Annual General Meeting
Roche Holding Ltd
14 March 2017

Address by Severin Schwan
CEO of the Roche Group

(Check against delivery.)

Dear Shareholders, Ladies and Gentlemen

I too would like to welcome you to the Annual General Meeting.

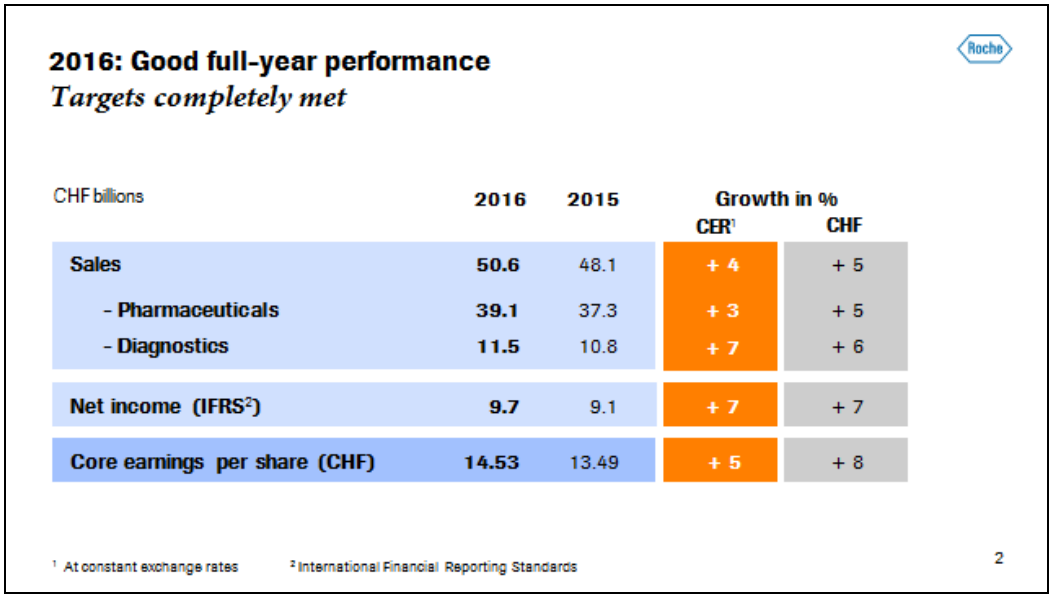
2016 was another extremely good year for your company. We again achieved strong financial results, while making significant strides in the development of a number of important medicines and diagnostics.

Today, I'd like to address two topics in greater detail:

- Firstly: the full-year results for 2016 and the outlook for the current financial year.
- Secondly: the progress we have made with our product pipeline, especially in relation to cancer immunotherapy – a treatment approach that offers patients new hope.

Now to my **first topic**. On 1 February we provided a detailed briefing on our full-year performance at our press conference. Allow me to summarise the key financial results.

Operating results



We met all the financial targets we set ourselves at the start of 2016.

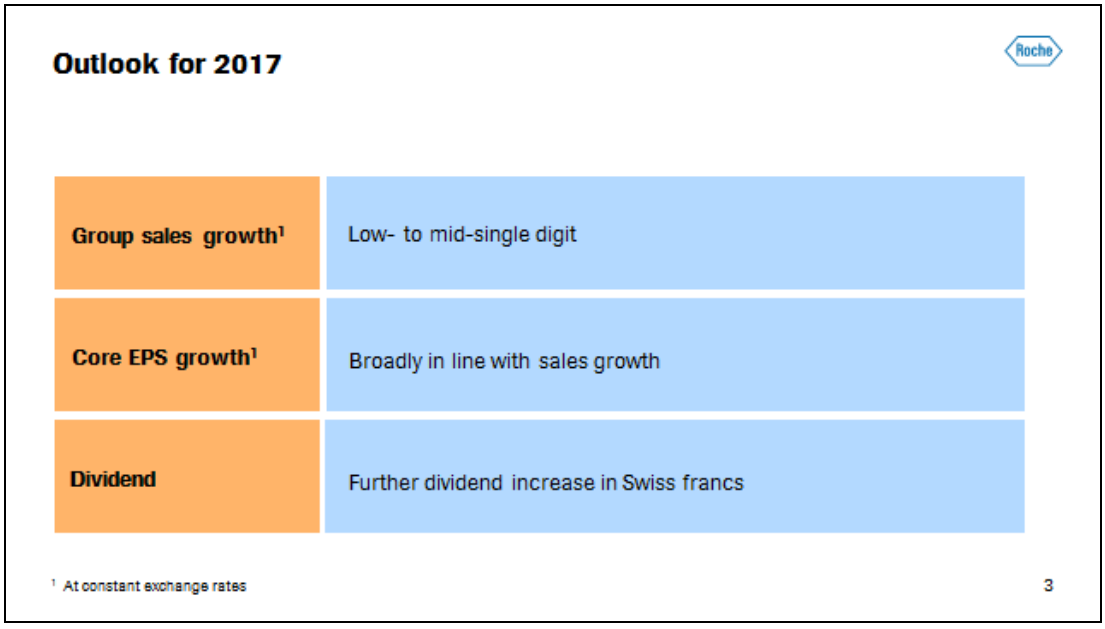
Sales in the Pharmaceuticals Division rose 3% at constant exchange rates. Our oncology portfolio continues to grow strongly, as does immunology.

