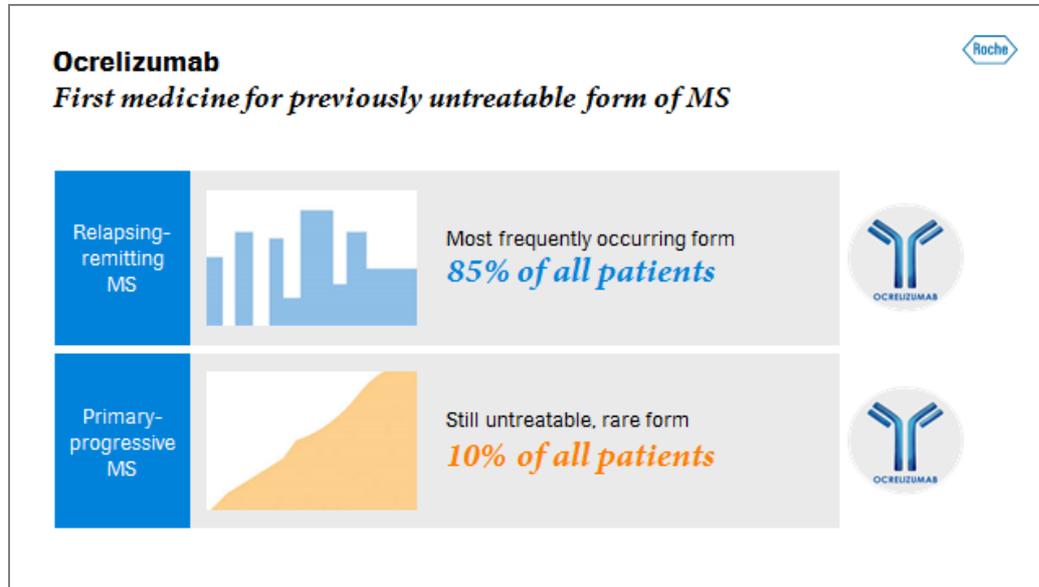
We started our first proof-of-concept MS studies in 2004 and have been pursuing this controversial hypothesis for over a decade since. We have also invested a great deal, not just in a small trial but also in various large-scale trials.

We have faced setbacks and learned from them. We have taken on (as Roche has done so often in the past) a comparatively high level of risk – based on our conviction that we were doing the right thing for patients.

Last year, it all came together: The study data for our new compound ocrelizumab were ready and the results we presented to the scientific community – as indicated earlier – met with great enthusiasm.

The data prove that ocrelizumab is not only highly effective, it also has a good safety profile. – So this would seem to prove that B cells play a bigger role in MS than was commonly thought to be the case.

## Ocrelizumab



The study results available to us show that ocrelizumab is effective in two (of the three) forms of MS (and thus in 95% of all patients): the medicine can be used to treat both the relapsing-remitting form of the disease – the most frequently encountered type of MS in which the symptoms suddenly come and go – but also in cases where the patient’s condition progressively deteriorates from the outset.

One in ten patients suffers from the second form of MS, which was untreatable up to now. Once ocrelizumab is approved, for the first time these patients too would have a treatment option available to them.

Ocrelizumab has another important advantage: It only has to be administered to patients twice a year (as an infusion).

I would now like to show you a short video about what ocrelizumab means for MS patients and for their families. It features an American lady called Beth, who gives an account of her experiences.

*(Video)*

Ladies and Gentlemen

Ocrelizumab illustrates perfectly, what sets Roche apart from other healthcare companies.

*Firstly:* Our strategy is clearly focused on innovation for patients. We are dedicated to developing better diagnostic tools and medicines. That is where our strengths lie. Put another way, we are not active in other areas such as OTC (prescription-free medicines) or generics.

*Secondly:* Real medical progress can only be achieved through a deep understanding of biological processes in the body. For this we need the world's best scientists.

*Thirdly:* Scientific success cannot be programmed, but we can create the conditions that will allow it to happen:

- We need to be open to new ideas, and to have the courage to take risks and challenge commonly-held views once in a while.
- Our researchers need to have the freedom to work on their ideas...
- ...and above all, they need plenty of time and staying power.

I would like to take this opportunity to thank all our people for the tireless effort that goes into success stories like ocrelizumab; to thank our researchers and every one of our over 91,000 employees who work with passion and commitment toward improving the health of patients. I also wish to thank you, valued shareholders, for your confidence in our company.

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