Diagnostics Division sales grew 7% at constant exchange rates – again well ahead of market growth. Immunodiagnostics was the main contributor.

Core earnings per share also developed well with a rise of 5% at constant exchange rates.

As you can see on the right (on the slide), the currency development has had a positive impact on growth in Swiss francs this time round. The reason for this is that in 2016 compared to 2015, the Swiss franc was weaker against major currencies (such as the US dollar, the Japanese yen and the euro).

Outlook



We expect the Roche Group to see low- to mid-single digit sales growth (at constant exchange rates) in the current year.

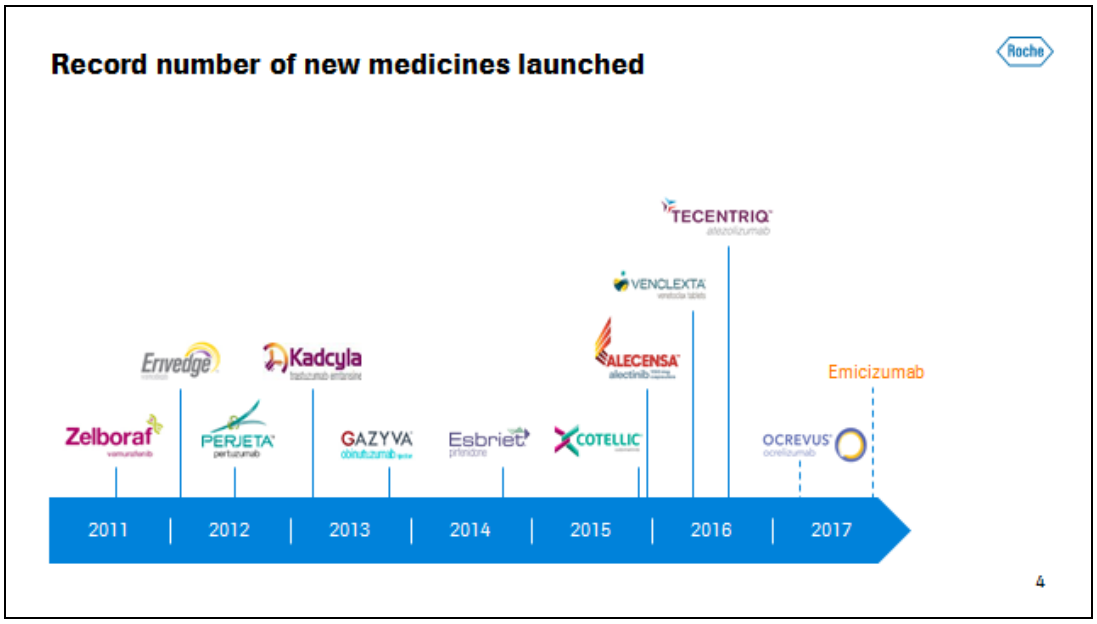
And we are aiming to grow core earnings per share (at constant exchange rates) broadly in line with sales growth.

Given these expectations, we also assume (as Christoph Franz mentioned) that we will be able to increase our dividend for 2017 as well.

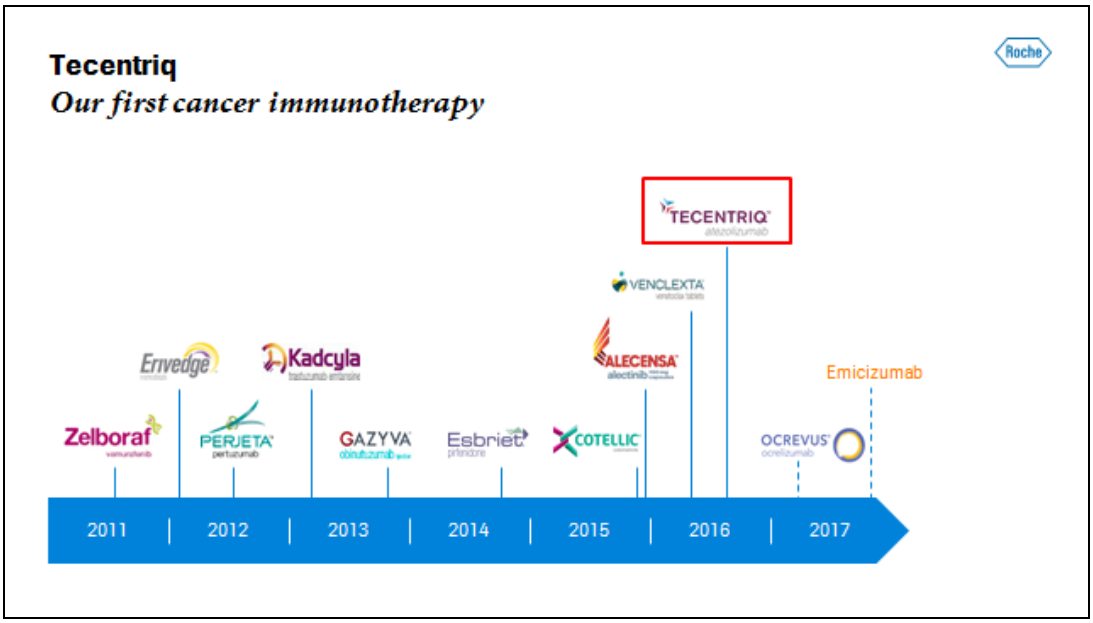
Pipeline

Our main objective is and remains to use scientific excellence to help patients. This focus on innovation also underpins our strategy – and our success, as Christoph Franz pointed out.

And this brings me to the **second part** of my speech: The advances we have made in the development of new medicines and, in particular, our achievements in cancer immunotherapy – an exceedingly promising area!



Let's look at the pipeline first: You can see here that in the very short span of the last few months, we have launched four new, innovative medicines – a first in the history of Roche! (We normally expect to average one to two medicines a year.)



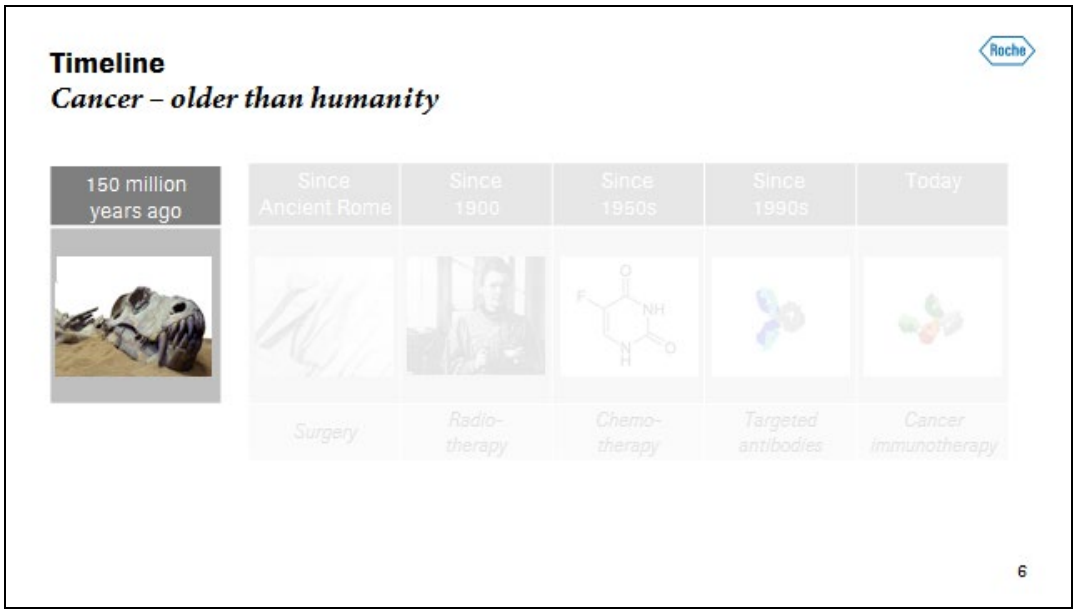
Roche's latest launch was **Tecentriq,** our first cancer immunotherapy. The medicine has been approved in the USA for the treatment of bladder and lung cancer (as have the companion diagnostic tests).

Tecentriq represents a milestone in the treatment of cancer – the US Food and Drug Administration granted the medicine Breakthrough Therapy Designation in both indications.

What makes Tecentriq so special? Or to put it another way: What is it about cancer immunotherapy? What has got the research and medical community so excited?

To understand the enthusiasm that this new type of treatment is generating, we should take a look back at the **history of medicine**. The fight against cancer is a tough one. For a long time there was no progress at all, and only recently have great strides been made.

Let's go back (a few million years) in time:

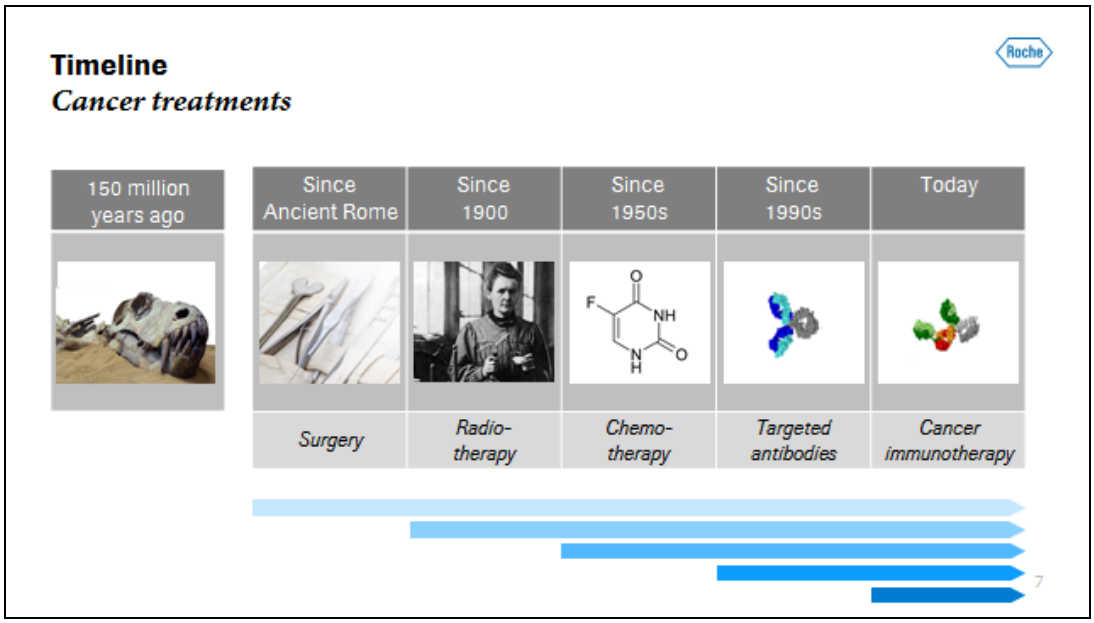


As a disease, cancer is older, very much older than humanity itself. Last year, a German researcher found evidence of cancer in 150-million-year-old dinosaur bones, providing (further) proof that even dinosaurs suffered from tumours.

There are widespread occurrences of cancer in nature – cats, birds and plants can also develop the disease.

One of the earliest descriptions of cancer is from ancient Egypt and includes a brief remark that there was no treatment for it.

What has been happening in the 5,000 or so years since then? – For a very long time nothing (or nothing useful).



(Operation) In first-century AD Rome, the scalpel came into increased use – but this method wasn't particularly popular, not least because there were no anaesthetics.

For around 2,000 (!) years (from antiquity to the 19th century), this remained the only actual (efficient) method of treatment. Ether was first used as an anaesthetic in the mid-19th century; surgery has since become established as a key (one might say the first) pillar of cancer therapy.

However, the excision of a tumour is only partially effective. It is never possible to be sure if all cancer cells really have been removed, especially if the cancer has already metastasised, i.e. it has spread to other parts of the body.

(Radiotherapy) In 1895, Wilhelm Conrad Röntgen discovered X-rays, also named Röntgen rays in his honour. A short while afterwards, Marie Curie (together with her husband) discovered radioactivity. These breakthroughs soon led to the first medical applications.

The rays were initially used to screen and diagnose patients – but it became apparent that cancer cells are so highly intolerant of radiation that they die. The second pillar of cancer therapy had been discovered.

(Chemotherapy) Another half a century was to elapse before a further (pharmaceutical) option could be added to the list of treatments in the form of chemotherapy.
And this discovery too was appropriated from quite a different area: Experiments with chemical agents intended for weapons during World War II resulted by chance in the identification of substances that inhibit cell growth – holding great promise for cancer treatment.

Since the 1950s (beginning in the USA) the use of chemotherapy has spread worldwide. Roche has always played a front-line role here: Our medicine fluorouracil was the world's first modern chemotherapeutic agent which (even to this day) can be used to treat many types of cancer.

Chemotherapy remained the standard treatment for cancer for several (more) decades, (and still is today). The problem is that chemotherapy (per se a poison) not only attacks sick cells, but also healthy ones, and so causes numerous side effects, some serious.

(Targeted antibodies) The late 1990s witnessed a quantum leap in cancer treatment in the form of biopharmaceuticals, or targeted antibodies – and Roche was among the pioneers. Approval for our cancer drugs MabThera/Rituxan and Herceptin marked the start of a new era in cancer treatment. These antibodies target harmful cells of a specific form of cancer. As a result, patients respond better to treatment, and experience fewer side effects.

That said, these treatments too are most effective in combination with chemotherapy – and, where feasible, in combination with surgery and, if appropriate, radiation.

(Cancer immunotherapy) Two decades passed until our recent initial successes with cancer immunotherapy. This is now the fifth column in the fight against cancer.

– Allow me to sum up: "Modern" surgical techniques (with anaesthetics) have been in place for around **170** years, radiotherapy for a good **100** years, chemotherapy for almost **70** years, biopharmaceuticals for **20** years, and now cancer immunotherapy since only recently.

After the first laborious baby steps, the last few decades of cancer research feel like a sprint. We have learned more in the last few decades than in the entire 5,000 years of medicine before.

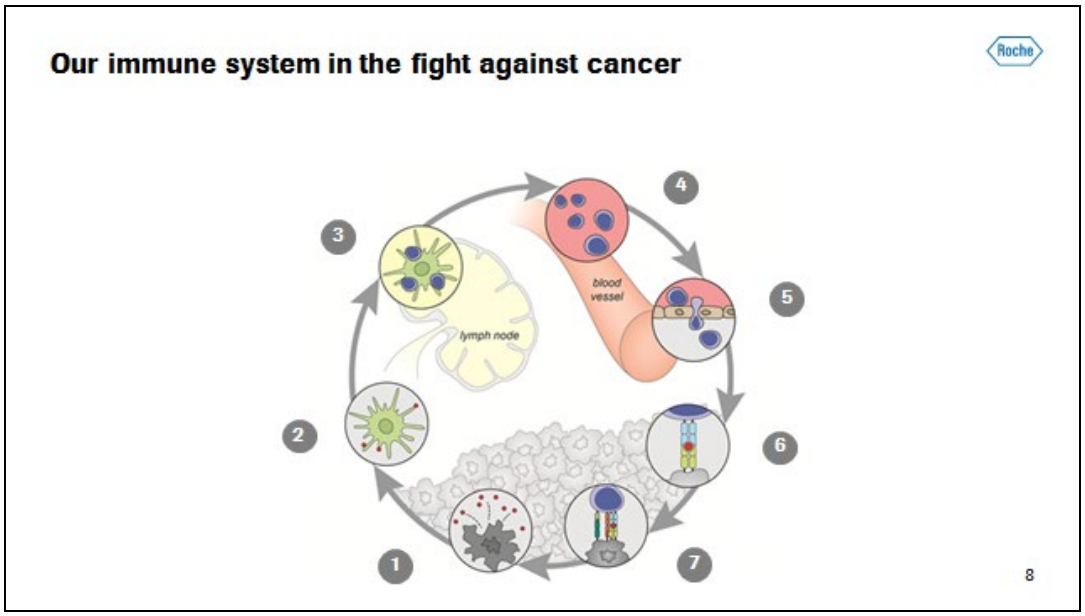
Cancer immunotherapy

Allow me now to take a slightly closer look at cancer immunotherapy and show how (and where) we can support our immune system in the fight against cancer.

As you know, as healthy human beings we have an outstanding immune system that protects us above all against “foreign invaders” such as viruses or bacteria. Without these natural defences we would all soon be dead.

Our immune system normally recognises a developing malignant tumour as something alien too, and destroys the abnormal cells. So why do people get cancer? What goes wrong with the immune system?

First we need to understand how our immune system works (or rather should work) against cancer.

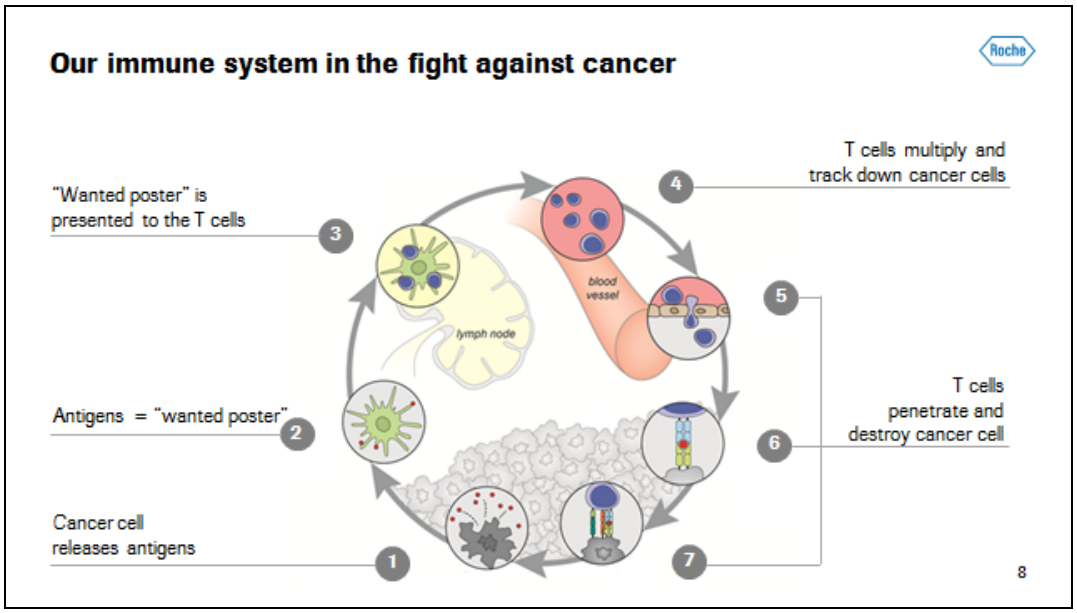


What you see here is a highly simplified representation of the process we call the **cancer-immunity cycle**.[1]

[1] The Cancer-Immunity Cycle: Daniel S. Chen, Ira Mellman

(Incidentally, this cycle was first described by two of our researchers, one of whom, Dan Chen, you will be seeing afterwards in a film clip. The two scientists had long been searching for a way to depict this complex process as simply as possible – until finally, one evening at a bar in San Francisco after work, this diagramme – which is still frequently used by scientists today – materialised, sketched out on a paper napkin.)

Our immune system has to fulfil three fundamental tasks; first it has to actually recognise the abnormal cells as a potential threat; secondly, it has to attack them effectively, and thirdly, it has to kill them (as it does with viruses and bacteria).



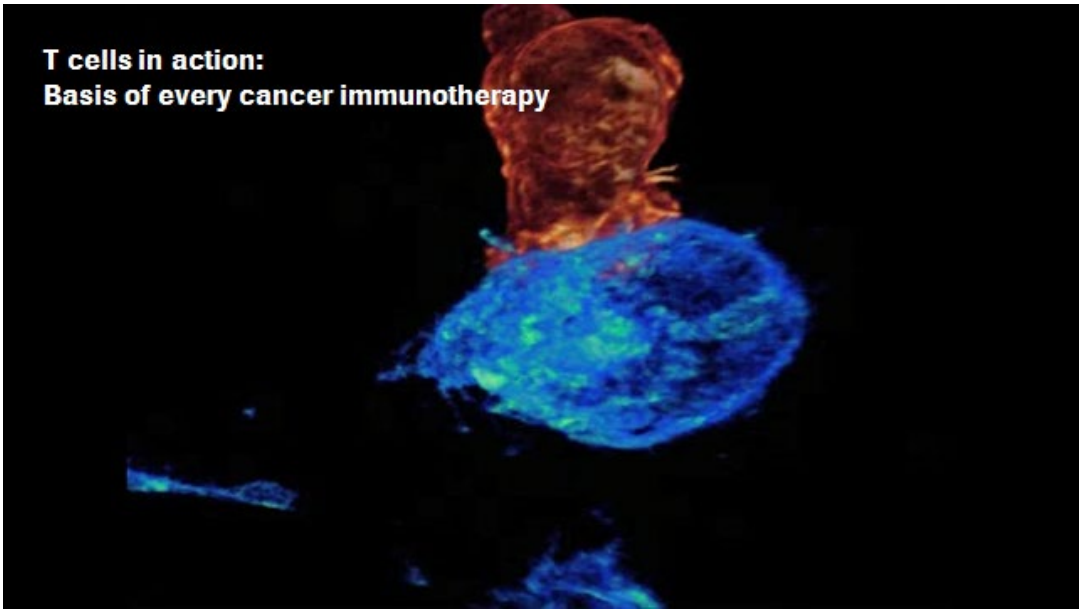
(1) At the beginning of this process is the cancer cell itself. Cancer cells are different to normal cells – they contain a variety of mutant proteins that enables tumour growth. Cancer cells release these mutant proteins (also known as cancer antigens).

(2,3) Certain cells in our immune system – known as dendritic cells (that are like police officers "on patrol" in our body) capture these antigens, transport them to one of the lymph nodes (to the "command centre") and present them there (like on a kind of "wanted poster") to the T cells.

T cells (we could also call them "good-guy killer cells") play a key role in our immune system: Using the "wanted poster" they recognise foreign bodies (such as viruses, bacteria) or sick cells and fight them.

(4) As soon as the T cells recognise the cancer antigens as a threat, they are activated and multiply – the immune system starts attacking the cancer. They migrate through the blood stream to the tumour, the "wanted poster" helping them to find the cancer cell.

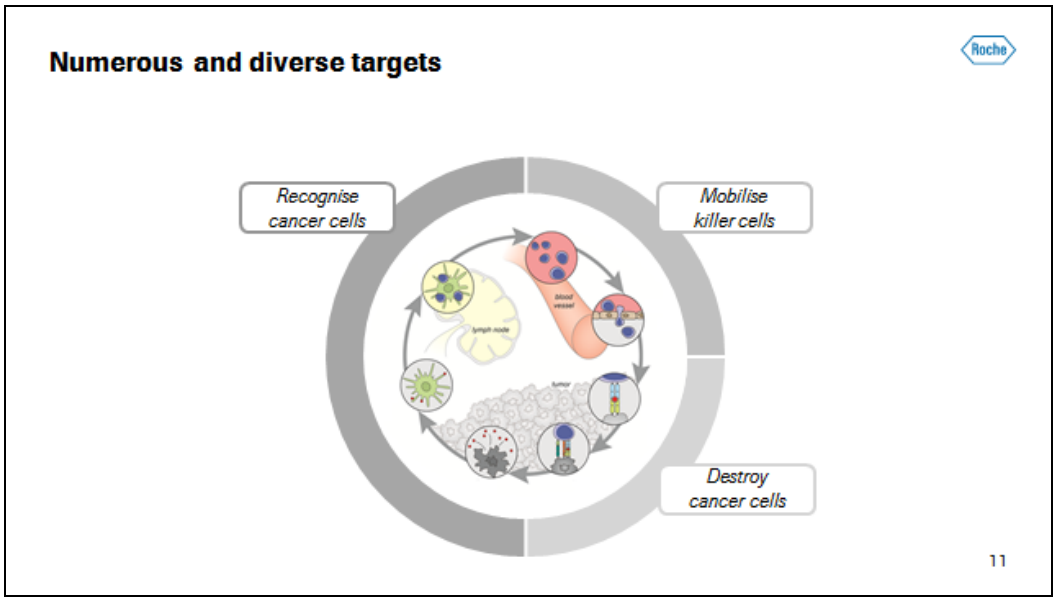
(5,6,7) When they get there, the killer cells penetrate the tumour and trigger a signal chain that ultimately leads to the death of the cancer cell. This releases more cancer antigens – and the cycle begins all over again.



The short film you can see here shows a T cell attacking a tumour cell. (By the way, this is not an animation; these are real cells filmed by one of our researchers using a newly developed high-tech microscope – it is in fact the first film of its kind taken with this particular microscope!)[2]

It's quite impressive to see the immense aggression and vehemence with which the killer cell attacks the cancer!

[2] Alex Ritter



Back to the cancer-immunity cycle. So this is what the cycle would look like if everything were to go smoothly. But this is often not the case, especially with cancer. There are numerous points in this process where things can go wrong.

And this is where we come in: Wherever a problem arises, we can use cancer immunotherapy either to “step on the gas” or “hit the brakes”.

Here in the **first phase** of the process, where we want the cancer cells to be recognised as a threat in the first place, we help the immune system, for example by increasing the number of dendritic cells (“police officers on patrol”) – inundating the “command centres” with cancer “wanted posters”.

Here (in the **second phase**), the T cells may recognise the tumour, but, for whatever reason, remain outside the tumour – they do not attack. We design drugs that try to “smuggle” the T cells into the tumour (usually with the help of targeted antibodies).

And here (finally; in the **third phase**), the killer cells are where they should be, but they are outsmarted by the cancer, which makes itself “invisible”, so to speak. Thanks to cancer immunotherapies such as Tecentriq, we can make cancer cells visible again – so the T cells can finally combat the cancer.

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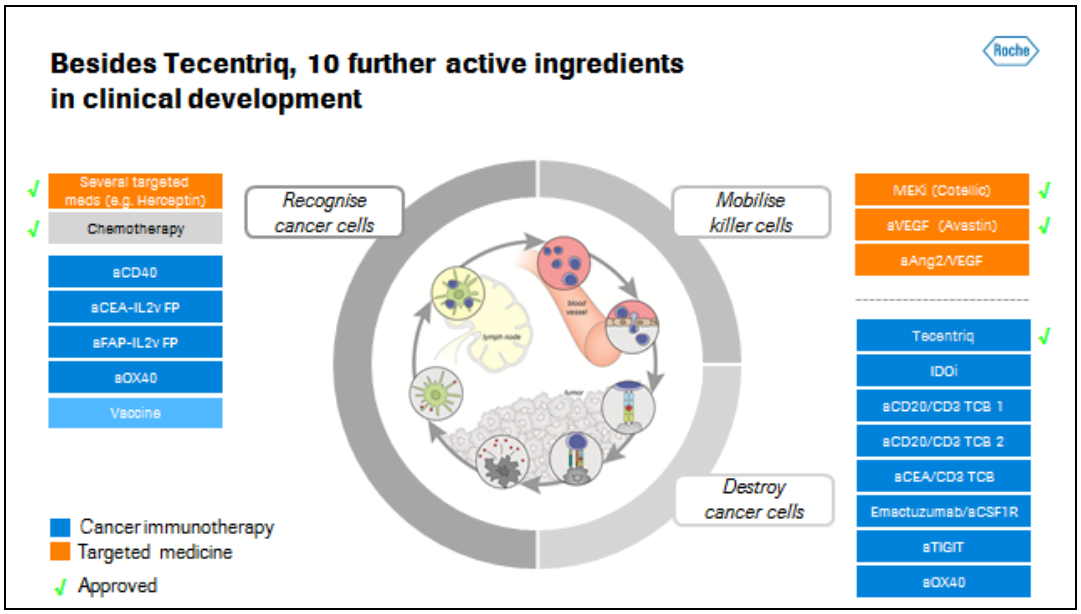
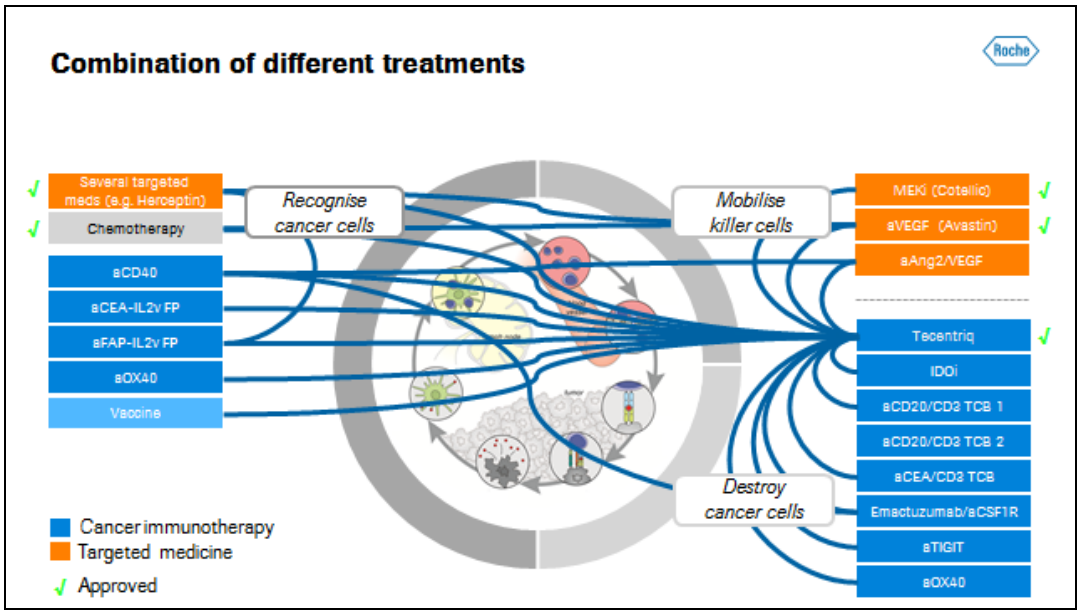
Roche invests huge sums in cancer immunotherapy and is an international leader in the field.



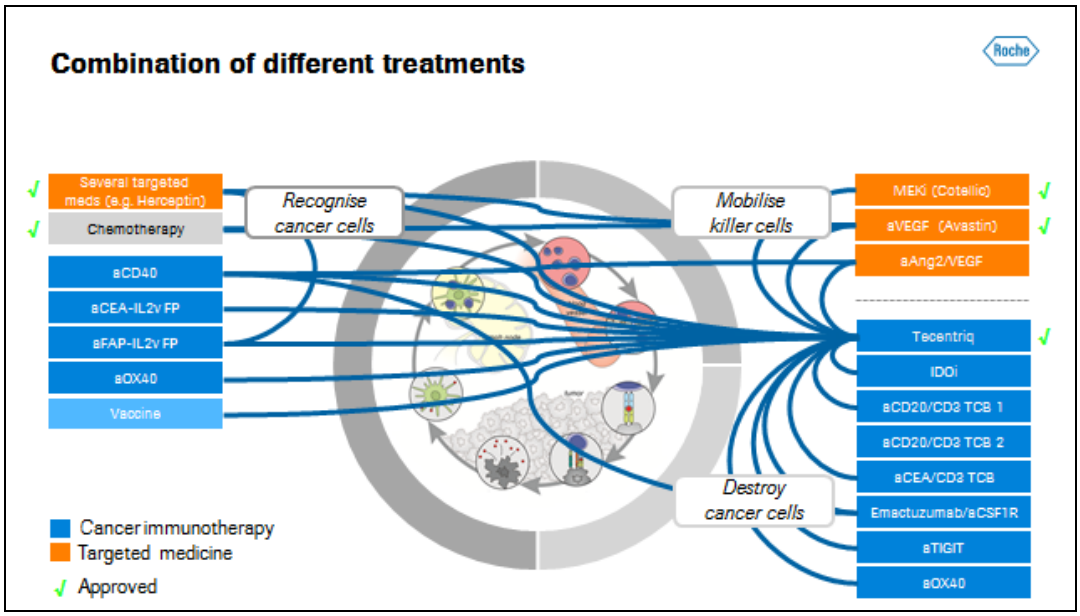
Besides Tecentriq, we currently have ten (!) new investigational candidates in clinical development – shown here in the blue boxes. The orange boxes represent our targeted medicines – there are actually far more than you can see here, but they would be too numerous to pack into one slide.

So where are we going from here? By developing highly specific **combination therapies**, most of which are based on Tecentriq, we aim to further improve treatment outcomes.

Combination therapy is nothing new in oncology; for half a century, patients have been treated simultaneously with different chemotherapeutic agents and other drugs. What is new is the precision with which we are targeting combination treatments to launch a multi-pronged attack against the molecular causes of cancer.



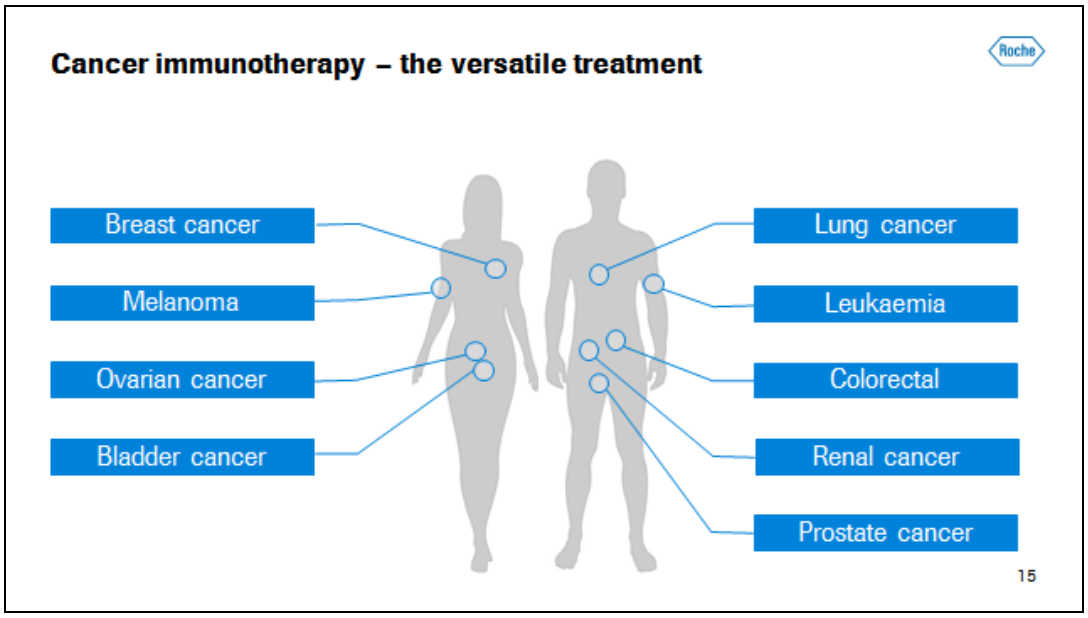
Here, for instance, we combine an immunotherapy (Tecentriq) with a chemotherapy and add a targeted antibody.



Or we combine cancer immunotherapies with one another, with other antibodies or only with chemotherapies – our options are (almost) limitless. Roche is presently pursuing more than 50 such programmes!

As the world's number one in oncology, in-house alone we have an incredibly large number of possible combinations available to us (something other firms can only dream of).

Then there are all the investigational candidates from outside Roche, which of course we also test wherever this makes sense.



And lastly, another fascinating advantage of these new therapies:
As soon as we re-enable the body's own immune system to do what it should be doing naturally, it will do so 24 hours a day, seven days a week. Moreover, it will do so everywhere in the body (not just in one specific organ).

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This is only the beginning: not all patient groups and not all types of cancer respond equally well to immunotherapies. But the first successes are impressive. Thanks to this new form of treatment, many patients suddenly regain control of their disease.

Cancer immunotherapy truly has the potential to revolutionise cancer treatment.

Esteemed Shareholders, Ladies and Gentlemen
I would like to show you a short film to demonstrate what a cancer immunotherapy such as Tecentriq means for patients and their families.

Two patients – she has breast cancer, he has bladder cancer – describe their experiences in the film. They are both still doing really well, by the way.

(Movie)

Thanks to cancer immunotherapy, for the first time there is justified hope that we will in future be able to provide highly effective life-extending treatment also to patients in the advanced stages, when the cancer has metastasised, and to do so for different types of cancer.

This is all incredibly fascinating – new doors are opening.

But these doors don't just “simply” open by themselves.

Ladies and gentlemen, I would like to thank our people most sincerely for their tremendous and tireless efforts. And you for the trust you place in our company.

– Thank you.

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